Diagnosing and Treating Depression
– Adult/Pediatric – Ambulatory
Clinical Practice Guideline

The UW Health Diagnosing and Treating Depression - Adult/Pediatric - Ambulatory Clinical Practice Guideline was approved by Unity’s Quality Improvement Committee (QIC) on June 12, 2017. Previous versions of the guideline were approved by Unity’s Clinical Quality Improvement Committee (CQIC) on May 22, 2015, May 17, 2013, November 16, 2012, November 19, 2010, November 21, 2008, November 17, 2006, November 18, 2005, November 19, 2004, and in August 2002 and September 2000. UW Health, Unity Health Insurance, and Group Health Cooperative participated in the development and revision of this guideline. The task force was a multidisciplinary work group comprised of physicians, behavioral health practitioners, a pharmacist, and quality improvement staff.
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Committee Approvals/Dates:
Clinical Knowledge Management (CKM) Council (04/23/2015)
• Interim revisions (12/17/2015)

Release Date: April 2015 | Next Review Date: April 2017
Executive Summary
Key Revisions (Interim Update 12/2015)
1. Modified recommendations for adolescent medications (page 24)

Key Practice Recommendations
1. Suspect and screen for major depressive disorder
2. Diagnose depression and rule out other disorders
3. Involve Behavioral Health when indicated
4. Develop and implement a treatment plan
5. Evaluate and monitor effectiveness of treatment plan

Companion Documents
1. Screening Algorithm
2. Treatment Algorithm- Adolescents
3. Treatment Algorithm- Adults
4. Treatment Algorithm- Pregnant Women
5. Table of Considerations of Concurrent Conditions
6. Table of Depression Medication Side Effect Profiles
7. Depression Medication Products and Dosage Chart

Related UW Health Clinical Practice Guidelines:
1. Preventive Health Care – Pediatric/Adult – Ambulatory Guideline
2. Attention Deficit and Hyperactivity Disorder (ADHD) – Adult – Ambulatory Guideline
3. Attention Deficit and Hyperactivity Disorder (ADHD) – Pediatric – Ambulatory Guideline
4. Diabetes – Adult/Pediatric – Inpatient/Ambulatory Guideline
5. Alcohol – Adult/Pediatric – Ambulatory Guideline
6. Tobacco Cessation – Adult/Pediatric – Inpatient/Ambulatory Guideline
7. Eating Disorders – Adult/Pediatric – Ambulatory Guideline

Related Patient Assessment Tools:
1. Patient Health Questionnaire-2 (PHQ-2)
2. Patient Health Questionnaire-9 (PHQ-9)
3. PHQ-9 Modified for Adolescents (PHQ-A)
4. Edinburgh Postnatal Depression Scale (EPDS)

External Resources:
1. State of Wisconsin Maternal & Child Health (MCH): provides information, resources, and referrals for women, family members and professionals. Maintains an online directory of mental health providers for perinatal mood disorders.
2. Postpartum Support International
3. Massachusetts General Hospital Center for Women’s Mental Health: provides a range of current information including discussion of new research findings in women’s mental health and how such investigations inform daily clinical practice.
Pertinent UW Health Policies & Procedures

1. UWMF Policy 114.009 – Person at Risk for Suicide
2. UWHC Policy 8.14 – Suicide Assessment and Intervention in Clinic
3. UWHC Policy 10.10 – Suicide Assessment and Prevention
4. UWHC Policy 10.14 – Emergency Detention – State Mental Health Act
5. UWHC Policy 10.17 – Involuntary Commitment – State Mental Health Act

Patient Resources (by population)

General
1. HFFY #4525: Depression - A Guide to Recognition and Treatment
2. HFFY #5299: Mental Health in Times of Crisis
3. HFFY #4472: Common Questions about ECT
4. Healthwise: Depression: Chronic Disease
5. Healthwise: Depression: Stopping Antidepressant: Deciding About
6. Healthwise: Mood Disorders: General Info
7. Healthwise: Suicidal Thoughts: Family Member
8. Health Information: Depressed Feeling
9. Health Information: Depression
10. Health Information: Depression (PDQ): Supportive Care - Health Professional Information
11. Health Information: Depression (PDQ): Supportive Care - Patient Information
12. Health Information: Depression and Suicide
13. Health Information: Depression and the Holidays
14. Health Information: Depression Evaluation Calculator
15. Health Information: Depression Screening
16. Health Information: Electroconvulsive Therapy for Depression
17. Health Information: Depression: Dealing With Medicine Side Effects
18. Health Information: Depression: Helping Someone Get Treatment
19. Health Information: Depression: Should I Stop Taking My Antidepressant?
20. Health Information: Depression: Should I Take an Antidepressant?
21. Health Information: Depression: Stop Negative Thoughts
22. Health Information: Depression: Supporting Someone Who Is Depressed
23. Health Information: Depression: Taking Antidepressants Safely

Pediatrics
1. HFFY #6327: How to Recognize and Treat Childhood Depression
2. Healthwise: Depression: Pediatric
3. Healthwise: Depression: Relapse Prevention: Teen
4. Healthwise: Depression: Self Care: Teen
5. Healthwise: Depression: Treatment: Teen
6. Healthwise: Depression: Treatment: Your Teen
7. Healthwise: Suicidal Thoughts: Your Teen
8. Health Information: Depression in Children and Teens
9. Health Information: Should My Child Take Medicine to Treat Depression?

Pregnant Adults
1. HFFY #5112: Postpartum (After Birth) Depression
2. Healthwise: Depression: Postpartum
3. Healthwise: Pregnancy: Depression: General Info
4. Health Information: Depression After Pregnancy
5. Health Information: Depression During Pregnancy
6. Health Information: Managing Postpartum Depression
7. Health Information: Depression: Should I Take an Antidepressant While I’m Pregnant?

Adults
1. HFFY #5267: Emotional Changes and Dementia
2. Healthwise: Depression: Relapse Prevention
3. Healthwise: Depression: Self Care
4. Healthwise: Depression: Treatment
5. Health Information: Depression in Older Adults

Scope
Disease/Condition(s): Major Depressive Disorder

Clinical Specialty: Internal Medicine, Family Medicine, Pediatrics, OB/GYN, Pharmacy, Psychiatry, Health Psychology

Intended Users: Primary Care Physicians, Physicians Assistants (PA), Registered Nurses, Licensed Practice Nurses (LPN), Psychiatrists, Health Psychologists, Licensed Practice Counselors (LPC), Pharmacists

CPG objective(s): To provide a framework for the diagnosis and treatment of depression in pediatric and adult primary care patients.

Target Population:
Pediatric (12-17 years) and adult (18 years+) primary care patients.

Interventions and Practices Considered:
1. Screening and assessment using validated assessment tools
2. Pharmacotherapy
3. Psychotherapy
4. Electroconvulsive therapy (ECT)
5. Light Therapy
6. Collaborative Care

Major Outcomes Considered:
1. Remission of depression
2. Reduction in depressive symptoms

Guideline Metrics:
ACO
1. GPRO PREV-12 (NQF 0418): Preventive Care and Screening: Screening for Clinical Depression and Follow-up Plan
2. GPRO MH-1 (NQF 0710): Depression Remission at Twelve Months
CPG-Derived
1. Percentage of patients who screen positive on the PHQ-2 and receive follow-up assessment (using the PHQ-9 or PHQ-A).
2. Percentage of pregnant patients screened for depression at the first prenatal visit and during the third trimester.
3. Percentage of postpartum patients screened for depression in the first year after childbirth.
4. Percentage of patients who screen positive on the PHQ-9 or PHQ-A and receive treatment (pharmacotherapy, psychotherapy, etc.).
5. Percentage of patients 12-18 years old with major depression and an initial PHQ-9 score ≥10 points who demonstrate remission at 12 months (defined as PHQ-9 score ≤4 points).
6. Rates of alcohol and drug use screening in patients who are depressed.

Methodology

Methods Used to Collect/Select the Evidence:
Electronic database searches were conducted by CCKM and workgroup members to collect evidence for review. Expert opinion and clinical experience was also considered during discussions of evidence.

Methods Used to Assess the Quality and Strength of the Evidence:
Recommendations developed by external organizations maintained the evidence grade assigned within the original guideline document and were adopted for use at UW Health. Recommendations developed internally during the workgroup meetings were evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) algorithm (See Figure 1 within Appendix A).

Methods Used to Formulate the Recommendations:
The interdisciplinary workgroup members agreed to adopt recommendations developed by external organizations and/or arrived at a consensus through discussion of the literature evidence and expert experiences. Recommendations developed by the workgroup were reviewed and approved by appropriate UW Health committees prior to full endorsement and implementation of the recommendations.

Rating Scheme for the Strength of the Evidence/Recommendations:
See Appendix A for the various rating schemes used within this document.

Introduction
According to the World Health Organization (WHO) major depression is the leading cause of disability worldwide, with more than 350 million people affected. The U.S. Preventive Services Task Force (2009) recommends depression screening in adolescents and adults when systems are in place to ensure accurate diagnosis, psychotherapy, and follow-up. Therefore, primary care physicians are in a unique position to provide initial assessment and diagnosis, as well as first line treatment to patients.
Recommendations

### Emergency “Same Day” Behavioral Health Consultation/Evaluation

is necessary when patients exhibit one or more of the following:
- suicidal thoughts and/or plans that make the patient’s safety uncertain
- assaultive and/or homicidal plans that make the safety of others uncertain
- loss of touch with reality (psychosis) in the context of depression

Reference:
- UWMF Policy 114.009 – Person at Risk for Suicide
- UWHC Policy 8.14 – Suicide Assessment and Intervention in Clinic

### Screening and Assessment

An algorithm for screening is included within Appendix B.

**Initial Screening in all Nonpregnant Patients (12 years or older)**

Depression screening in adolescents and adults is recommended by the U.S. Preventive Services Task Force when systems are in place to ensure accurate diagnosis, psychotherapy, and follow-up. Although an optimal interval for screening is currently unknown, it is recommended (and required by an ACO Quality measure) to perform annual universal depression screening in all nonpregnant patients older than 12 years of age. (UW Health Very low quality evidence, strong recommendation) Initial screening should be completed using the Patient Health Questionnaire-2 (PHQ-2).

A total score of 3 points or greater on the PHQ-2 constitutes a positive screen and need for further age appropriate follow-up assessment using the PHQ-9 or PHQ-A.

<table>
<thead>
<tr>
<th>Patient Health Questionnaire-2 (PHQ-2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
</tr>
<tr>
<td>Number of Questions</td>
</tr>
<tr>
<td>Administrator</td>
</tr>
<tr>
<td>Scoring:</td>
</tr>
<tr>
<td>Max Score</td>
</tr>
<tr>
<td>Positive Threshold (At-Risk)</td>
</tr>
</tbody>
</table>

### Assessment in Nonpregnant Adolescents (12-17 years)

If a nonpregnant adolescent patient scores positive on the PHQ-2 (score of 3 points or greater), it is recommended to complete additional assessment using the Patient Health Questionnaire-9 (PHQ-9) or Patient Health Questionnaire-A (PHQ-A). (UW Health Low quality evidence, strong recommendation)

Assessment using the PHQ-9 or PHQ-A may also be completed at any time based upon patient presentation or risk and symptomology (i.e., emotional problems as the chief complaint) in adolescents. (AAP Grade B, very strong recommendation)
A total score of 10 points or greater on the PHQ-9 or PHQ-A indicates the need for clinical evaluation and documentation of a follow-up plan.\textsuperscript{7,9,10,12}

### Patient Health Questionnaire-A (PHQ-A)

<table>
<thead>
<tr>
<th>Population</th>
<th>All patients 12-17 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Questions</td>
<td>13 (9 scored)</td>
</tr>
<tr>
<td>Administrator</td>
<td>Self-administered by patient</td>
</tr>
</tbody>
</table>

**Scoring:**

<table>
<thead>
<tr>
<th>Positive Threshold (Need for clinical evaluation)</th>
<th>Max Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>27 points</td>
</tr>
</tbody>
</table>

**Scoring Interpretation:**

- Mild depressive symptoms; disorder is unlikely
- Moderate depressive symptoms; disorder is possible
- Moderately severe depressive symptoms; disorder is likely
- Severe depressive symptoms; disorder is very likely

### Patient Health Questionnaire-9 (PHQ-9)

<table>
<thead>
<tr>
<th>Population</th>
<th>All patients 18 years or older</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Questions</td>
<td>9</td>
</tr>
<tr>
<td>Administrator</td>
<td>Self-administered by patient</td>
</tr>
</tbody>
</table>

**Scoring:**

<table>
<thead>
<tr>
<th>Positive Threshold (Need for clinical evaluation)</th>
<th>Max Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Threshold (Suicide Risk)</td>
<td>27 points</td>
</tr>
<tr>
<td>None</td>
<td>10 points or greater</td>
</tr>
</tbody>
</table>

**Scoring Interpretation:**

- None
- Mild depressive symptoms; disorder is unlikely
- Moderate depressive symptoms; disorder is possible
- Moderately severe depressive symptoms; disorder is likely
- Severe depressive symptoms; disorder is very likely

### Assessment in Nonpregnant Adults (18 years or older)

If a nonpregnant adult patient scores positive on the PHQ-2 (score of 3 points or greater), it is recommended to complete additional assessment using the PHQ-9.\textsuperscript{7,12,13} (UW Health Low quality evidence, strong recommendation)

Assessment using the PHQ-9 may also be completed at any time based upon patient presentation or risk and symptomology (i.e., emotional problems as the chief complaint) in adults.\textsuperscript{14} (ICSI Low quality evidence, strong recommendation)

A score of 10 points or greater on the PHQ-9 indicates the need for clinical evaluation and documentation of a follow-up plan.\textsuperscript{7,12,13}
Patients who are Pregnant (12 years or older)
Diagnosing depression in pregnant women is difficult because many common ‘normal’
symptoms during pregnancy may be misconstrued as depressive symptomatology.
Depressive symptoms may also falsely be interpreted as pregnancy-related. Examples
may include changes in appetite, sleep, libido, and loss of energy.

Pregnant adolescents or adults should be screened at the first prenatal visit, during the
third trimester (24-32 weeks), and at six weeks postpartum.\(^{14-17}\) (\textit{UW Health Low quality
evidence, strong recommendation}) Screening may be completed using the \textit{Edinburgh
Postnatal Depression Scale (EPDS), Patient Health Questionnaire-9 (PHQ-9) or Patient
Health Questionnaire-A (PHQ-A)} assessment tools.\(^{13,15}\)

A total score of 10 points of greater on the EPDS constitutes the need for clinical
evaluation and documentation of a follow-up plan. An affirmative response to Question
10 (suicidality) constitutes the need to access crisis intervention services.\(^{18}\)

<table>
<thead>
<tr>
<th>Edinburgh Postnatal Depression Scale (EPDS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
</tr>
<tr>
<td>Number of Questions</td>
</tr>
<tr>
<td>Administrator</td>
</tr>
<tr>
<td>Scoring:</td>
</tr>
<tr>
<td>Positive Threshold (At-Risk)</td>
</tr>
<tr>
<td>Positive Threshold (Suicide Risk)</td>
</tr>
<tr>
<td><strong>Affirmative response to Question 10</strong></td>
</tr>
</tbody>
</table>

A total score of 10 points or greater on the PHQ-9 or PHQ-A indicates the need for
clinical evaluation and documentation of a follow-up plan.\(^{7,12}\)

<table>
<thead>
<tr>
<th>Patient Health Questionnaire-A (PHQ-A)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
</tr>
<tr>
<td>Number of Questions</td>
</tr>
<tr>
<td>Administrator</td>
</tr>
<tr>
<td>Scoring:</td>
</tr>
<tr>
<td>Positive Threshold (Need for clinical evaluation)</td>
</tr>
<tr>
<td><strong>10 points or greater</strong></td>
</tr>
</tbody>
</table>
### Scoring Interpretation:

<table>
<thead>
<tr>
<th>Score Range</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 points</td>
<td>None</td>
</tr>
<tr>
<td>5-9 points</td>
<td>Mild depressive symptoms; disorder is unlikely</td>
</tr>
<tr>
<td>10-14 points</td>
<td>Moderate depressive symptoms; disorder is possible</td>
</tr>
<tr>
<td>15-19 points</td>
<td>Moderately severe depressive symptoms; disorder is likely</td>
</tr>
<tr>
<td>20-27 points</td>
<td>Severe depressive symptoms; disorder is very likely</td>
</tr>
</tbody>
</table>

### Patient Health Questionnaire-9 (PHQ-9)

<table>
<thead>
<tr>
<th>Population</th>
<th>All patients 18 years or older</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Questions</td>
<td>9</td>
</tr>
<tr>
<td>Administrator</td>
<td>Self-administered by patient</td>
</tr>
</tbody>
</table>

#### Scoring:

<table>
<thead>
<tr>
<th>Max Score</th>
<th>Positive Threshold (Need for clinical evaluation)</th>
<th>Positive Threshold (Suicide Risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>27 points</td>
<td>10 points or greater</td>
<td>Affirmative response to Question 9</td>
</tr>
</tbody>
</table>

#### Scoring Interpretation:

<table>
<thead>
<tr>
<th>Score Range</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 points</td>
<td>None</td>
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<tr>
<td>5-9 points</td>
<td>Mild depressive symptoms; disorder is unlikely</td>
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<td>10-14 points</td>
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<td>Moderately severe depressive symptoms; disorder is likely</td>
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<tr>
<td>20-27 points</td>
<td>Severe depressive symptoms; disorder is very likely</td>
</tr>
</tbody>
</table>

### Patients in Postpartum (12 years or older)

Many medical professionals often rely on their clinical impressions alone to determine whether a woman appears depressed, but several studies have shown that up to 50% of mothers with major depression are missed by primary care practitioners when screening instruments are not used. If left untreated, the disorder can have serious adverse effects for the mother, her infant’s development, and her relationship with others.

Postpartum Depression (PPD) may begin 24 hours to several months after delivery. When its onset is abrupt and symptoms are severe, women are more likely to seek help early in the illness. In cases with an insidious onset, treatment is often delayed, if it is ever sought. Untreated, PPD may resolve within several months but can linger into the second year postpartum. After the initial episode, women who have had PPD are at risk for both non-puerperal and puerperal relapses.

Postpartum depression assessment should be conducted at 4-10 weeks (i.e., 6 week OB visit) and 3-6 months (i.e., during Well-Child visits). (UW Health Low quality evidence, weak recommendation) The EPDS addresses depressive and anxiety symptomatology, and is therefore preferred as anxiety frequently co-occurs with depression in the postpartum period. However, some clinicians may be prefer to use the PHQ-9 or PHQ-A because of familiarity and continuity.

A total score of 10 points or greater on the EPDS constitutes the need for clinical evaluation and documentation of a follow-up plan. An affirmative response to Question 10 (suicidality) constitutes the need to access crisis intervention services.
Edinburgh Postnatal Depression Scale (EPDS)

<table>
<thead>
<tr>
<th>Population</th>
<th>Postpartum patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Questions</td>
<td>10</td>
</tr>
<tr>
<td>Administrator</td>
<td>Self-administered by patient</td>
</tr>
<tr>
<td>Scoring:</td>
<td></td>
</tr>
<tr>
<td>Max Score</td>
<td>30 points</td>
</tr>
<tr>
<td>Positive Threshold (At-Risk)</td>
<td>10 points or greater</td>
</tr>
<tr>
<td>Positive Threshold (Suicide Risk)</td>
<td>Affirmative response to Question 10</td>
</tr>
</tbody>
</table>

A total score of 10 points or greater on the PHQ-9 or PHQ-A indicates the need for clinical evaluation and documentation of a follow-up plan.⁷,¹²

Patient Health Questionnaire-A (PHQ-A)

<table>
<thead>
<tr>
<th>Population</th>
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</tr>
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<tbody>
<tr>
<td>Number of Questions</td>
<td>13 (9 scored)</td>
</tr>
<tr>
<td>Administrator</td>
<td>Self-administered by patient</td>
</tr>
<tr>
<td>Scoring:</td>
<td></td>
</tr>
<tr>
<td>Max Score</td>
<td>27 points</td>
</tr>
<tr>
<td>Positive Threshold (Need for clinical evaluation)</td>
<td>10 points or greater</td>
</tr>
</tbody>
</table>

Patient Health Questionnaire-9 (PHQ-9)

<table>
<thead>
<tr>
<th>Population</th>
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<tbody>
<tr>
<td>Number of Questions</td>
<td>9</td>
</tr>
<tr>
<td>Administrator</td>
<td>Self-administered by patient</td>
</tr>
<tr>
<td>Scoring:</td>
<td></td>
</tr>
<tr>
<td>Max Score</td>
<td>27 points</td>
</tr>
<tr>
<td>Positive Threshold (Need for clinical evaluation)</td>
<td>10 points or greater</td>
</tr>
<tr>
<td>Positive Threshold (Suicide Risk)</td>
<td>Affirmative response to Question 9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Scoring Interpretation:</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild depressive symptoms; disorder is unlikely</td>
<td>0-4 points</td>
</tr>
<tr>
<td>Moderate depressive symptoms; disorder is possible</td>
<td>5-9 points</td>
</tr>
<tr>
<td>Moderately severe depressive symptoms; disorder is likely</td>
<td>10-14 points</td>
</tr>
<tr>
<td>Severe depressive symptoms; disorder is very likely</td>
<td>15-19 points</td>
</tr>
<tr>
<td></td>
<td>20-27 points</td>
</tr>
</tbody>
</table>

Follow-up Plan Documentation

According to the ACO Quality measure, all patients who screen positive on a validated depression screening tool must have a documented follow-up plan on the date of the positive screen. This plan must contain one or more of the following:

- Additional evaluation for depression
- Suicide Risk Assessment
- Referral to a practitioner who is qualified to diagnose and treat depression
- Pharmacological interventions
- Other interventions or follow-up for the diagnosis or treatment of depression.
**Patient Presentation and Risk Factors**

Physical complaints are extremely common in depression and are often the primary manifestation of the illness. Somatic manifestations of depression include fatigue, insomnia, anorexia, weight loss, gastrointestinal disturbances, and a variety of pain complaints. Anxiety and agitation are common as secondary symptoms. It is important that clinicians keep in mind that patients who have depression or any mental illness are often stigmatized and may be at risk of not having medical complaints adequately addressed.

Common presentations of patients with depression may include\textsuperscript{14,22,23}:

- multiple patient-initiated office visits (more than five per year)
- numerous unexplained symptoms
- work or relationship dysfunction
- sleep disturbance
- multiple worries and distress (irritable mood in adolescents)
- fatigue
- irritable bowel syndrome

**Risk Factors**

Risk factors are often intertwined and related, and may vary based upon patient age and experiences. Patients with chronic illnesses such as diabetes, cardiovascular disease, and chronic pain are at a higher risk for depression.\textsuperscript{14,24} Risk factors associated with patient age or postpartum status are listed below. Older adults, especially white men over age 65 years, are at a higher risk of suicide.\textsuperscript{25}

**Table 1. Risk Factors in Adolescents\textsuperscript{11,23,24}**

<table>
<thead>
<tr>
<th>Biological</th>
<th>Psychological</th>
<th>Environmental</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal history of depression</td>
<td>Emotional dependence</td>
<td>Antisocial peer group</td>
</tr>
<tr>
<td>Family history of depression</td>
<td>History of suicide attempts</td>
<td>Decreased physical activity</td>
</tr>
<tr>
<td>Female gender</td>
<td>Ineffective coping skills</td>
<td>Increased parental conflict</td>
</tr>
<tr>
<td>Hormonal changes during puberty</td>
<td>Low self-esteem</td>
<td>Loss of relationship (i.e., death of family member, romantic relationship, friendship)</td>
</tr>
<tr>
<td>Low birth weight</td>
<td></td>
<td>Low socioeconomic status</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Overeating</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poor academic performance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poor peer relationships</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Substance use</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Traumatic event (i.e., accident, physical or sexual abuse)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Risk Factors in Adults\textsuperscript{14,22,23,25}

<table>
<thead>
<tr>
<th>Biological</th>
<th>Psychological</th>
<th>Environmental</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Personal history of depression</td>
<td>• Medical co-morbidity</td>
<td>• Men over age 65 years are at a higher risk of suicide</td>
</tr>
<tr>
<td>• Family history of depression (first-degree relative)</td>
<td>• Postpartum period</td>
<td>• Substance use</td>
</tr>
<tr>
<td>• Female gender</td>
<td>• Peri/postmenopausal period</td>
<td>• Major life change (i.e., job change, financial difficulties)</td>
</tr>
</tbody>
</table>

Psychological

• Negative thinking styles (i.e., “nothing will ever work out”)  
• Feelings of hopelessness

Environmental

• Lack of social support  
• Loss of relationship (i.e., being widowed, death of family member, romantic relationship, friendship)  
• Substance use  
• Major life change (i.e., job change, financial difficulties)  
• Traumatic event (i.e., accident, physical or sexual abuse)

Table 3. Risk Factors for Postpartum Depression\textsuperscript{14,26}

<table>
<thead>
<tr>
<th>Biological</th>
<th>Psychological</th>
<th>Environmental</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Personal history of depressive episode or psychiatric illness</td>
<td>• Fragmented or poor sleep</td>
<td>• Low socioeconomic status</td>
</tr>
<tr>
<td>• Depression or anxiety during pregnancy</td>
<td>• Premorbid or gestational diabetes</td>
<td>• Past or current abuse</td>
</tr>
<tr>
<td>• Family history of mood or anxiety disorders</td>
<td>• Difficulty breastfeeding in the first two months postpartum</td>
<td></td>
</tr>
</tbody>
</table>

Psychological

• Dissatisfaction with the amount of social support from a spouse or significant other  
• Low self-esteem

Environmental

• Lack of psychosocial support  
• Recent stressful life event  
• Child care stress

Establish a Diagnosis

To diagnose a depressive disorder, the clinician should determine that criteria outlined within the Diagnostic and Statistical Manual of Mood Disorders, Fifth Edition (DSM-5) have been met using a detailed clinical interview.\textsuperscript{14,22,23} (ICSI Low quality evidence, strong recommendation) It is recommended to conduct direct interviews with adolescent patients and their families or caregivers.\textsuperscript{11} (AAP Grade B, very strong recommendation) The diagnostic DSM-5 criteria for major depressive disorder are listed below.

DSM-5 Diagnostic Criteria:\textsuperscript{23}

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.  
Note: Do not include symptoms that are clearly attributable to another medical condition.
1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, and hopeless) or observation made by others (e.g., appears tearful). (Note: In children and adolescents, can be irritable mood).

2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).

3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (Note: In children, consider failure to make expected weight gain).

4. Insomnia or hypersomnia nearly every day.

5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).

6. Fatigue or loss of energy nearly every day.

7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).

8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).

9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The episode is not attributable to the physiological effects of a substance or to another medical condition.

Note: Criteria A–C represent a major depressive episode.

Note: Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgment based on the individual’s history and the cultural norms for the expression of distress in the context of loss.

In distinguishing grief from a major depressive episode (MDE), it is useful to consider that in grief the predominant affect is feelings of emptiness and loss, while in MDE it is persistent depressed mood and the inability to anticipate happiness or pleasure. The dysphoria in grief is likely to decrease in intensity over days to weeks and occurs in waves, the so-called pangs of grief. These waves tend to be associated with thoughts or reminders of the deceased. The depressed mood of MDE is more persistent and not tied to specific thoughts or preoccupations. The pain of grief may be accompanied by positive emotions and humor that are uncharacteristic of the pervasive unhappiness and misery characteristic of MDE. The thought content associated with grief generally features a preoccupation with thoughts and memories of
the deceased, rather than the self-critical or pessimistic ruminations seen in MDE. In grief, self-esteem is generally preserved, whereas in MDE feelings of worthlessness and self-loathing are common. If self-deprecatory ideation is present in grief, it typically involves perceived failings vis-à-vis the deceased (e.g., not visiting frequently enough, not telling the deceased how much he or she was loved). If a bereaved individual thinks about death and dying, such thoughts are generally focused on the deceased and possibly about “joining” the deceased, whereas in MDE such thoughts are focused on ending one’s own life because of feeling worthless, undeserving of life, or unable to cope with the pain of depression.

D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.

E. There has never been a manic episode or a hypomaniac episode.

Note: This exclusion does not apply if all of the manic-like or hypomaniac-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.

Interview for Key Symptoms
Patients should receive a thorough evaluation in order to establish a diagnosis of major depressive disorder, identify other psychiatric or medical conditions that may require attention, and develop a treatment plan. (UW Health High quality evidence, strong recommendation) In adolescent patients, the clinician should also assess the functional impairment across different domains.¹¹ (AAP Grade B, very strong recommendation)

This evaluation may include:⁵,¹⁴
- History of present illness and current symptoms
- Psychiatric history including past symptoms of mania, hypomania, or mixed episodes and responses to previous treatments
- General medical history
- Personal history including information about psychological development and responses to life transitions and major life events
- Social, occupational, and family history including mood disorder and suicide
- Review of prescribed and over-the-counter medications

It should be noted that older adults may be less likely to endorse low mood and worthlessness; rather loss of interest and pleasure may be core symptoms of depression.

Questions which are asked during the clinical interview should elaborate on answers provided on the initial assessment(s) (i.e., PHQ-9, PHQ-A, or EPDS), and assess for suicidal or homicidal intent, plan, and access to means.

Detecting Postpartum Depression (PPD)
The detection of PPD is often complicated by several factors, including:
- Most women expect a period of adjustment after having a baby
- Stigma and societal pressures to be a “good mother”
- Concern that sharing depressive thoughts might mean that their child could be taken from them
• Delayed detection of PPD by providers’ minimizing a woman’s distress in an effort to be reassuring.

Symptoms of PPD include:
• Depressed mood
• Lack of pleasure or interest including in her baby
• Agitation or motor retardation
• Frequent thoughts of death or suicide
• Sleep disturbance (insomnia or hypersomnia)
• Appetite disturbance (weight loss or gain)
• Loss of energy
• Feelings of worthlessness, inappropriate guilt, or being overwhelmed
• Diminished concentration or indecisiveness
• Symptoms that may be confused with normal sequelae of childbirth

Anxiety may be a prominent feature and more readily apparent than traditional depressive symptoms. Co-morbid anxiety has been found to be present in 60% of women with major depression in the postpartum period. Other co-morbid disorders often present may include: social phobia, agoraphobia, obsessive compulsive and avoidant personality disorders, all of which may contribute to social isolation. **One of the most concerning features of postpartum mood or anxiety disorders is intrusive thoughts of harming the infant.** These thoughts are most commonly associated with postpartum depression but are also prominent in postpartum psychosis and OCD, which are less common but important to recognize. These thoughts are usually distressing to the mother and she may worry that discussing them might call into questions her ability to parent. It is imperative to ask all postpartum women with any mood or anxiety symptoms if they have experienced any intrusive thoughts of harming their child. This is best accomplished by acknowledging that such thoughts are common and usually transient in the postpartum period. In the absence of psychosis, the likelihood of a woman acting on these thoughts is low; however, formal psychiatric assessment is essential to clarify the diagnosis and initiate treatment. Any woman endorsing thoughts of harming her infant should be referred immediately for psychiatric care.

Consider a Differential Diagnosis
Many other psychiatric disorders, physical conditions or medications can cause depressive symptoms. In evaluating adolescent (AAP Grade B, very strong recommendation) and adult (UW Health High quality evidence, strong recommendation) patients with symptoms of depression, the primary care practitioner should determine if the depression is a primary process or whether it is a symptom of other medical conditions.  

**Medical Conditions:** Screening for other medical conditions should be based on clinical judgment. Many medical conditions (i.e. hypothyroidism, hyperthyroidism, cancer, coronary artery disease, diabetes mellitus, cerebral vascular accident, chronic pain, HIV, Parkinson’s disease, multiple sclerosis) are risk factors for depression.
patient presents with prominent symptoms of low energy or hypersomnia, consider an evaluation for sleep apnea.\textsuperscript{27}

In patients who are at risk for low levels of B12 (i.e., vegetarians, poor diet, drink heavily, or are elderly), obtaining a baseline value may be considered. Repletion of B12 can improve mood and increase the efficacy of antidepressant medications.

In older adults, it is important to consider obtaining a baseline TSH value given the higher rates of hypothyroidism in this population.\textsuperscript{5} Older patients may also be screened for cognitive impairment through clinical assessment or use of a validated tool(s) such as the 6-item screener with the St. Louis University Mental Status Examination (SLUMS) or Montreal Cognitive Assessment (MoCA) as follow-up.

Depressive disorder, when present, should be considered an independent condition and specifically treated. Treatment may include optimizing treatment for the medical condition and/or providing specific treatment for the depression. When depression and a medical condition co-exist, there are several plausible explanations:\textsuperscript{5}

- The medical disorder biologically causes the depression (i.e., hypothyroidism).
- The medical disorder triggers the onset of depression in those who are genetically predisposed to depression.
- The perceived severity of the illness causes depression (i.e., a patient with cancer becomes depressed as a psychological reaction to prognosis and pain).
- The medical disorder and the depression are not causally linked.

It is important for the practitioner to differentiate among these several explanations in patients with concomitant medical disorder(s) and depression.

**Medications:** Some medications may cause depressive symptoms:

<table>
<thead>
<tr>
<th>Drug Causing Depression</th>
<th>Potential Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonidine, Metyldopa, Reserpine</td>
<td>Other antihypertensive agent (diuretics, ACE-I, CCB, ARB, etc)</td>
</tr>
<tr>
<td>Lipophilic beta blockers (propranolol)</td>
<td>Use lowest effective dose (atenolol or metoprolol). For heart rate control consider non-dyhydropyridine calcium channel blocker</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Minimize dose as allowed</td>
</tr>
<tr>
<td>Sedatives/Hypnotics</td>
<td>Consider taper off</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Minimize use</td>
</tr>
<tr>
<td>Estrogens/Progesterones</td>
<td>Addition of Vitamin B6, use lower progestin</td>
</tr>
<tr>
<td>Anti-Parkinson Medications</td>
<td>No alternatives</td>
</tr>
<tr>
<td>Anti-convulsants (Especially levetiracetam, phenytoin)</td>
<td>Consider lamotrigine and other alternative anti-epileptic drugs</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>Other NSAIDS</td>
</tr>
<tr>
<td>Interferons (Hep C, MS)</td>
<td>No alternatives</td>
</tr>
<tr>
<td>Isotretinoin</td>
<td>No alternatives</td>
</tr>
<tr>
<td>Opioids</td>
<td>Minimize/taper off opioids or use NSAIDS</td>
</tr>
</tbody>
</table>
**Bipolar disorder**: Use of antidepressants can precipitate mania or hypomania. Although the DSM-5 diagnostic criteria for an episode of major depression in bipolar disorder are the same as the criteria for unipolar major depression, the treatment for both disorders is different. Therefore, screening for bipolar disorder and any previous episodes of hypomania and mania should always be done before initiating treatment for depression.\(^\text{14,22}\)

The following symptoms of mania (lasting at least a week) or hypomania (lasting at least 4 days) may be used to differentiate bipolar disorder from depression:\(^\text{23}\)

- Inflated self-esteem or grandiosity
- Decreased need for sleep (i.e., feels rested after only 3 hours of sleep)
- More talkative than usual or pressure to keep talking
- Flight of ideas or subjective experience that thoughts are racing
- Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed
- Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation (i.e., purposeless non-goal-directed activity)
- Excessive involvement in activities that have a high potential for painful consequences (i.e., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

**Anxiety, panic, obsessive-compulsive or phobic disorders**: More often than not depression is accompanied by a co-morbid anxiety disorder which can impact the treatment approach. Depression can also mask underlying psychiatric disorders. Anxiety symptoms are frequent in depressive episodes. The depression may precede the panic or anxiety disorder, or the anxiety disorder may be part of the longitudinal course of the mood disorder. When a patient has anxiety symptoms, the existence of depressive symptoms should be evaluated. For those patients whose disorder has some obsessive features, the mood disorder is the initial focus of treatment.

**Bereavement**: is considered a normal state that most often resolves without treatment. In those bereaved patients who meet the diagnostic criteria for a depression following the loss, the diagnosis of a depressive disorder may be made.\(^\text{23}\)

**Substance abuse**: Major depressive disorder frequently occurs with alcohol or other substance use disorders. A patient with major depressive disorder who has a co-occurring substance use disorder is more likely to require hospitalization, more likely to attempt suicide, and less likely to adhere to treatment than a patient with major depressive disorder of similar severity uncomplicated by substance use. Therefore, a history of the patient's substance use, including current use, should be obtained. For recommendations related to alcohol or tobacco screening and treatment, refer to the [UW Health Alcohol Assessment and Intervention – Adult/Pediatric – Ambulatory](#) or [UW Health Tobacco Cessation – Adult/Pediatric – Inpatient/Ambulatory](#) Clinical Practice Guidelines.
Patients should be advised to stop substance use. Patients with significant alcohol, sedative or opioid use should be monitored for withdrawal and managed accordingly. Referral to AODA services should be considered for patients who have difficulty stopping on their own or who are facing significant interpersonal, occupational, medical, financial or legal consequences from substance use.\(^5\)

**Eating disorders**: It is recommended that young adults who present with any mood disorder be interviewed for symptoms of anorexia nervosa and/or bulimia at some point during treatment. One-third to one-half of patients with eating disorders has a concurrent depressive syndrome. If both depression and an eating disorder are present, the eating disorder, generally, should be the principal therapeutic target.\(^5\) For recommendations related to screening and assessment, refer to the [UW Health Eating Disorders – Adult/Pediatric – Ambulatory Clinical Practice Guideline](#).

**Attention Deficit and Hyperactivity Disorder (ADHD)**: It is recommended that adolescents and adults who present with inattention be interviewed for symptoms of ADHD as par of the evaluation. For recommendations related to ADHD diagnosis, refer to the [UW Health ADHD – Pediatric – Ambulatory](#) and [UW Health ADHD – Adult – Ambulatory](#) Clinical Practice Guidelines.

**Other Postpartum Conditions**: The criteria for diagnosing postpartum depression (PPD) apply to the diagnosis of PPD as well, with symptoms occurring nearly every day, most of the day, for at least two weeks. PPD often begins later than baby blues and postpartum psychosis, which often occur right away.

**Postpartum Blues**: The "baby blues" are subclinical mood fluctuations characterized by mild depressive symptoms that typically peak 3 to 5 days after delivery and resolve by the 10th postnatal day. These symptoms include tearfulness, irritability, fatigue, anger, insomnia, anxiety, mood liability, and sensitivity. All women with postpartum baby blues should be monitored for the onset of continuing or worsening symptoms.\(^26\)

**Postpartum Psychosis**: Postpartum depression must be distinguished from postpartum psychosis, which occurs in 0.1% of childbearing women. The most significant risk factors for postpartum psychosis are a personal or family history of bipolar disorder or a previous psychotic episode. Most puerperal psychoses have their onset within the first month of delivery and are manic in nature. Warning signs heralding the onset of puerperal psychosis include:

- An inability to sleep for several nights
- Irritable mood
- Agitation
- Avoidance of the infant
- Delusion or hallucinations often involve the infant
- Racing thoughts
- Rapid speech
Perplexed affect

Of women who develop a postpartum psychosis, there is a 5% infanticide or suicide rate; thus postpartum psychosis is a medical emergency and requires immediate psychiatric evaluation and usually requires psychiatric admission for medication management and safety.\(^26\)

**Involve Behavioral Health**

Referral to a Behavioral Health Specialist is recommended when there is:\(^14\)

- possibility of bipolar disorder
- psychiatric co-morbidity (for example, substance abuse, anxiety, obsessive compulsive disorder, or eating disorders)
- concern regarding the possibility of suicide and/or homicide
- substance abuse
- psychosis with the depression
- no improvement with medications prescribed by the primary prescriber despite multiple dose adjustments and trials of different medication classes
- significant or prolonged inability to work and care for self and/or family
- diagnostic uncertainty

**Provide Treatment**

The objectives of treatment are:

- Reduction and ultimately resolution (remission) of all signs and symptoms of the depressive syndrome. This may be assessed objectively through administration of an assessment tool such as the PHQ-9. The ACO Quality measure defines remission in adults 18 years or older as a PHQ-9 score < 5 within one year of positive screening (PHQ-9 score > 9 points).
- Restoration of psychosocial and occupational function to that of the baseline asymptomatic state.
- Reduction of the likelihood of relapse or recurrence.

Primary care clinicians should develop a treatment plan with patients and their families in adolescence (AAP Grade C, very strong recommendation) or adulthood (ICSI Low quality evidence, strong recommendation), and set specific treatment goals in key functional areas such as home, peer and school settings.\(^14,28\) (AAP Grade D, very strong recommendation)

It is recommended to use evidence-based treatments, such as psychotherapy, pharmacotherapy, electroconvulsive therapy, or light therapy, whenever possible and appropriate to achieve the goals of the treatment plan.\(^28\) (AAP Grade A, very strong)
The Collaborative Care model is recommended for all patients with depression in primary care.\textsuperscript{14,29-31} (ICSI High quality evidence, strong recommendation)

The Collaborative Care model expands the primary care team to include a consulting psychiatrist and care manager. Key principles of this model include:\textsuperscript{32}

- **Measurement-based treatment to target** (or stepped care) where each patient’s treatment goals and outcomes are clearly identified and routinely measured by validated tools, such as the PHQ-9. If no improvement is seen, treatments are actively modified until the expected result or outcome is achieved.

- **Population-based care** requires care teams to share a defined group of patients tracked in a registry. Care managers track patient symptoms and promote adherence to the treatment plan, while others provide pharmacotherapy and psychotherapy.

- **Patient-centered team care** involves collaboration between the patient, primary care provider, behavioral health provider and other team members to develop treatment goals and plans. Immersion of behavioral health providers into primary care clinics reduces the need for duplicate assessments and enhances the effectiveness of referrals.

Factors to consider in making treatment recommendations (Table 4) are the severity of symptoms, presence of psychosocial stressors, presence of co-morbid conditions, insurance coverage, pregnancy status, and patient preferences or prior treatment experiences.\textsuperscript{5,12}

**Table 4. Suggested Treatment Modalities Based on Depression Severity or Other Factors**

<table>
<thead>
<tr>
<th>Factors</th>
<th>Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptom Severity</strong> (based on total PHQ-9 or PHQ-A scores)</td>
<td></td>
</tr>
<tr>
<td>Mild (5-9 pts.)</td>
<td>Psychotherapy (IPT, CBT)</td>
</tr>
<tr>
<td>Moderate (10-14 pts.)</td>
<td>Pharmacotherapy (SSRIs) in combination with psychotherapy (IPT, CBT)</td>
</tr>
<tr>
<td>Moderately severe (15-19 pts.)</td>
<td></td>
</tr>
<tr>
<td>Severe (20-27 pts.)</td>
<td></td>
</tr>
<tr>
<td><strong>Psychosocial Stressors</strong></td>
<td>Psychotherapy</td>
</tr>
<tr>
<td><strong>Patient is Pregnant</strong></td>
<td>Psychotherapy</td>
</tr>
<tr>
<td><strong>Seasonal episodes</strong></td>
<td>Light therapy</td>
</tr>
</tbody>
</table>
Treatment Modalities

Psychotherapy: Cognitive-behavioral therapy, interpersonal psychotherapy (IPT) and behavioral psychotherapies (i.e., behavioral activation) have demonstrated acute efficacy in treating major depressive disorder.\(^5\)

- **Behavioral Activation:** A therapy that encourages behavioral changes using motivational interviewing. Recommend increase in activities such as adding 20 minutes of exercise 3-4 times per week, improving diet, increase social activities, engage in enjoyable activities, stress reduction (mindfulness practice, relaxation) and sleep hygiene.\(^5,22\)

- **Cognitive-behavioral Therapy (CBT):** A therapy founded on the perspective that irrational beliefs and distorted attitudes towards the self, environment, and future perpetuate depressive affects and compromise functioning. The goal of CBT is to reduce depressive symptoms by challenging and reversing these beliefs and attitudes and encourage patients to change their maladaptive preconceptions and behaviors.\(^5\)

- **Interpersonal Psychotherapy (IPT):** A therapy which focuses on current life changes including loss, role disputes and role transition (i.e., becoming a new mother, divorce, primary caretaker for an elderly family member), social isolation, deficits in social skills, and other interpersonal factors that may interact with the development of depression. The goal of IPT is to intervene by identifying the current trigger for the depressive episode, facilitating mourning in the case of bereavement, promoting recognition of related affects, resolving role disputes, and transitions, and building social skills.\(^5\)

Pharmacotherapy: For essentially all patients, the clinician who provides the medication also provides support, advice, reassurance, instills optimism as well as medication monitoring. This “clinical management” is critical with depressed patients whose pessimism, low motivation, low energy, and sense of social isolation or guilt lead them to give up, not comply with treatment, or to drop out of treatment.

Many drug interactions occur with antidepressant therapy; many of these occur with medications commonly prescribed in primary care.

Selection of a particular medication should take into consideration the following:\(^5,14\)

- Prior positive/negative response to medication (personal or family history)
- Clinician experience with specific antidepressants
- Patient preference
- Other health conditions (i.e., ADHD, smoking cessation) (see Appendix F)
- Side effect profiles (see Appendix G)
- Safety in overdose (i.e., 10 days of a TCA can be a lethal overdose)
- Concurrent medications that make selected medications more or less risky
- History of first degree relatives’ responses to medication
- Cost and insurance coverage
Drug information on antidepressant therapies is included in Appendix H.

Pediatric and adult patients with a major depressive disorder may experience worsening of their depression, emergence of suicidal ideation and suicidality, whether or not they are taking antidepressants and this may persist until significant remission occurs. Patient education on depression is important for patient adherence with therapy. For antidepressant medications, compliance with a therapeutic dose is more important than the specific drug selected.

- Take medication daily as prescribed.
- Antidepressants must be taken daily for 2-4 weeks for a noticeable effect.
- Be educated on potential side effects. Many side effects resolve after 1-2 weeks.
- Continue to take medication even if you are feeling better, increased risk of relapse if stopped before 6 months.
- Do not stop taking antidepressant without checking with your provider. Some antidepressants may have uncomfortable withdrawal symptoms.
- Contact your provider if you have questions about your medication.
- Be sure to make and keep follow-up appointments. This is important to ensure full response to your medication.
- The medication is not addictive and will not change your personality. Depression alters brain functioning and the medication helps restore normal patterns, so you eat and sleep more normally, think more clearly and have more energy.
- The medication should help you benefit from the psychotherapy you are receiving.
- Do not drink alcohol with medication.

**Patients with Substance Abuse and Use of Antidepressants**

Detoxifying patients before initiating antidepressant medication therapy is advisable when possible. Antidepressants may be used to treat depressive symptoms following initiation of abstinence if symptoms do not improve over time. It is difficult to identify patients who should begin a regimen of antidepressant medication therapy soon after initiation of abstinence, because depressive symptoms may have been induced by intoxication and/or withdrawal of the substance. A family history of major depressive disorder, a history of major depressive disorder preceding alcohol or other substance abuse, or a history of major depressive disorder during periods of sobriety raises the likelihood that the patient might benefit from antidepressant medication, which may then be started early in treatment. Comparing the temporal pattern of symptoms with the periods of use and abstinence of the substance may help to clarify the patient’s diagnosis. Repeated, longitudinal assessments may be necessary to distinguish substance-induced depressive disorder from co-occurring major depressive disorder, particularly because some individuals with substance use disorders reduce their substance consumption once they achieve remission of a co-occurring major depressive disorder.

Benzodiazepines and other sedative-hypnotics carry the potential for abuse or dependence and should rarely be prescribed to patients with co-occurring substance use disorders, except as part of a brief detoxification regimen. Hepatic dysfunction and
hepatic enzyme induction frequently complicate pharmacotherapy of patients with alcoholism and other drug abuse. These conditions may require careful monitoring of blood levels (as appropriate for the medication), therapeutic effects, and side effects to avoid the opposing risks of either psychotropic medication intoxication or under dosing.

**Electroconvulsive Therapy (ECT):** ECT may be administered unilaterally or bilaterally (using a bitemporal or bifrontal electrode placement). This therapy is typically administered 2-3 times per week for 6-12 treatments or until symptoms have remitted.\(^5\)

**Light Therapy:** Light therapy is an FDA approved treatment for seasonal depression and is covered by most insurance companies.\(^22\) Use of a light box (10,000 lux for 30 minutes every morning) in the dark months of the year (September – March) can be considered as a treatment option.\(^5\)

**Treatment in Nonpregnant Adolescents (12-17 years)**

An algorithm for treatment in adolescents is included within Appendix C.

Interpersonal or cognitive behavioral psychotherapy (individual or group) should be considered a first-line treatment option for mild depression in adolescent patients.\(^24,28,34\) (AAP Grade A, very strong recommendation) Psychotherapy alone is not recommended for the acute treatment of patients with severe and/or psychotic depressive disorders and has not been shown to reduce the risk for suicide attempts in adolescent patients.\(^35\)

Psychotherapy in combination with antidepressant medication may be needed for moderate to severe depression in adolescents\(^24\) (AAFP Grade A) or if any of the following symptoms are present: severe insomnia, severe anxiety, marked anhedonia, or thoughts of suicide. Medication may also be the preferred method of treatment in individuals who decline psychotherapy or who have required medication to treat depression in the past.

Selective serotonin reuptake inhibitors (SSRIs) have demonstrated efficacy in adolescent patients and may be considered as the first-line pharmacotherapy treatment option.\(^3,24,28,34\) Preference should be given to the two FDA-approved agents (fluoxetine and escitalopram); however off-label use of citalopram or sertraline may be considered.\(^36,37\) (UW Health Moderate quality evidence, weak recommendation) While patients are more likely to benefit from antidepressant treatment than commit suicide, the risks and benefits of SSRI use should be weighed due to risk of suicidal thoughts (suicide ideation).\(^3,28,34\) Side effects of SSRIs may include: irritability, insomnia, appetite change, gastrointestinal symptoms, headaches, diaphoresis, restlessness, or sexual dysfunction.\(^38\)

Atypical antidepressants (bupropion, venlafaxine, mirtazapine, duloxetine) may be considered as a second-line pharmacotherapy option only after at least two SSRIs have proven to be ineffective.\(^34,39\) (UW Health Very low quality evidence, weak recommendation) Side effects to these medications may include: irritability, nausea, anorexia, headaches, or insomnia. Blood pressure changes may also occur with venlafaxine.\(^38\)
Treatment in Nonpregnant Adults (18 years or older)

An algorithm for treatment in adults is included within Appendix D.

Clinicians should provide antidepressant medications and/or referral to psychotherapy as treatment for major depression. \(^\text{14}\) \((\text{ICSI Low quality evidence, strong recommendation})\) Treatment decisions may be completed through a shared-decision making process which considers the patient’s willingness to invest time in psychotherapy, the presence of psychosocial stressors, disease severity, and patient preference.

Mild to moderate levels of depression in adults have been treated as effectively with psychotherapy as with pharmacotherapy. Therefore, cognitive-behavioral therapy or interpersonal therapy may be recommended as a treatment option in adults. \(^\text{14}\) \((\text{UW Health Low quality evidence, weak recommendation})\) Psychotherapy in combination with antidepressant medication may be needed for moderate to severe depression in adults \(^\text{14}\) \((\text{UW Health High quality evidence, weak recommendation})\) or if any of the following symptoms are present: severe insomnia, severe anxiety, marked anhedonia, or thoughts of suicide.

Medication may also be the preferred method of treatment in individuals who decline psychotherapy, or who have required medication to treat depression in the past. Medication class may be determined through a discussion with the patient using the concurrent condition and product list information outlined in Appendix F and Appendix H, respectively.

When prescribing medications in older adults age 65 years or older, careful consideration should be taken of how the drug metabolism may be affected by physiologic changes, comorbid illnesses, and/or concomitant medications. \(^\text{14}\) \((\text{ICSI Low quality evidence, strong recommendation})\) Antidepressants should be initiated in older adults at \(\frac{1}{2}\) (or even \(\frac{1}{4}\)) of the usual starting doses. \(^\text{5}\) Note: Some tablets are not scored and pharmacies (including UW Health) may not split the tablet. Thus, they will not fill some prescriptions. It is important to keep in mind renal and hepatic status of a patient when choosing antidepressant doses, as well as to consider drug-drug interactions (including the risk of serotonin syndrome). \(^\text{5}\)

NOTE: Adult patients with a diagnosis of major depression on an antidepressant medication are subject to follow requirements established by the Healthcare Effectiveness Data and Information Set (HEDIS). For more information, see Appendix I.

ECT is most commonly recommended for adults with severe depression accompanied by psychosis, suicidal intent, or refusal to eat. \(^\text{5}\) \((\text{APA Grade I})\) It may be tried when medications are not tolerated or other forms of therapy haven’t proved effective \((\text{APA Grade I})\), by patient preference, or in patients who have had a previously positive response to ECT. \(^\text{5}\) \((\text{APA Grade II})\) A full psychiatric assessment is recommended before considering this treatment method. \(^\text{5,22}\)
Use of a light box (10,000 lux for 30 minutes every morning) in the dark months of the year (September – March) can be considered as a treatment option, especially in patients who suffer from seasonal depressive episodes. (APA Grade III)

**Treatment in Patients who are Pregnant (12 years or older)**

Algorithms for treatment in patients who are pregnant are included within Appendix E.

The treatment of depression during pregnancy should be completed using a shared-decision making process which weighs the potential risk of fetal exposure to psychotropic medication against the potential adverse effects of an untreated disorder. (UW Health Low quality evidence, weak recommendation) It is important to engage the patient and significant others in this discussion about what is best for their situation (patient preference), the different treatment options available, and that the ultimate goal is for the patient and baby to be as safe as possible. The treatment decision may also depend on the patient's history of depression before the pregnancy, their previous experience with medications, the severity of the depression, support available, response to alternative treatment modalities, etc.

Psychotherapy (IPT or CBT) is recommended whenever possible for mild to moderate depression, in patients who have exhibited a positive response in the past, or by patient preference. (APA Grade I) Interpersonal therapy is considered to be particularly useful during pregnancy as it directly addresses issues associated with role transitions and relationships with the partner.

Patients, who have become significantly depressed while off antidepressant medication in the past, will likely need to continue taking antidepressant medication in pregnancy to prevent recurrence of symptoms. Pregnant patients with new onset of moderate to severe depression in pregnancy may also need psychiatric medication in addition to psychotherapy to ensure the best treatment response. (APA Grade II) The goal of pharmacotherapy is to treat to remission to avoid exposing the infant to both the antidepressant medication and maternal depression.

Current evidence is insufficient to establish a direct relationship between antidepressant use during pregnancy and risks or adverse birth outcomes. SSRIs (except for paroxetine) and TCAs may be used if preferred by the patient. (UW Health Low quality evidence, weak recommendation) Paroxetine (FDA category D) is not recommended in women who are planning to become pregnant or those who are pregnant and in their first trimester, as some studies have found increased risk of cardiac defects with more than 25 mg/day of paroxetine use in the first trimester. (UW Health Low quality evidence, weak recommendation)

ECT is an additional treatment option for patients who are pregnant with depression and psychotic or catatonic feature, moderate to severe depression unresponsive to pharmacotherapy or psychotherapy, or by patient preference. (APA Grade II)
Treatment in Patients in Postpartum (12 years or older)

Interpersonal psychotherapy (individual or group) or cognitive behavioral therapy should be considered a first-line treatment option for mild-moderate postpartum depression, by patient preference, or in patients who have exhibited a positive response in the past.\(^5,45\) \((UW\ Health\ Moderate\ quality\ evidence,\ weak\ recommendation)\) Women with severe depression, suicidal ideation, or psychosis should be referred for psychiatric care. Such women require a comprehensive, multifaceted approach to treatment, including crisis intervention, pharmacotherapy, psychotherapy, and strengthening of social support networks.

Psychotherapy in combination with antidepressant medication may be needed if any of the following symptoms are present: severe insomnia, severe anxiety, marked anhedonia, thoughts of suicide, or intrusive thoughts of harm to the infant.\(^5\) Medication may also be the preferred method of treatment in women who decline psychotherapy, or who have required medication to treat depression in the past.

Postpartum Medications and Lactation

While there are not absolute contraindications to using a particular antidepressant medication while breastfeeding, there are no specific FDA-approved antidepressants labeled for peripartum use.\(^46\) If pharmacotherapy is preferred during the postpartum period, it is recommended to use SSRIs as the first line of therapy.\(^47\) \((UW\ Health\ Low\ quality\ evidence,\ weak\ recommendation)\) Therefore, initiation or continuation of medication should not interfere with the decision to begin or continue breastfeeding.

If the woman is breastfeeding, some agents may be preferred over others. Despite differences in relative infant exposure between individual SSRIs, the probability of an adverse event with SSRIs is remote.\(^42,47-51\) Mothers should be maintained on SSRIs that work best for them. If a medication is effective for the management of depression, it is not advisable to change breastfeeding mothers to another SSRI.\(^47\)

Sertraline and paroxetine may be preferred SSRIs, based on the relatively low exposure through breast milk.\(^47\) Exposure is determined by evaluating the concentration of the medication in the mother’s milk factored by the amount of milk the infant usually receives. The remaining SSRIs, as well as bupropion and venlafaxine, are not known to be contraindicated in nursing women, but less information is known about these medications during lactation. A decision to use these medications should be based on a patient-specific risk-benefit evaluation, and the infant should be observed closely for side effects.\(^52\)

Fluoxetine is not considered a first-line agent for women who are breastfeeding. The relative exposure of the infant through breast milk is higher than other SSRIs (9%) probably due to the long half-life and active metabolite.\(^47\) Fluoxetine has had several case reports of adverse effects in the infant, including colic, delayed weight gain, irritability, and disturbed sleep.\(^43,53\) For this reason, fluoxetine should generally not be considered first line treatment with a new diagnosis of depression.
The relative infant exposure to tri-cyclic antidepressants is low and they are well tolerated by the infant. TCAs are seldom used due to maternal adverse effects, but may present a safe option when SSRIs are not effective or tolerated.\textsuperscript{47}

**Perform Follow-up Care**

**Acute phase of treatment (first 6-12 weeks)** aims to resolve all signs and symptoms of the current episode of depression and to restore psychological and occupational functioning (a remission).\textsuperscript{5}

Patient non-compliance is high in those with depression, and the practitioner must assertively engage the patient in follow-up care and assessments. Proactive follow-up contacts (by telephone or in person clinic visits) based on the Collaborative Care model can significantly decrease depression severity.\textsuperscript{14,29-31}

Recommended contacts for adult patients based upon depression severity are outlined below (Table 5)\textsuperscript{14} (UW Health Low quality evidence, weak recommendation), however certain patient populations (i.e., new onset, unstable) may require more frequent contacts and closer observation. Similar contact frequencies for adolescents are appropriate, with the addition of monthly contacts to parents to discuss treatment adherence and response.\textsuperscript{54} (UW Health Moderate quality evidence, weak recommendation)

All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy or at times of dose changes, either increases or decreases.

**Table 5. Suggested Follow-up Contacts Based on Depression Severity\textsuperscript{14,54}**

<table>
<thead>
<tr>
<th>Symptom Severity (based on total PHQ-9 or PHQ-A scores)</th>
<th>Mild (5-9 pts.)</th>
<th>If no improvement after one month, consider referral to Behavioral Health for evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate (10-14 pts.)</td>
<td>Initially consider weekly contacts to ensure adequate engagement, then repeat monthly</td>
<td></td>
</tr>
<tr>
<td>Moderately severe (15-19 pts.)</td>
<td>Initially consider weekly contacts to ensure adequate engagement, then repeat a minimum of every 2-4 weeks</td>
<td></td>
</tr>
<tr>
<td>Severe (20-27 pts.)</td>
<td>Weekly contacts until less severe</td>
<td></td>
</tr>
</tbody>
</table>

Note: Parents of adolescent patients may be contacted monthly to discuss treatment adherence and response.

**Assessment of Treatment Response**

No psychotherapy should be continued unmodified if there is no symptomatic improvement after one month.\textsuperscript{5} (APA Grade I)
Treatment response should be assessed using the PHQ-9 or PHQ-A within 4-6 weeks of initiation in patients on drug therapy (alone or in combination with psychotherapy).\textsuperscript{5,34} (APA Grade II) Most patients respond partially to medication within 2-3 weeks and full symptom remission is typically seen in 6-8 weeks.\textsuperscript{5} Patients receiving psychotherapy alone should be assessed using the PHQ-9 or PHQ-A within 6-12 weeks of initiation, depending on the expectation of the given type of therapy.\textsuperscript{5} Patients who demonstrate remission or a response (defined as a 50% or greater reduction in symptoms as measured by the PHQ-9 or PHQ-A) should move into the continuation phase.\textsuperscript{14,34}

Treatment response should be assessed using the PHQ-9 or PHQ-A within 4-8 weeks for adults or 8-10 weeks for adolescents, following any change in treatment particularly if the change was due to a lack of response to previous therapy.\textsuperscript{5,34} (APA Grade I)

Adjusting Treatment if No Response- Stepped Care Approach
Treatment in the acute phase should not be discontinued prematurely in patients who do not fully respond at the initial assessment. (APA Grade I) If the patient does not demonstrate a response to pharmacotherapy (alone or in combination with psychotherapy) within 6 weeks (4 weeks in severely ill) of initiation, or responds only partially by 12 weeks, other treatment options should be considered (APA Grade I) including:

- Assess medication adherence
- Continue medication at a corrected dose
- Change medication (APA Grade II)
- Augment with a second medication (not advised until initial trial adequate in time and dosage)
- Refer for professional psychotherapy. Most patients receiving time-limited psychotherapy respond partially by 5-6 weeks and fully by 10-12 weeks.
- Obtain a Behavioral Health consultation

Patients receiving psychotherapy alone who do not respond initially to treatment should consider augmentation with pharmacotherapy, assessing the frequency of sessions and whether the type of therapy or therapeutic alliance is addressing the patient’s needs.\textsuperscript{5} (APA Grade I)

Continuation phase (4 - 9 months beyond acute treatment) is intended to prevent relapse by continuing the treatment of antidepressants, psychotherapy, or other therapies (i.e., ECT). Given the significant risk of relapse during the continuation phase, it is essential to assess depressive symptoms, functional status, and quality of life using the PHQ-9 or PHQ-A.\textsuperscript{5} (APA Grade II) Following remission or a response, patients should be contacted monthly during the continuation phase to monitor for relapse.\textsuperscript{30,54} (UW Health Moderate quality evidence, weak recommendation)

It is strongly recommended that adult patients on pharmacotherapy continue therapy for 4-9 months following successful acute phase treatment.\textsuperscript{5} (APA Grade I) Adolescent patients should continue medication for 6-12 months.\textsuperscript{34} Continuation of psychotherapy such as CBT is also recommended.\textsuperscript{5} (APA Grade I) Patients who continue psychotherapy should be reassessed every 3-4 months to ensure adequate improvement.\textsuperscript{5}
Once the patient has been asymptomatic for at least 4 to 9 months following a depressive episode, recovery from the episode is declared. At recovery, treatment may be stopped unless the patient is considered at high risk for recurrence. Maintenance therapy should be considered in high risk patients experiencing three or more prior major depressive episodes (APA Grade I), or two prior episodes and any of the following risk factors (APA Grade II):

- Chronic major depressive disorder (severe prior episodes)
- Presence of residual symptoms
- Ongoing psychosocial stressors
- Early age at onset
- Family history of mood disorders

Prior to discontinuation of treatment, patients should be informed of the potential for relapse and a plan should be established to seek treatment if symptoms reoccur. The discontinuation of antidepressant therapy should be tapered over at least several weeks in adults (APA Grade I) and over 2-3 months in adolescents. It is important to notify patients receiving psychotherapy of discontinuation, well in advance of the last session.

**Maintenance phase (1 year to lifetime beyond continuation therapy)** is aimed at preventing new or future depressive episodes. Adult (APA Grade I) or adolescent (UW Health Very low quality evidence, weak recommendation) patients who have had three or more episodes of depression or at high risk for recurrence should be considered for long-term maintenance medication therapy (antidepressant). Patients should be contacted throughout the maintenance phase every 3-12 months if stable.

Recurrent depression is common in elderly patients. Therefore, maintenance therapy with an SSRI is recommended. Interpersonal psychotherapy alone is not effective in this population. (UW Health High quality evidence, strong recommendation)

**Management of Medication Side Effects**

Side effects are common with SSRIs, SNRIs, mirtazapine, and bupropion but can be managed for most patients. See Appendix G for a list of common side effects and alternative options.

To minimize GI distress, headache, and agitation associated with starting an SSRI or SNRI, start at half of the target dose for 1 week then increase to the full amount. If the patient complains of side effects, you can recommend cutting the dose in half and titrating even more slowly (e.g., starting with 5 mg of citalopram, increasing to 10, then 15, then 20 mg). Taking at bedtime with a little food will also minimize nausea. If slow titration is not effective in minimizing these side effects, (GI distress, agitation, or headache), you may need to consider using another SSRI, SNRI, bupropion, mirtazapine, duloxetine, or a TCA instead. Mirtazapine is particularly helpful for patients who experience akathisia, or intense restlessness that causes them to pace. While the above side effects usually go away with time, sedation and sexual side effects of SSRIs and SNRIs persist and are dose dependent. For sedation, switching to
escitalopram, venlafaxine, or bupropion is often helpful, as these are the least sedating antidepressants. An initial strategy for reducing sexual side effects can be lowering the dose by 25-50% if the patient is stable and willing. Alternatively, bupropion can be added to an SSRI to minimize sexual side effects by as much as 80%. A dose of 300 mg a day is recommended – lower doses are not as effective. Bupropion may also be helpful for patients who complain of lethargy, amotivation, tobacco dependence, or poor concentration. A final option is to add buspirone to the SSRI/SNRI. This is the best choice when the patient has comorbid anxiety that might worsen with bupropion. Start with 5 mg BID for 1 week then increase by 10 mg a week to a target dose of 30-60 mg a day. The dose-limiting side effect for most people is dizziness, which can be managed by giving a higher dose at night than in the morning.

The chronic side effects of bupropion are similar to the effects of caffeine: jitteriness, anxiety, sleeplessness, and tremor. Short term side effects include decreased appetite, and nausea. If a person becomes too stimulated with bupropion, you will have to either lower the dose or change to another medication.

Mirtazapine’s two persistent side effects are sedation and weight gain. There is little that can be done to minimize these, although the daytime sedation does improve with time; therefore, switching to another medication is warranted if these side effects are problematic.

Venlafaxine should always be started at 37.5 mg and titrated by this amount every 4-5 days to a target dose of 75-150 mg. A more abrupt titration will almost always cause agitation. It does not become an “SNRI” until at least 112.5 mg – so if it is being used for this purpose, it is best to increase to a target dose of 150 mg at the start of treatment.

In patients who are sensitive to most medication, duloxetine or escitalopram are often well tolerated when started at the lowest possible dose (2.5 mg for escitalopram and 20 mg for duloxetine) and titrated very slowly.

**Special Considerations for Older Adult Patients (65 years or older)**

Older adults are also more likely to experience the side effects such as falls, sedation or cognitive impairment. In adults age 65 and older SSRI’s and SNRI’s may cause hyponatremia. A plasma sodium should be checked at baseline 2-3 weeks after initiation and 2-3 weeks after each titration. Patients should be educated about the symptoms of hyponatremia.

Citalopram should not be prescribed at doses higher than 40 mg per day due to a risk of QT prolongation. In patients 60 years and older the maximum dose is 20 mg per day.
UW Health Implementation

Potential Benefits:
• Appropriate screening, diagnosis and treatment of depression
• Improved patient outcomes in terms of symptoms, quality of life, functioning, and medical utilization

Potential Harms:
• Side effects and adverse effects associated with various treatments (i.e., increased risk for suicidal ideation in adolescents taking SSRIs)

Implementation Plan/Tools
1. Guideline will be housed on U-Connect on the UW Health CPG webpage.
2. Release of the guideline will be advertised in the Clinical Knowledge Management Corner within the Best Practice newsletter.
3. Links to this guideline will be updated and/or added in appropriate Health Link or equivalent tools, including:
   Smart Sets
   Depression [77]

Disclaimer
CPGs are described to assist clinicians by providing a framework for the evaluation and treatment of patients. This Clinical Practice Guideline outlines the preferred approach for most patients. It is not intended to replace a clinician’s judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

References
1. Organization WH. Depression. Fact Sheet No. 3692012.


33. Administration SAaMHS. General Principles for the Use of Pharmacological Agents to Treat Individuals with Co-Occurring Mental and Substance Use Disorders. Rockville, MD: HHS Publication; 2012.


Appendix A. Rating Schemes for the Strength of the Evidence/Recommendations

Grading of Recommendations Assessment, Development, and Evaluation (GRADE)

**Figure 1: GRADE Algorithm**

**GRADE Ranking of Evidence**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>We are confident that the effect in the study reflects the actual effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.</td>
</tr>
<tr>
<td>Low</td>
<td>The true effect may differ significantly from the estimate.</td>
</tr>
<tr>
<td>Very Low</td>
<td>The true effect is likely to be substantially different from the estimated effect.</td>
</tr>
</tbody>
</table>

**GRADE Ratings for Recommendations**

<table>
<thead>
<tr>
<th>Strength</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong for using/Strong against using</td>
<td>The net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.</td>
</tr>
<tr>
<td>Weak for using/Weak against using</td>
<td>The evidence is weak or the balance of positive and negative effects is vague.</td>
</tr>
</tbody>
</table>

**American Academy of Family Physicians**

**SORT Evidence Rating System**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Consistent, good-quality patient-oriented evidence</td>
</tr>
<tr>
<td>B</td>
<td>Inconsistent or limited-quality patient-oriented evidence</td>
</tr>
<tr>
<td>C</td>
<td>Consensus, disease-oriented evidence, usual practice, expert opinion or case series</td>
</tr>
</tbody>
</table>
American Academy of Pediatrics\textsuperscript{11,28}

**Level of Supporting Evidence- Oxford Centre for Evidence-based Medicine**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Consistent, good-quality patient-oriented evidence</td>
</tr>
<tr>
<td>B</td>
<td>Inconsistent or limited-quality patient-oriented evidence</td>
</tr>
<tr>
<td>C</td>
<td>Consensus, disease-oriented evidence, usual practice, expert opinion or case series</td>
</tr>
</tbody>
</table>

**AAP Recommendation Strength**

<table>
<thead>
<tr>
<th>Strength</th>
<th>Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very strong</td>
<td>&gt; 90% agreement</td>
</tr>
<tr>
<td>Strong</td>
<td>&gt; 70% agreement</td>
</tr>
<tr>
<td>Fair</td>
<td>&gt; 50% agreement</td>
</tr>
<tr>
<td>Weak</td>
<td>&lt; 50% agreement</td>
</tr>
</tbody>
</table>

American Psychiatric Association\textsuperscript{5}

**APA Grading Scheme**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Recommended with substantial clinical confidence</td>
</tr>
<tr>
<td>II</td>
<td>Recommended with moderate clinical confidence</td>
</tr>
<tr>
<td>III</td>
<td>May be recommended on the basis of individual circumstances</td>
</tr>
</tbody>
</table>

United States Preventive Services Task Force (USPSTF)

**USPSTF Grade Definitions**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>The USPSTF recommends this service. There is high certainty that the net benefit is substantial.</td>
</tr>
<tr>
<td>B</td>
<td>The USPSTF recommends this service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.</td>
</tr>
<tr>
<td>C</td>
<td>The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.</td>
</tr>
<tr>
<td>D</td>
<td>The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.</td>
</tr>
<tr>
<td>I</td>
<td>Statement</td>
</tr>
<tr>
<td></td>
<td>The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefit and harms cannot be determined.</td>
</tr>
</tbody>
</table>
Appendix B. Depression Screening Algorithm

### Adolescents (12-17 years)

- Perform universal annual screening or assessment based on symptoms/patient presentation using the PHQ-2
  - PHQ-2 score 3 or greater?
    - Yes → Perform follow-up assessment using the PHQ-9 or PHQ-A
      - PHQ-9 or PHQ-A score ≥ 10?
        - Yes → Complete documentation. Repeat screening in one year or next visit.
        - No
          - No → Complete documentation. Repeat screening in one year or next visit.
    - No → Complete documentation. Repeat screening in one year or next visit.

### Adults (18 years or older)

- Perform universal annual screening or assessment based on symptoms/patient presentation using the PHQ-2
  - PHQ-2 score 3 or greater?
    - Yes → Perform follow-up assessment using the PHQ-9
      - PHQ-9 score ≥ 10?
        - Yes → Complete documentation. Repeat screening in one year or next visit.
        - No → Complete documentation. Repeat screening in one year or next visit.
    - No → Complete documentation. Repeat screening in one year or next visit.

### Pregnant Women (12 years or older)

- Screen at the first prenatal visit, during the 3rd trimester (24-32 weeks), and 6 weeks postpartum using the EPDS, PHQ-9 or PHQ-A.
  - EPDS score > 10?
    - Yes → Affirmative response to Question 10?
      - Yes → Perform suicide assessment. Consider accessing crisis intervention services.
      - No → Complete documentation. Repeat screening if necessary.
    - No → PHQ-9 or PHQ-A score > 10?
      - Yes → Complete documentation. Repeat screening if necessary.
      - No
        - No
          - No → Complete documentation. Repeat screening if necessary.

Document follow-up plan (which must contain one or more of the following):
- additional evaluation for depression
- suicide risk assessment
- referral to a practitioner who is qualified to diagnose and treat depression
- pharmacological interventions
- other interventions or follow-up for the diagnosis and treatment of depression

Establish a diagnosis using DSM-5 Criteria

Provide treatment
- Refer to Treatment Algorithm for Depression in Adults
- Refer to Treatment Algorithm for Depression in Pregnant Women
- Refer to Treatment Algorithm for Depression in Adolescents

Contact CCKM for questions.
Depression – Pediatric/Adult – Ambulatory Clinical Practice Guideline

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Contact: CCKM@uwhealth.org  Last Revised: 04/2015
Appendix C. Depression Treatment in Adolescents Algorithm

Diagnosis of Depression

Mild Severity
(PHQ-9 or PHQ-A score 5-9 points)
- Initiate psychotherapy alone (i.e., CBT or IPT)

Moderate Severity
(PHQ-9 or PHQ-A score 10-19 points)
- Initiate psychotherapy alone (i.e., CBT or IPT), pharmacotherapy alone, or combination therapy (psychotherapy and medications)

Severe Severity
(PHQ-9 or PHQ-A score 20-27 points)
- Initiate pharmacotherapy or ECT

Assess Initial Response using PHQ-9 or PHQ-A
- At 4-6 weeks if pharmacotherapy (alone or in combination) or 6-12 weeks if psychotherapy alone

Response?*
- Yes
  - Prevent Relapse
    - If on medications, continue for 6-12 months.
    - If receiving psychotherapy alone, continue for 3-4 months.
  - Assess Response using PHQ-9 or PHQ-A
    - 8-10 weeks following change in treatment

- No
  - Adjust or Change Therapy
    - Consider:
      - Assessing therapy adherence
      - Adjusting medication dose or class
      - Increasing number of therapy sessions
      - Augmenting or changing therapy type
      - Referral to Behavioral Health

CONTINUATION PHASE
(4-9 months)
- Contact patient monthly for up to 12 months.

Assess Response using PHQ-9 or PHQ-A
- Full symptom remission?**
  - Yes
    - Continue pharmacotherapy and contact patient every 3-12 months if stable.
  - No
    - Adjust Treatment and return to Acute Phase

Risk factors for recurrence:
- 3 or more major depressive episodes OR 2 prior episodes and any of the following factors:
  - Chronic major depressive disorder
  - Presence or residual symptoms
  - Ongoing psychosocial stressors
  - Early age at onset
  - Family history of mood disorders

MAINTENANCE PHASE
(1 year to lifetime)
- Contact patient every 3-12 months if stable.

*Response: a 50% or greater reduction in symptoms (as measure by the PHQ-9).
**Remission: the absence of depressive symptoms, or the presence of minimal depressive symptoms (PHQ-9 score < 5 points)
Appendix D. Depression Treatment in Adults Algorithm

**ACUTE PHASE (6-12 weeks)**

- Contact patient weekly, then monthly (moderate severity), or every 2-4 weeks (moderately severe). Patients with severe depression should be contacted weekly until symptoms less severe.

**Diagnosis of Depression**

<table>
<thead>
<tr>
<th>Mild Severity (PHQ-9 score 5-9 points)</th>
<th>Moderate Severity (PHQ-9 score 10-19 points)</th>
<th>Severe Severity (PHQ-9 score 20-27 points)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiate psychotherapy alone and/or behavioral activation</td>
<td>Initiate psychotherapy alone (i.e., CBT or IPT), pharmacotherapy alone, or combination therapy (psychotherapy and medications)</td>
<td>Initiate pharmacotherapy or ECT</td>
</tr>
</tbody>
</table>

**Assess Initial Response using PHQ-9**
- At 4-6 weeks if pharmacotherapy (alone or in combination) or 6-12 weeks if psychotherapy alone

**Response?**
- Yes
- No

**CONTINUATION PHASE (4-9 months)**

- Contact patient monthly for up to 12 months.

**Prevent Relapse**
- If on medications, continue for 4-9 months.
- If receiving psychotherapy alone, continue for 3-4 months.

**Assess Response Monthly using PHQ-9**
- Full symptom remission?**
  - Yes
  - No

**MAINTENANCE PHASE (1 year to lifetime)**

- Continue pharmacotherapy and contact patient every 3-12 months if stable.

**Risk factors for recurrence:**
- 3 or more major depressive episodes OR 2 prior episodes and any of the following factors:
  - Chronic major depressive disorder
  - Presence or residual symptoms
  - Ongoing psychosocial stressors
  - Early age at onset
  - Family history of mood disorders

**Response:** a 50% or greater reduction in symptoms (as measured by the PHQ-9).

**Remission:** the absence of depressive symptoms, or the presence of minimal depressive symptoms (PHQ-9 score < 5 points)

**Adjust or Change Therapy Stepped Care Approach**
- Consider:
  - Assessing therapy adherence
  - Adjusting medication dose
  - Increasing number of therapy sessions
  - Augmenting or changing therapy type
  - Referral to Behavioral Health

**Adjust Treatment and return to Acute Phase**

**Discontinue Treatment**
- Taper antidepressants over several weeks
- Notify patient prior to final psychotherapy session

**Consider referral to Behavioral Health at any time, especially if:**
- Possibility of bipolar disorder
- Psychiatric co-morbidity (i.e., substance abuse, anxiety, OCD, eating disorder)
- Concern regarding the possibility of suicide and/or homicide
- Psychosis with depression
- No improvement with medications despite multiple dose adjustments and trials of different medication classes
- Significant or prolonged inability to work and care for self and/or family
- Diagnostic uncertainty

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Contact: CCKM@uwhealth.org

Last Revised: 04/2015

Contact CCKM with questions.

Depression- Pediatric/Adult – Ambulatory Clinical Practice Guideline
Appendix E. Depression Treatment during Pregnancy Algorithm

Pregnant Patient Diagnosed with Depression

- New diagnosis?
  - Yes
    - Currently taking antidepressant?
      - No
        - Willing to discontinue?
          - Yes
            - Continue pharmacotherapy after discussion of risks and benefits; monitor symptoms
          - No
            - Consider tapering antidepressant, monitor for relapse and refer to psychotherapy
      - Yes
        - Past relapse after stopping medication?
          - No
            - Consider medication in addition to psychotherapy; monitor symptoms
          - Yes
            - Consider referral to Psychiatry
    - No
      - Mild/Moderate Severity
        - Psychotherapy (IPT or CBT)
          - Positive response?
            - Yes
              - Continue psychotherapy; monitor symptoms
            - No
              - Willing to consider medication?
                - Yes
                  - Consider medication in addition to psychotherapy; monitor symptoms
                - No
                  - Severity moderate to severe?
                    - Yes
                      - Consider referral to Psychiatry
                    - No
                      - Consider medication in addition to psychotherapy; monitor symptoms

Reference: Yonkers KA, Wisner KL, Stewart DE, et al. The management of depression during pregnancy: a report from the American Copyright © 2015 University of Wisconsin Hospitals and Clinics Authority Contact: CCKM@uwhealth.org Last Revised: 04/2015
## Appendix F. Consideration of Concurrent Conditions

<table>
<thead>
<tr>
<th>Depression With</th>
<th>First-Line Therapeutic Options*</th>
<th>May be Problematic</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Additional Comorbid Conditions</td>
<td>Fluoxetine, Citalopram, Escitalopram, Paroxetine, Sertraline, Trazodone, Mirtazapine, Venlafaxine, Desvenlafaxine, Bupropion</td>
<td>TCA-side effect profile less desirable Nefazodone-hepatotoxicity</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Sertraline, Citalopram, Fluoxetine, TCA</td>
<td>Paroxetine, Venlafaxine, Duloxetine</td>
</tr>
<tr>
<td>Elderly patients</td>
<td></td>
<td>Fluoxetine, Paroxetine</td>
</tr>
<tr>
<td>Alcohol Use</td>
<td></td>
<td>Duloxetine=Liver injury, as manifested by ALT and total Bilirubin elevations, with evidence of obstruction have occurred with coadministration of alcohol and Duloxetine.</td>
</tr>
<tr>
<td>Anxiety or Panic Disorder</td>
<td>Paroxetine, Fluoxetine, Mirtazapine, Sertraline, Citalopram, Escitalopram Venlafaxine, Sertraline</td>
<td>Bupropion-may increase anxiety</td>
</tr>
<tr>
<td>Cardiac Condition</td>
<td>Sertraline</td>
<td>TCA Venlafaxine Desvenlafaxine, Bupropion (increases blood pressure), Mirtazapine (increases cholesterol), Citalopram</td>
</tr>
<tr>
<td>Chronic Pain</td>
<td>TCA, SNRI such as Duloxetine</td>
<td></td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>TCA, Mirtazapine</td>
<td>Venlafaxine Desvenlafaxine SSRI</td>
</tr>
<tr>
<td>Dementia</td>
<td>Bupropion, Mirtazapine, Citalopram</td>
<td></td>
</tr>
<tr>
<td>Dementia, Head Injury, Post-Stroke Patients</td>
<td>Citalopram, Escitalopram, Sertraline</td>
<td>TCAs, Paroxetine, Mirtazapine, Bupropion</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Fluoxetine, Citalopram, Escitalopram, Paroxetine, Sertraline</td>
<td>TCAs, Mirtazapine (may increase carbohydrate cravings), Duloxetine (causes slowed gastric emptying), Paroxetine</td>
</tr>
<tr>
<td>Eating Disorders (anorexia, bulimia)</td>
<td>Fluoxetine, Paroxetine, Sertraline</td>
<td>Bupropion, Mirtazapine</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>Duloxetine, Venlafaxine</td>
<td></td>
</tr>
<tr>
<td>Glaucoma</td>
<td>Fluoxetine, Citalopram, Escitalopram, Sertraline, Bupropion</td>
<td>TCA, Paroxetine, Duloxetine, Venlafaxine, Desvenlafaxine</td>
</tr>
<tr>
<td>Lactation</td>
<td>Sertraline, Paroxetine</td>
<td>Fluoxetine</td>
</tr>
<tr>
<td>Liver Disease</td>
<td>Sertraline, Venlafaxine (use at low dose), Desvenlafaxine (use at low dose)</td>
<td>TCAs, Fluoxetine, Paroxetine, Citalopram, Escitalopram, Trazodone, Mirtazapine, Nefazodone, Duloxetine</td>
</tr>
<tr>
<td>Obsessive Compulsive Disorder</td>
<td>Fluoxetine, Citalopram, Escitalopram, Paroxetine</td>
<td></td>
</tr>
<tr>
<td>Parkinson's Disease</td>
<td>Bupropion, Trazodone, Desipramine, Amoxapine, Nortriptyline, Protryptyline</td>
<td>SSRIs, Venlafaxine, Desvenlafaxine, Nefazodone, Mirtazapine</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td></td>
<td>Selegiline patch</td>
</tr>
<tr>
<td>Renal Disease</td>
<td>Fluoxetine, Citalopram, Escitalopram, Sertraline</td>
<td>Mirtazapine, Paroxetine, Venlafaxine, Desvenlafaxine, TCA-levels not predictive</td>
</tr>
<tr>
<td>Seizures/Seizure Disorder</td>
<td>Fluoxetine, Citalopram, Escitalopram, Sertraline, Paroxetine</td>
<td>Bupropion, Maprotiline, TCA (in overdose), Duloxetine, Venlafaxine Desvenlafaxine</td>
</tr>
<tr>
<td>Symptoms of: insomnia, weight loss, or overstimulation</td>
<td>Mirtazapine, Trazodone, TCAs, Paroxetine</td>
<td>Venlafaxine, Desvenlafaxine, SSRI, Bupropion</td>
</tr>
<tr>
<td>Symptoms of: oversedation, weight gain, or lethargy</td>
<td>Bupropion, Venlafaxine, Desvenlafaxine</td>
<td>Mirtazapine, TCA, Trazodone, Fluoxetine, Sertraline, Citalopram, Escitalopram, Paroxetine</td>
</tr>
</tbody>
</table>

*Prior to selecting an individual agent for therapy, prescribers should screen for other medications and supplements that may cause problematic effects for the patient.*
### Appendix G. Depression Side Effect Profiles

Side effects may be observed early in pharmacotherapy treatment and improve over time. If side effects persist, alternatives may be considered.\(^5\)

<table>
<thead>
<tr>
<th>Presenting Symptom</th>
<th>First Line Therapeutic Options</th>
<th>May Be Problematic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agitation/Insomnia</td>
<td>Mirtazapine, TCA</td>
<td>Selegiline Patch, Fluoxetine, Sertraline, Paroxetine, Citalopram, Escitalopram, Bupropion, Venlafaxine, Desvenlafaxine</td>
</tr>
<tr>
<td>Anticholinergic Side Effects</td>
<td>Citalopram, Escitalopram, Fluoxetine, Sertraline, Venlafaxine, Desvenlafaxine, Bupropion</td>
<td>TCA, Mirtazapine, Paroxetine, Duloxetine, Selegiline Patch</td>
</tr>
<tr>
<td>GI Sensitivity</td>
<td>Bupropion, TCA, Mirtazapine</td>
<td>Fluoxetine, Sertraline, Paroxetine, Citalopram, Escitalopram, Nefazodone, Venlafaxine, Desvenlafaxine, Duloxetine (20% pts nausea)</td>
</tr>
<tr>
<td>Headache</td>
<td>TCA, Mirtazapine</td>
<td>Fluoxetine, Sertraline, Paroxetine, Citalopram, Escitalopram, Nefazodone, Venlafaxine, Desvenlafaxine, Bupropion, Selegiline Patch</td>
</tr>
<tr>
<td>Orthostatic Hypotension</td>
<td>Fluoxetine, Sertraline, Paroxetine, Citalopram, Escitalopram, Venlafaxine, Desvenlafaxine, Bupropion</td>
<td>TCA, Mirtazapine, Trazodone, Selegiline Patch</td>
</tr>
<tr>
<td>Sedation</td>
<td>Fluoxetine, Sertraline, Paroxetine, Citalopram, Escitalopram, Venlafaxine, Desvenlafaxine, Bupropion</td>
<td>TCA, Nefazodone, Trazodone, Mirtazapine, Selegiline Patch, Paroxetine</td>
</tr>
<tr>
<td>Sexual Dysfunction</td>
<td>Bupropion, Mirtazapine</td>
<td>Fluoxetine, Sertraline, Paroxetine, Citalopram, Escitalopram, Venlafaxine, Desvenlafaxine, Bupropion, Trazodone</td>
</tr>
<tr>
<td>Weight Gain</td>
<td>Fluoxetine, Sertraline, Citalopram, Escitalopram, Venlafaxine, Desvenlafaxine, Bupropion</td>
<td>TCA, Paroxetine, Mirtazapine, Trazodone</td>
</tr>
</tbody>
</table>

### Special Considerations for Older Adults (age 65 years or older) \(^5,59,61\)

<table>
<thead>
<tr>
<th>Presenting Symptom</th>
<th>First Line Therapeutic Options</th>
<th>May Be Problematic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor sleep/Insomnia</td>
<td>Mirtazapine</td>
<td>Benzodiazepines, Paroxetine</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Mirtazapine</td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>SSRIs, SNRIs</td>
<td></td>
</tr>
<tr>
<td>Hypersomnia and low energy</td>
<td>Bupropion</td>
<td></td>
</tr>
</tbody>
</table>
# Appendix H. Product and Dosage Chart

<table>
<thead>
<tr>
<th>Product</th>
<th>How Supplied</th>
<th>Dosage Ranges</th>
<th>Generic?**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SELECTIVE SEROTONIN REUPTAKE INHIBITORS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram (Celexa)</td>
<td>10, 20, 40mg scored tab 10mg/4mL soln</td>
<td>20-40mg daily</td>
<td>Yes</td>
</tr>
<tr>
<td>Escitalopram (Lexapro)</td>
<td>5mg unscored, 10 and 20mg scored tab 5mg/5mL soln</td>
<td>10-20mg daily</td>
<td>Yes</td>
</tr>
<tr>
<td>Fluoxetine (Prozac)</td>
<td>10, 20, 40mg tab 90mg delayed release cap 10mg, 20mg tab 20mg/5mL soln</td>
<td>10-80mg daily or 90mg weekly</td>
<td>Yes</td>
</tr>
<tr>
<td>Paroxetine (Paxil, Paxil CR)</td>
<td>10, 20mg scored tab 30, 40mg tab 12.5, 25mg, 37.5mg CR</td>
<td>10-60mg IR daily or 25-62.5mg CR daily (includes CR)</td>
<td>Yes</td>
</tr>
<tr>
<td>Sertraline (Zoloft)</td>
<td>25, 50, 100mg scored tab 20mg/mL concentrate</td>
<td>50-200mg daily</td>
<td>Yes</td>
</tr>
<tr>
<td>Trazodone* (Oleptro)</td>
<td>50, 100, 150, 300mg IR tab ER 150, 300mg</td>
<td>150-600mg IR daily in divided doses 150mg ER daily</td>
<td>Yes</td>
</tr>
<tr>
<td>Vilazodone (Viibryd)</td>
<td>10, 20, 40mg tablets 20 – 40mg once daily</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Vortioxetine (Brintellix)</td>
<td>5, 10, 15, 20 mg tablets 5 – 20mg once daily</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td><strong>NOREPINEPHERINE SEROTONIN REUPTAKE INHIBITORS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desvenlafaxine (Pristiq)</td>
<td>50, 100mg tab</td>
<td>50 daily</td>
<td>Yes</td>
</tr>
<tr>
<td>Duloxetine (Cymbalta)</td>
<td>20, 30, 60mg cap</td>
<td>40-60mg daily</td>
<td>Yes</td>
</tr>
<tr>
<td>Levomilnacipran (Fetzima)</td>
<td>20, 40, 80, 120mg ER capsules</td>
<td>40 – 120mg daily following 20mg X2day titration</td>
<td>No</td>
</tr>
<tr>
<td>Mirtazapine (Remeron)</td>
<td>7.5, 15, 30, 45mg tab 15, 30, 45mg ODT</td>
<td>15-45mg daily (includes ODT)</td>
<td>Yes</td>
</tr>
<tr>
<td>Venlafaxine (Effexor, Effexor XR)</td>
<td>25, 37.5, 50, 75, 100mg IR tab 37.5, 75, 150, 225mg ER tab 37.5, 75, 150mg ER cap</td>
<td>75-225mg IR daily in divided doses 37.5-75mg ER daily (includes ER)</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>DOPAMINE REUPTAKE INHIBITOR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion (Wellbutrin, Aplenzin)</td>
<td>75, 100mg IR tab 100, 150, 200mg SR tab 150, 300mg XL tab 174, 348, 522mg ER tab</td>
<td>100-150 mg IR TID 150-200mg SR BID 150-450 mg XL daily (hydrochloride salt) 174-522 mg ER daily (hydrobromide salt) (includes ER &amp; XL but not Aplenzin products)</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>TRI-CYCLIC ANTIDEPRESSANTS</strong>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>amitriptyline</td>
<td>10, 25, 50, 75, 100, 150mg tab</td>
<td>50-150mg daily at bedtime or in divided doses</td>
<td>Yes</td>
</tr>
<tr>
<td>amoxapine</td>
<td>25, 50, 100, 150mg tab</td>
<td>50mg BID-TID</td>
<td>Yes</td>
</tr>
<tr>
<td>desipramine</td>
<td>10, 25, 50, 75, 100, 150mg tab</td>
<td>100-300mg daily in divided or single doses</td>
<td>Yes</td>
</tr>
<tr>
<td>doxepin</td>
<td>10, 25, 50, 75, 100, 150mg cap 10mg/mL conc</td>
<td>25-300mg daily in divided or single doses</td>
<td>Yes</td>
</tr>
<tr>
<td>imipramine</td>
<td>10, 25, 50mg tab 75, 100, 125, 150mg cap</td>
<td>75-200mg daily</td>
<td>Yes</td>
</tr>
<tr>
<td>maprotiline</td>
<td>25, 50, 75mg tab</td>
<td>75-150mg daily in divided or single dose</td>
<td>Yes</td>
</tr>
<tr>
<td>nortriptyline</td>
<td>10, 25, 50, 75mg cap 10mg/5mL soln</td>
<td>75-150mg daily in divided or single doses</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>MONOAMINE OXIDASE INHIBITORS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>phenelzine (Nardil)</td>
<td>15mg tab</td>
<td>15mg TID</td>
<td>Yes</td>
</tr>
<tr>
<td>selegiline transdermal (Emsam)</td>
<td>6, 9, 12mg/25 hr patch</td>
<td>6mg/24hr patch every 24 hours</td>
<td>No</td>
</tr>
<tr>
<td>Tranylcypromine (parimate)</td>
<td>10mg tab</td>
<td>30mg daily in divided doses</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*For TCA’s and trazodone, there are therapeutic blood levels that should be done if patient does not respond to therapeutic dose. **Insurance coverage varies. Patients are less likely to take their medication if they cannot afford it.
Appendix I. Depression HEDIS Measure

**Antidepressant Medication Management (AMM)**

The percentage of members 18 years of age and older with a diagnosis of major depression and prescription for an antidepressant medication, who remained on antidepressant medication treatment. Two rates are reported:

- **Effective Acute Phase Treatment** – percentage of members who remained on an antidepressant medication for at least 84 days (12 weeks.) *Members are allowed 30 gap days in treatment, so actually looking for 84 days of medication treatment over the course of 114 days from the Index Prescription Start Date (IPSD.)*

- **Effective Continuation Phase Treatment** – percentage of members who remained on an antidepressant medication for at least 180 days (6 months.) *Members are allowed 51 gap days in treatment, so actually looking for 180 days of medication treatment over the course of 231 days from IPSD.*

**Intake period** – The 12-month window starting on May 1 of the year prior to the measurement year and ending on April 30 of the measurement year.

**Index Prescription Start Date (IPSD)** – Earliest Rx for an antidepressant during the Intake Period (for example, for HEDIS™ 2015, we are looking for the 1st Rx filled between May 1, 2013 and April 30, 2014.)

Member must not have filled an Rx for an antidepressant within 105 days prior to the IPSD.

Ok to switch between antidepressants as long as you meet the rules of continuous use, as described above.

**Product line** – Commercial, Medicaid, Medicare