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Executive Summary

Guideline Title:
Diagnosing and Treating Depression – Adult – Primary Care Clinical Practice Guideline

Guideline Overview
Recommendations for diagnosing and treating depression in primary care adult patients.

Practice Recommendations
- Suspect and Screen for Major Depression
- Diagnose Depression and Rule Out Related Disorders
- Involve Behavioral Health When Indicated
- Develop and Implement a Treatment Plan
- Evaluate and Monitor Effectiveness of Treatment Plan

Companion Documents
- Health Facts For You (HFFY): Depression – A guide to Recognition and Treatment #4525
  [https://uconnect.wisc.edu/extranet/hffy/4525.pdf](https://uconnect.wisc.edu/extranet/hffy/4525.pdf)
- Health Facts For You (HFFY): Postpartum (After Birth) Depression #5112
  [https://uconnect.wisc.edu/extranet/hffy/5112.pdf](https://uconnect.wisc.edu/extranet/hffy/5112.pdf)
Scope
Disease/Condition(s): Depression

Clinical Specialty: Primary Care

Intended Users: Primary Care Clinicians

CPG objective(s): To assist clinicians by providing a framework for the diagnosis and treatment of depression in adult patients

Target Population: Primary care adult patients

Methodology
The steps used to develop this report include:
(1) Completing a comprehensive search of the literature
(2) Conducting an in-depth review of relevant abstracts and articles
(3) Conducting thoughtful discussion and interpretation of findings
(4) Ranking strength of evidence underlying the current recommendations that are made
(5) Updating text, tables, figures, and references of the existing guidelines with new findings from the evidence review.

Methods Used to Assess the Quality and Strength of the Evidence:
Comprehensive review of literature from 1994 to 2012.

Rating Scheme for the Strength of the Evidence:
A modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology (Figure 1) has been used to assess the Quality and Strength of the Evidence in this Clinical Practice Guideline.
**Figure 1: Quality of Evidence and Strength of Recommendation Grading Matrix**

*Modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology

**Description of Methods Used to Formulate the Recommendations:**
Clinical expertise of the clinicians on the workgroup.

**Description of Method of Guideline Validation:**
Clinical Knowledge Management Council
Introduction
It is important to recognize the prevalence of depressive disorder in the Western industrialized nations. In primary care settings the prevalence for major depressive disorder is 5-13%.\(^1\)

Major depression is characterized by:

**DSM-IV TR Criteria: Major Depressive Episode**
A. Five or more of the following symptoms having been present and documented during the same two-week period and representing 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 due to a general medical condition, or mood-incongruent delusions or hallucinations.

- depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful)
- 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 made by others)
- 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
- insomnia or hypersomnia nearly every day
- psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
- fatigue or loss of energy nearly every day
- feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
- diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)
- 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 do not meet criteria for a Mixed Episode.

C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

E. The symptoms are not better accounted for by Bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.²

There are multiple mood disorders to be aware of i.e. bipolar type I or II, major depressive episode, bereavement, dysthymic disorder, or cyclothymic disorder.
Recommendations

Major Recommendations:

1. **Suspect and Screen for Major Depression**
   (Class IIa, Level B)
   
   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. Please keep in mind that patients that 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 include:\(^3\)
   - multiple office visits
   - numerous unexplained symptoms
   - work or relationship dysfunction
   - sleep disturbance
   - multiple worries and distress

   **Risk Factors** for depression include:\(^3\)
   - prior episode(s)
   - family history of depressive disorder
   - female gender
   - postpartum period
   - peri/postmenopausal period
   - medical co-morbidity
   - lack of social support
   - major life stressor (loss of loved one or other members of social network)
   - substance abuse
   - history of adverse childhood events
   - negative cognitive style

   **Screening Instruments** have been developed for use in various clinical settings, including ambulatory primary care. The primary objective of these well-tested tools is to obtain input from the patient regarding their symptoms related to depression.

   The Patient Health Questionnaires (PHQ-2 & PHQ-9) and the Center for Epidemiological Studies Depression Scale for Children (CES-DC) are examples of screening tools used to aid in diagnosing depression. These tools tend to be fairly sensitive but not very specific in the diagnosis of depression. Generally, these tools are self-administered and then reviewed by the practitioner.

   All patients age 12 and older should be screened annually using a validated tool such as the PHQ-2. Patients who screen positive on the PHQ-2 should be
administered an age appropriate follow up screen, such as the CES-DC or the PHQ-9, for further diagnosis.

- **Use the PHQ-2 to screen patients 12 years of age and older**
  - A score of 2 or greater indicates a positive screen

- **For patients age 18 and greater:**
  - If a patient screens positive on the PHQ-2, administer the PHQ-9
  - A score of 10 or greater on the PHQ-9 indicates clinically significant depressive symptoms and the need for clinical evaluation (see section 2) to confirm the diagnosis. Once confirmed, a treatment plan should be documented (see section 4).

- **For patients age 12-17:**
  - If a patient screens positive on the PHQ-2 administer the CES-DC or the PHQ-9
  - A score of 15 or greater on the CES-DC indicates clinically significant depressive symptoms and the need for clinical evaluation (see section 2) to confirm the diagnosis. Once confirmed, a treatment plan should be documented (see section 4).

- **Treatment plan documentation should include the following:**
  - The treatment plan should include whether the patient is receiving any of the following treatment modalities:
    - Behavioral Activation
    - Psychotherapy
    - Medications
    - Psychoeducation
    - Collaborative Care
    - Social Services
  - The follow up plan should include:
    - Additional evaluation
    - Suicide risk assessment
    - Referral to a practitioner who is qualified to diagnose and treat depression

<table>
<thead>
<tr>
<th>Depression Screening Tools</th>
<th>Contact</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHQ-2, Patient Health Questionnaire</td>
<td><a href="http://www.phqscreeners.com">http://www.phqscreeners.com</a> Tool included in this guideline – Appendix pg. 34</td>
<td>No charge</td>
</tr>
<tr>
<td>PHQ-9, Patient Health Questionnaire</td>
<td><a href="http://www.phqscreeners.com">http://www.phqscreeners.com</a> Tool included in this guideline – Appendix pg. 35</td>
<td>No charge</td>
</tr>
<tr>
<td>EPDS, Edinburgh Postnatal Depression Scale</td>
<td><a href="http://www.perinatalweb.org">http://www.perinatalweb.org</a> Tool included in this guideline – Appendix pg. 37</td>
<td>No charge</td>
</tr>
</tbody>
</table>
2. Diagnosis
A detailed clinical interview is used to confirm the diagnosis of depression. Questions asked should elaborate on questions from the PHQ-9 or the CES-DC and assess for suicidal or homicidal intent, plan, and access to means.

Interview for Key Symptoms of Depression
(Class I, Level A)
Patients should receive a thorough assessment in order to establish a diagnosis of major depressive disorder, identify other psychiatric or other medical conditions that may require attention, and develop a treatment plan. This evaluation may include:
- 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

Consider a Differential Diagnosis
Many other psychiatric disorders can cause depressive symptoms. In evaluating patients with the symptoms of depression, the primary care practitioner must determine if the depression is a primary process or 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. cancer, coronary artery disease, diabetes mellitus, cerebral vascular accident, hypothyroidism, hyperthyroidism, chronic pain) are risk factors for depression. 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:
  - The medical disorder biologically causes the depression (for example, hypothyroidism may cause depression).
  - The medical disorder triggers the onset of depression in those who are genetically predisposed to depression.
  - The perceived severity of the illness causes depression (for example, 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, Methyldopa, 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 diagnosis and alternatives</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>Other NSAIDS</td>
</tr>
<tr>
<td>Interferons (HepC, 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. Screening for bipolar should always be done before initiating treatment for depression.³

Have you ever experienced 4 or more days of:
- Needing less sleep
- Having a lot of energy
- Talking faster than normal
- Being more social than normal
- Doing things you normally wouldn’t do like: having more sex or spending more money

• **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.
• **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.

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 substance 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.

Patients should be advised to stop substance use. Patients with significant alcohol 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.4

• **Eating disorders**: young women who present with any mood disorder should be interviewed for symptoms of anorexia nervosa and/or bulimia. 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.4
• **Bereavement**: is depressive symptoms beginning within 2-3 weeks of the loss of a loved one. 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.

• **Other Psychiatric Disorders**: Patients with depressive symptoms or in a depressive episode may have a co-existent mood psychiatric disorder

3. **Involve Behavioral Health**
   (Class IIa, Level C)
   **Emergency “Same Day” Behavioral Health Consultation/Evaluation** is necessary for:
   - suicidal thoughts and/or plans that make the patient’s safety uncertain
   - assaultive and/or homicidal plans which make the safety of others uncertain
   - loss of touch with reality (psychosis) in the context of depression

   **Referral to a Behavioral Health Specialist** is recommended when there is:
   - possibility of bipolar
   - psychiatric co-morbidity (for example, substance abuse, anxiety, obsessive compulsive disorder, or eating disorders)
   - concern regarding the possibility of suicide and/or homicide
   - alcohol or 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

4. **Treatment Plan**
   (Class IIa, Level B)
   **The Objectives of Treatment** are:
   - Reduction and ultimately resolution of all signs and symptoms of the depressive syndrome.
   - Restoration of psychosocial and occupational function to that of the asymptomatic state.
   - Reduction of the likelihood of relapse or recurrence.

   **Treatment Modalities for Depressive Disorder**
   Factors considered in making treatment recommendations are the severity of symptoms, presence of psychosocial stressors, presence of co-morbid conditions, insurance coverage and patient preferences.

   i. **Engagement in Behavioral Activation 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)
- Sleep hygiene

ii. Psychotherapy: Interpersonal or cognitive behavioral psychotherapy, individual or group, is the mainstay for mild-moderate depression, although antidepressant medication may be needed if any of the following 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. Psychotherapy alone is not recommended for the acute treatment of patients with severe and/or psychotic depressive disorders.

iii. Medication: 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. To determine if the interaction is clinically important, refer to Epocrates, Micromedex or eFacts for details or discuss concerns with a pharmacist.

Selection of a particular medication should take into consideration:
- Prior positive/negative response to medication
- Concurrent medications that make selected medications more or less risky
- Other health conditions
- History of first degree relatives’ responses to medication

See cost and drug information on antidepressant therapies at the end of this guideline.

- Adult and pediatric 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.

- 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.

iv. **Light Therapy:** use of a light box in the dark months of the year (September – March). Light therapy is an FDA approved treatment for seasonal depression and is covered by most insurance companies.³
- 10,000 lux for 30 minutes every morning

v. **Electroconvulsive Therapy (ECT)** – Most commonly recommended for people with severe depression accompanied by psychosis, suicidal intent or refusal to eat. It may be tried when medications are not tolerated or other forms of therapy haven’t proved effective. Recommend full psychiatric assessment before considering.³, ⁴

**NOTE: Some of the treatment modalities can be used in combination**

**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.

**Treatment Plan Phases**

- See Appendix (page 32) for Treatment Plan Flow Chart
- **Acute Treatment (first 12 Weeks)** aims to resolve all signs and symptoms of the current episode of depression and to restore psychological and occupational functioning (a remission).

The patient should be seen a minimum of three times during the acute phase.
At least one of those encounters should be with the prescriber. Patient non-compliance is high in those with depression, and the practitioner must assertively engage the patient in follow-up care and assessments.

- Patients should have a minimum of three contacts during the acute phase (first 12 weeks)
- Patients should be reminded to call if they experience unexpected adverse medication reactions
- Consider referral to behavioral health if more severe symptoms present.
- Certain patients (new, unstable, those on many medications, those with sudden onset) may need to be seen more often and may require close observation
- Once the depression has resolved, visits every 4-12 weeks are reasonable.

Treatment response should be assessed every 4-6 weeks for drug therapy and every 6-12 weeks for psychotherapy. Most patients respond partially to medication within 2-3 weeks and full symptom remission is typically seen in 6-8 weeks. If the patient does not respond at all by 6 weeks (4 weeks in severely ill), or responds only partially by 12 weeks, other treatment options should be considered including:

- Assess medication adherence
- Continue medication at a corrected dose
- Change medication
- 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

- **Continuation Therapy (next 4 - 9 months)** is intended to prevent relapse.
  - The patient should remain on medication for at least 4-9 months after symptoms resolve.
  - Once the patient has been asymptomatic for at least 4 to 9 months following an episode, recovery from the episode is declared. At recovery, treatment may be stopped.

- **Maintenance Therapy (1 Year to lifetime)** is aimed at preventing a new episode. Patients who have had three or more episodes of depression should be considered for long-term maintenance medication therapy.

**Monitoring Tools**
(Class IIa, Level C)
- PHQ-9’s should be repeated monthly
- Declines of less than 5 points per month should prompt for reconsideration of treatment plan
**Side Effect Management**  
(Class IIa, Level B)

Side effects are common with SSRIs, SNRIs, mirtazapine and bupropion but can be managed for most patients. 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 (eg, 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, buproprian, 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.9, 10

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.28

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.

5. Detection and Treatment During Pregnancy
The incidence of a depressive disorder in women during pregnancy is between 14-23%.12 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 include changes in appetite, sleep, libido and loss of energy.

Depression during pregnancy does not differ from depression during other periods of life. Therefore, screening tools such as the Edinburgh Postnatal Depression Scale (EPDS) or the PHQ-9 should be administered if the woman has risks for depression or depression is suspected. The EPDS scale was developed to detect women with postnatal depressive symptoms, but has also been validated for use in pregnancy.11

Treatment
(Class IIa, Level B)
Depression in pregnancy is not without risk to the mother or the infant. It commonly leads to poor self-care in women, thus jeopardizing fetal health in the process. Prenatal depression is the most robust predictor of postpartum depression. There is evidence that prenatal and postnatal depression increases the likelihood of maladaptive stress responsiveness in offspring later on. Thus, the clinician, the patient, and the patient’s partner should work together to determine appropriate treatment for prenatal depression using a risk/benefit analysis. Algorithms for this decision-making process can be found in the APA and ACOG consensus statement.12

Psychotherapy is recommended whenever possible for mild to moderate depression that has not required antidepressant treatment in the past. Psychotherapy has been considered to be particularly useful for patients with mild to moderate depression during pregnancy in that it directly addresses issues associated with role transitions and relationship with the partner. It is important to engage the patient and significant others in risk/benefit discussions about what is best for their situation, that there are different options, and that the issue is for the patient and the baby to be as safe as possible.24 The decision will depend on the patient's history before the pregnancy
and their previous experience with medications, the severity of the depression, support available, response to alternative treatment modalities, etc.

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. Patients with new onset of severe depression in pregnancy may also need psychiatric medication in addition to psychotherapy to ensure the best treatment response. The goal of pharmacotherapy is to treat to remission to avoid exposing the infant to both the antidepressant medication and maternal depression.

SSRIs have been studied extensively in pregnancy. The most common complication of SSRI use in pregnancy is decreased gestation length and lower birth weight. Of note, these complications also occur with depression alone. Mothers taking antidepressants deliver on average 1 week earlier than non depressed mothers and their babies are on average a few ounces smaller. Because of this, it is prudent to remind women to do everything possible to minimize other causes of early labor including: maintaining adequate hydration, avoiding tobacco and alcohol, eating well, and managing stress. The next most common risk of antidepressants in pregnancy is neonatal adaptation syndrome, which occurs in 15-30% of infants born to mothers taking SSRIs/SNRIs/TCAs in the last trimester. Symptoms most often include irritability, tremor, jitteriness, convulsions, and hyperreflexia. This is a self limited condition that usually goes away on its own within two weeks or sooner. Infants may be monitored in the NICU during this time; treatment is supportive care. A review by Yonkers et al of the limited information available about the possible long term effects of SSRI and TCA exposure in utero does not indicate an association with adverse neurocognitive effects in infancy or general behavior or cognitive functioning in young children. However the authors note that further work is needed to identify the specific effects of prenatal psychotropic medication exposure from the effects of antenatal and postnatal depression.12

The remaining potential risks of antidepressant treatment remain somewhat controversial. Three out of six studies have found an association with persistent pulmonary hypertension (PPH) in infants exposed to SSRIs in utero in the second half of pregnancy. The FDA added -- and then removed -- a black box warning about this risk. The absolute risk, if present, is between 1-6/1000. There have been no deaths associated in the literature with SSRI-related PPH. Finally, there is much controversy about SSRIs and birth defects, particularly cardiac defects. In the consensus statement published in 2009, the APA and ACOG12 jointly reported that the data at that time were inconclusive in this area. Thus, there is no convincing evidence to support an association between structural defects with SSRIs in pregnancy, with the possible exception of paroxetine in the first trimester. Notably, TCAs have not been shown to be associated with PPH or cardiac defects and thus are used more commonly than SSRIs in pregnancy in many parts of Europe.23
Currently, many OB/GYNs are most comfortable prescribing sertraline in pregnancy because it has been studied extensively in pregnancy and because of its favorable nursing profile. Other SSRIs, except for paroxetine, may also be used if preferred by the patient. Paroxetine is not recommended in women who are planning to become pregnant, because there are some studies, though not all, that have found increased risk of cardiac defects with more than 25 mg/day of paroxetine use in the first trimester.\textsuperscript{13}

6. Postpartum Depression: Detection and Treatment

Postpartum depression (PPD) occurs in approximately 8-15\% of women postpartum and up to 50\% of women living in poverty.\textsuperscript{25} Many medical professionals 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.\textsuperscript{11} If left untreated, the disorder can have serious adverse effects for the mother, her infant’s development, and her relationship with others.

PPD may begin 24 hours to several months after delivery.\textsuperscript{26} 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.

A simple screening tool can be used to increase the detection of postpartum depression. The EPDS tool included in this guideline is appropriate to use in postpartum assessment and diagnosis. The EPDS screening tool also addresses anxiety which frequently co-occurs with depression. It was developed specifically to identify significant depressive symptoms among pregnant women and new mothers, is well validated, translated into many languages, is in the public domain and is available on-line.

Interpersonal psychotherapy, individual or group, is the mainstay for mild-moderate postpartum depression, although antidepressant medication may be needed if any of the following are present: severe insomnia, severe anxiety, marked anhedonia, thoughts of suicide, or intrusive thoughts of harm to the infant. 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.

7. Recognizing Postpartum Depression

Risk Factors
- Previous history of depressive episode
- Family history of mood or anxiety disorders
- Depression or anxiety during pregnancy
- Dissatisfaction with the amount of social support from a spouse or significant other
Screening for PPD
The detection of PPD is often complicated by several factors.

- 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

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.

Distinguishing PPD
- Postpartum Blues
  The “baby blues” are the most common disorder affecting 50-80% of new mothers. They 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 include:
  - tearfulness
  - irritability
  - fatigue
  - anger
  - insomnia
  - anxiety
  - mood liability
  - sensitivity
• **Postpartum Depression**
  The criteria for diagnosing depression 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.

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 or inappropriate guilt
  • Diminished concentration or indecisiveness
  • Feeling of being overwhelmed
  • Symptoms that may be confused with normal sequelae of childbirth

• **Postpartum Psychosis**
  PPD must be distinguished from postpartum psychosis, which occurs in 0.1% of childbearing women. Most puerperal psychoses have their onset within the first month of delivery and are manic in nature. Postpartum psychosis is a medical emergency and requires immediate psychiatric evaluation and usually requires psychiatric admission for medication management and safety. 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

  The most significant risk factors for postpartum psychosis are a personal or family history of bipolar disorder or a previous psychotic episode. Of women who develop a postpartum psychosis, there is a 5% infanticide or suicide rate; thus, this is an emergency and immediate referral to the ER or to a psychiatrist who can evaluate the same day is necessary.

8. **Treatment for Postpartum Depression**
   (Class IIa, Level B)
   Psychotherapy, particularly individual or group has been shown to be an effective treatment for Postpartum Depression and does not hold the risk to breastfeeding that medication can, making it a preferable first order of treatment. 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.\textsuperscript{14}

\textbf{Medications and Lactation}

The majority of expert opinion feels the benefit outweighs the risk in treatment with a SSRI. SSRI's should be a first choice recommendation.\textsuperscript{15, 27}
- The goal is to effectively treat the depression.
- Initiating or continuing medication should not interfere with the decision to start or continue to breastfeed.

If the woman is breastfeeding, some agents may be preferred over others.
- \textbf{Sertraline or paroxetine} may be preferred SSRIs, since no adverse effects have been reported thus far in nursing infants.\textsuperscript{16,17} Several studies have shown infant serum levels of sertraline to be nondetectable or less than 5ng/ml and its metabolite concentration to be less than 10ng/ml.\textsuperscript{18, 19} In six reports, paroxetine serum concentrations were measured in 27 infants and were found to be nondetectable in 24 infants and less than 20 ng/mL in the remaining three.\textsuperscript{19,17}

- 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.\textsuperscript{20}

\textbf{Fluoxetine} is not considered a first-line agent for women who are breastfeeding.
- \textbf{Fluoxetine} has had several case reports of adverse effects in the infant, including colic, delayed weight gain, irritability, and disturbed sleep.\textsuperscript{13,22} For this reason, fluoxetine should generally not be considered first line treatment with a new diagnosis of depression.

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 social support networks.

\textbf{Resources:}
- \textbf{State of Wisconsin Maternal & Child Health (MCH)}
  Provides information, resources, and referrals for women, family members, and professionals. Maintains an on-line directory of mental health providers who can evaluate and treat perinatal mood disorders.
  \url{http://www.mch-hotlines.org/}
  Hotline: 1-800-722-2295
  Hotlines are operated 24 hours a day
Postpartum Support International
http://www.postpartum.net/

Algorithm for Management of Unipolar Depression in Pregnant and Postpartum Women

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 day-to-day clinical practice.
http://www.womensmentalhealth.org/

References for Supporting Evidence


References for Supporting Evidence
Postpartum Depression References:

27. The Transfer of Drugs and other Chemicals into Human Milk. Pediatrics. 2001; 108; 776
HEDIS Measure Information Related to Depression
The percentage of members 18 years of age and older who were diagnosed with a new episode of major depression, treated with antidepressant medication, and who remained on an antidepressant medication treatment. Two rates are reported.

- **Effective Acute Phase Treatment.** The percentage of newly diagnosed and treated members who remained on an antidepressant medication for at least 84 days (12 weeks).
- **Effective Continuation Phase Treatment.** The percentage of newly diagnosed and treated members who remained on an antidepressant medication for at least 180 days (6 months).

Benefits/Harms of Implementation
**Potential Benefits:**
- Increased percentage of patients who are screened for depression
- Appropriate 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 events associated with various treatments for depression

Implementation Tools/Plan
- Guideline will be housed in the Care Guidelines tab of the Provider section at [www.pplusic.com](http://www.pplusic.com) or on UConnect in a dedicated folder for Clinical Practice Guidelines

Disclaimer
Guidelines are designed to assist clinicians by providing a framework for the evaluation and treatment of patients. This 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.
# 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>Alcohol Use</td>
<td>Paroxetine, Fluoxetine, Mirtazapine, Sertraline, Citalopram, Escitalopram, Venlafaxine, Desvenlafaxine</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, Desvenlafaxine</td>
<td>Bupropion-may increase anxiety</td>
</tr>
<tr>
<td>Cardiac Condition</td>
<td>Paroxetine, Fluoxetine, Mirtazapine, Sertraline, Citalopram, Escitalopram, Venlafaxine, Desvenlafaxine</td>
<td>TCA Venlafaxine Desvenlafaxine, Bupropion (increases blood pressure). Mirtazapine (increases cholesterol), Citalopram</td>
</tr>
<tr>
<td>Chronic Pain</td>
<td>TCA, SNRI, Duloxetine</td>
<td></td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>TCA, Mirtazapine</td>
<td>Sertraline Desvenlafaxine SSRI</td>
</tr>
<tr>
<td>Dementia</td>
<td>Bupropion</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)</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 (See Post Partum Depression)</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, Sertraline, Paroxetine</td>
<td></td>
</tr>
<tr>
<td>Parkinson’s Disease</td>
<td>Bupropion, Trazodone, Desipramine, Amoxapine, Nortriptyline, Protriptyline</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>
<tr>
<td>Pregnancy</td>
<td>Paroxetine, Venlafaxine, Duloxetine</td>
<td></td>
</tr>
<tr>
<td>Elderly patients</td>
<td></td>
<td>Fluoxetine</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.*
# Depression Side Effect Profiles

Side effects may be observed early in treatment and improve over time. If side effects persist, alternatives may be considered.

<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 (dry mouth, blurred vision, constipation, urinary retention)</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, Duloxetine, 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>
### Product and Dosage Chart

<table>
<thead>
<tr>
<th>Product</th>
<th>How Supplied</th>
<th>Dosage Range/Comments</th>
<th>Relative Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram (Celexa)</td>
<td>10, 20, 40mg scored tab</td>
<td>20-40mg daily</td>
<td>$</td>
</tr>
<tr>
<td></td>
<td>10mg/4mL soln</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escitalopram (Lexapro)</td>
<td>5mg unscored, 10 and 20mg scored tab</td>
<td>10-20mg daily</td>
<td>$$$</td>
</tr>
<tr>
<td></td>
<td>5mg/5mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine (Prozac)</td>
<td>10, 20, 40 cap</td>
<td>10-80mg daily or 90mg weekly</td>
<td>$</td>
</tr>
<tr>
<td></td>
<td>90mg delayed release cap</td>
<td></td>
<td>$$$ 90mg cap</td>
</tr>
<tr>
<td></td>
<td>10 mg, 20mg tab</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20mg/5mL soln</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxetine (Paxil, Paxil CR)</td>
<td>10, 20mg scored tab</td>
<td>10-60mg IR daily or 25-62.5mg CR daily</td>
<td>$</td>
</tr>
<tr>
<td></td>
<td>30, 40mg tab</td>
<td></td>
<td>$$$</td>
</tr>
<tr>
<td></td>
<td>10mg/5mL susp</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>12.5, 25 mg, 37.5mg CR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sertraline (Zoloft)</td>
<td>25, 50, 100mg scored tab</td>
<td>50-200mg daily</td>
<td>$</td>
</tr>
<tr>
<td></td>
<td>20mg/mL concentrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trazodone* (Oleptro)</td>
<td>50, 100, 150, 300mg IR tab</td>
<td>150-600mg IR daily in divided doses</td>
<td>$</td>
</tr>
<tr>
<td></td>
<td>ER 150, 300mg</td>
<td>150 mg ER daily</td>
<td>$$$$</td>
</tr>
<tr>
<td></td>
<td>20mg/5mL soln</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desvenlafaxine (Pristiq)</td>
<td>50, 100mg tab</td>
<td>50 daily</td>
<td>$$$$-$$$$$$</td>
</tr>
<tr>
<td>Duloxetine (Cymbalta)</td>
<td>20, 30, 60mg cap</td>
<td>40-60mg daily</td>
<td>$$$</td>
</tr>
<tr>
<td>Mirtazapine (Remeron)</td>
<td>7.5, 15, 30, 45 mg tab</td>
<td>15-45mg daily</td>
<td>$ tab</td>
</tr>
<tr>
<td></td>
<td>15, 30, 45mg ODT</td>
<td></td>
<td>$$$ ODT</td>
</tr>
<tr>
<td>Venlafaxine (Effexor, Effexor XR)</td>
<td>25, 37.5, 50, 75, 100mg IR tab</td>
<td>75-225mg IR daily in divided doses</td>
<td>$$$$$</td>
</tr>
<tr>
<td></td>
<td>37.5, 75, 150, 225mg ER tab</td>
<td>37.5-75mg ER daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>37.5, 75, 150mg ER cap</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion (Wellbutrin, Aplenzin)</td>
<td>75, 100mg IR tab</td>
<td>100-150 mg IR TID</td>
<td>$</td>
</tr>
<tr>
<td></td>
<td>100, 150, 200mg SR tab</td>
<td>150-200mg SR BID</td>
<td>$$$</td>
</tr>
<tr>
<td></td>
<td>150, 300mg XL tab</td>
<td>150-450 mg XL daily (hydrochloride salt)</td>
<td>$$$$$</td>
</tr>
<tr>
<td></td>
<td>174, 348, 522mg ER tab</td>
<td>174-522 mg ER daily (hydrobromide salt)</td>
<td></td>
</tr>
<tr>
<td>amitriptyline</td>
<td>10, 25, 50, 75, 100, 150 mg tab</td>
<td>50-150mg daily at bedtime or in divided doses</td>
<td>$</td>
</tr>
<tr>
<td>amoxapine</td>
<td>25, 50, 100, 150mg tab</td>
<td>50mg BID-TID</td>
<td>$</td>
</tr>
<tr>
<td>desipramine</td>
<td>10, 25, 50, 75, 100, 150mg tab</td>
<td>100-300mg daily in divided or single doses</td>
<td>$$$</td>
</tr>
<tr>
<td>doxepin</td>
<td>10, 25, 50, 75, 100, 150mg cap</td>
<td>25-300mg daily in divided or single doses</td>
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<tr>
<td></td>
<td>10mg/mL conc</td>
<td></td>
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<tr>
<td>imipramine</td>
<td>10, 25, 50mg tab</td>
<td>75-200mg daily</td>
<td>$</td>
</tr>
<tr>
<td></td>
<td>75, 100, 125, 150mg cap</td>
<td></td>
<td></td>
</tr>
<tr>
<td>maprotiline</td>
<td>25, 50, 75mg tab</td>
<td>75-150 mg daily in divided or single dose</td>
<td>$$$$-$$$$$</td>
</tr>
<tr>
<td>nortriptyline</td>
<td>10, 25, 50, 75mg cap</td>
<td>75-150mg daily in divided or single doses</td>
<td>$</td>
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<tr>
<td></td>
<td>10mg/5mL soln</td>
<td></td>
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<tr>
<td>phenelzine (Nardil)</td>
<td>15mg tab</td>
<td>15mg TID</td>
<td>$$$</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>$$$$$</td>
</tr>
<tr>
<td>Tranylcypromine (parnate)</td>
<td>10mg tab</td>
<td>30mg daily in divided doses</td>
<td>$$$</td>
</tr>
</tbody>
</table>

*For TCA’s and trazadone, there are therapeutic blood levels that should be done if patient does not respond to therapeutic dose.

Insurance coverage for antidepressants varies. Refer to ePocrates for local plan listings:
https://online.epocrates.com/noFrame/ Patients are less likely to take their medication if they cannot afford it.
**Depression Monitoring Flow Sheet #1**

**Patient Name:** ___________________________  **DOB/Age:** __________________

**Date of Diagnosis:** ___________________________

**Date/Type of Contact**

<p>| | | | | | | | | | |</p>
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</table>

**Assessment of Progress:**

<table>
<thead>
<tr>
<th>Score 1 if symptoms are worse</th>
<th>Score 2 if there is no change in symptoms</th>
<th>Score 3 if symptoms have improved</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>PHQ-9 score / Assessment Score</th>
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<table>
<thead>
<tr>
<th>Thoughts of death or suicidal ideation</th>
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<tr>
<th>Patient impression of progress</th>
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**New stressors**

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</table>

**Other concerns or Assessments**

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</table>

**Assessment of Treatment**

**Current Medications**

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</table>

<table>
<thead>
<tr>
<th>Medication compliance</th>
<th>Y</th>
<th>N</th>
<th>Y</th>
<th>N</th>
<th>Y</th>
<th>N</th>
<th>Y</th>
<th>N</th>
<th>Y</th>
<th>N</th>
<th>Y</th>
<th>N</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Medication side-effect *</th>
<th>Sedation/agitation</th>
<th>Dry mouth</th>
<th>Headache</th>
<th>Nausea/GI distress</th>
<th>Constipation</th>
<th>Diarrhea</th>
<th>Dizziness</th>
<th>Sexual dysfunction</th>
<th>Other</th>
</tr>
</thead>
<tbody>
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</table>

<table>
<thead>
<tr>
<th>Psychotherapy</th>
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<table>
<thead>
<tr>
<th>Initials of Provider Completing the Assessment</th>
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</table>

* Place check mark for presence of side-effect. Track progress by noting ongoing presence of side-effect.
**Depression Monitoring Flow Sheet #2**

<table>
<thead>
<tr>
<th>Date/Type of Contact</th>
<th>Mood</th>
<th>Interest in activities</th>
<th>Appetite</th>
<th>Sleep</th>
<th>Psychomotor agitation or lethargy</th>
<th>Energy level</th>
<th>Self-esteem</th>
<th>Concentration</th>
<th>Thoughts of death or suicidal ideation</th>
<th>Patient impression of progress</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

| Medication side-effect * | | | | | | | | | | |
|--------------------------| | | | | | | | | | |
| Sedation/agitation       | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ |
| Dry mouth                | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ |
| Headache                 | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ |
| Nausea/GI distress       | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ |
| Constipation             | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ |
| Diarrhea                 | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ |
| Dizziness                | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ |
| Sexual dysfunction       | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ |
| Other                    | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ |

<table>
<thead>
<tr>
<th>Other concerns or assessments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Initials of Provider Completing the Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

* Place check mark for presence of side-effect. Track progress by noting ongoing presence of side-effect.
Educate about Depression and Medications
For antidepressant medications, compliance with a therapeutic dose is more important than the specific drug selected. The following educational messages may increase adherence:

A) Take the medication daily as prescribed.
B) Some treatment response may occur in 10 – 14 days, but full effect requires continuous treatment for four to six weeks.
C) Continue to take medication even if you are feeling better: increased risk of relapse if stopped before 6 months.
D) Do not stop taking antidepressant without checking with your provider. Some antidepressants may have uncomfortable withdrawal symptoms.
E) Contact your provider if you have questions about your medication.
F) Be sure to make and keep an appropriate follow-up appointment. This is important to ensure full response to your medication.
G) The medication is not mood altering. 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.
H) The medication should help you benefit from the psychotherapy you are receiving.

Consider Medication When:
• Depression is moderate to severe
• Patient has had prior positive response to medication
• Patient has had recurrent depressive episodes
• As adjunct to psychotherapy or if symptoms are not remitting or if psychotherapy is unavailable

Monitor Acute Treatment (first 12 weeks)
• Patients should have a minimum of three contacts during the acute phase
• Patients should be reminded to call as needed if they experience adverse medication reactions or suicidal ideation
• Ask patient whether psychotherapy has been started, if that was recommended
• Young adults ages 18-24 should be monitored for suicidal ideation regularly for at least several months
• Consider referral to behavioral health if more severe symptoms present (i.e. risk of harm to self or others, presence of major psychosocial stressors likely to require psychotherapy, patients with history of antidepressant failure in the past, or already on complex medication regimens)
• Certain patients (new, unstable, those on many medications, those with sudden onset) may need to be seen more often and require close observation
• Check PHQ-9 at baseline and at follow-up visits to assess response

Select and Initiate Therapy
A) Mild Depressive Disorder* - Psychotherapy or Pharmacotherapy
B) Moderate / Severe Depressive Disorder** - Psychotherapy with Pharmacotherapy

* Mild depressive disorder: Depression without prominent vegetative symptoms, suicidal ideation, or significant functional impairment.
** Moderate to severe depression disorder: Depression with significant neurovegetative symptoms, hopelessness, or suicidal ideation.

Adjust Therapy
• Pharmacotherapy – consider adjusting dose
• Psychotherapy – consider augmenting with medical therapy, have conversation with specialist

Consider medication taper over a period of weeks to several months for patients who have had only one prior episode of major depression, have no significant family history, no severe symptoms.

Consider maintenance therapy for patients who have had two previous episodes of major depression, or who have had two episodes of major depression but have also had rapid recurrence of episodes, or are older in age at the onset of major depression (more than 60 years of age), have had severe episodes of major depression or a family history of a mood disorder, at-risk patients with double depression and patients with comorbid anxiety disorder or substance abuse, or patients whose major depression has a seasonal pattern. For maintenance medication, contacts can occur every 3 to 12 months if everything else is stable.
Health Care Guideline:  
Major Depression in Adults in Primary Care

Suspect and screen for major depression: (see also box #1a)
- Presentations (in addition to obvious sadness)
- Risk Factors
Use measurable tool at screening for baseline intensity and at follow-up for adequate response

Diagnose and characterize major depression with clinical interview to include:
- DSM-IV TR criteria (see box #2a)
- History of present illness (onset and severity of symptoms, functional impairment, past episodes and psychosocial stressors)
- Pertinent medical history, especially illness that can cause depression
- Assess for current substance abuse, withdrawal or medications that can cause depression

≥ 5 DSM-IV TR criteria present?  

Is patient unsafe to self or others?  

Involves behavioral/chemical health

Consider other mood and anxiety disorders or somatoform disorders, especially bipolar disorder

Address secondary causes and/or adapt a plan for the special population

Comprehensive Treatment Plan
- Collaborative Care Model
- Educate and engage patient
- Discuss treatment options
- Establish follow-up plan
- Use measurable tool at screening for baseline intensity and at follow-up for adequate response

Is patient responding adequately?

Evaluate dose, duration, type and adherence with medication and/or psychotherapy. Reconsider accuracy of diagnosis or impact of comorbidities.

Consider other strategies:
- Augmentation therapy
- Hospitalization
- Light therapy
- Electroconvulsive treatment (ECT)

The two-question screen:
Over the past two weeks have you been bothered by:
1. Little interest or pleasure in doing things?
2. Feeling down, depressed or hopeless?

DSM-IV TR Criteria for Major Depressive Episode:
Must have a total of 5 symptoms for at least 2 weeks. One of the symptoms must be depressed mood or loss of interest.
1. Depressed mood.
2. Markedly diminished interest or pleasure in all or almost all activities.
3. Significant (> 5% body weight) weight loss or gain, or increase or decrease in appetite.
4. Insomnia or hypersomnia.
5. Psychomotor agitation or retardation.
6. Fatigue or loss of energy.
7. Feeling of worthlessness or inappropriate guilt.
8. Diminished concentration or indecisiveness.
9. Recurrent thoughts of death or suicide.

A = Annotation

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### PATIENT HEALTH QUESTIONNAIRE-2

<table>
<thead>
<tr>
<th>Over the last 2 weeks, how often have you been bothered by any of the following problems?</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

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## PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems?  
(Use “✔” to indicate your answer)

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

For office coding: $0 + \_\_\_ + \_\_\_ + \_\_\_ = \text{Total Score:} \_\_\_\_\_\_

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

<table>
<thead>
<tr>
<th>Not difficult at all</th>
<th>Somewhat difficult</th>
<th>Very difficult</th>
<th>Extremely difficult</th>
</tr>
</thead>
<tbody>
<tr>
<td>✅</td>
<td></td>
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</table>

Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. No permission required to reproduce, translate, display or distribute.
## Center for Epidemiological Studies Depression Scale for Children (CES-DC)

### INSTRUCTIONS
Below is a list of the ways you might have felt or acted. Please check how much you have felt this way during the past week.

<table>
<thead>
<tr>
<th>DURING THE PAST WEEK</th>
<th>Not At All</th>
<th>A Little</th>
<th>Some</th>
<th>A Lot</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I was bothered by things that usually don’t bother me.</td>
<td></td>
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<tr>
<td>2. I did not feel like eating, I wasn’t very hungry.</td>
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<tr>
<td>3. I wasn’t able to feel happy, even when my family or friends tried to help me feel better.</td>
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<tr>
<td>4. I felt like I was just as good as other kids.</td>
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<tr>
<td>5. I felt like I couldn’t pay attention to what I was doing.</td>
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</tr>
<tr>
<td>6. I felt down and unhappy.</td>
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<td></td>
</tr>
<tr>
<td>7. I felt like I was too tired to do things.</td>
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<tr>
<td>8. I felt like something good was going to happen.</td>
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</tr>
<tr>
<td>9. I felt like things I did before didn’t work out right.</td>
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<tr>
<td>10. I felt scared.</td>
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<tr>
<td>11. I didn’t sleep as well as I usually sleep.</td>
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<tr>
<td>12. I was happy.</td>
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<tr>
<td>13. I was more quiet than usual.</td>
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<tr>
<td>14. I felt lonely, like I didn’t have any friends.</td>
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<tr>
<td>15. I felt like kids I know were not friendly or that they didn’t want to be with me.</td>
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</tr>
<tr>
<td>16. I had a good time.</td>
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<tr>
<td>17. I felt like crying.</td>
<td></td>
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<tr>
<td>18. I felt sad.</td>
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<tr>
<td>19. I felt people didn’t like me.</td>
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<tr>
<td>20. It was hard to get started doing things.</td>
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</tbody>
</table>

Number ____________________
Score ____________________
Circle the number for each statement, which best describes how often you felt or behaved this way in the past 7 days....

I have been able to laugh and see the funny side of things.

0  As much as I always could
1  Not quite so much now
2  Definitely not so much now
3  Not at all

I have looked forward with enjoyment to things.

0  As much as I ever did
1  Rather less than I used to
2  Definitely less than I used to
3  Hardly at all

I have blamed myself unnecessarily when things went wrong.

0  No not at all
1  Hardly ever
2  Yes, sometimes
3  Yes, very often

I have been anxious or worried for no good reason.

3  Yes, quite a lot
2  Yes, sometimes
1  No, not much
0  No, not at all

I felt scared or panicky for no very good reason.

3  Yes, quite a lot
2  Yes, sometimes
1  No, not much
0  No, not at all

Things have been getting on top of me.

3  Yes, most of the time I have not been able to cope at all
2  Yes, sometimes I have not been coping as well as usual
1  No, most of the time I have coped quite well
0  No, I have been coping as well as ever

I have felt so unhappy that I have had difficulty sleeping.

3  Yes, most of the time
2  Yes, sometimes
1  Not very often
0  No, not at all

I have felt sad and miserable.

3  Yes, most of the time
2  Yes, quite often
1  Not very often
0  No, not at all

I have been so unhappy that I have been crying.

3  Yes, most of the time
2  Yes, quite often
1  Only occasionally
0  No, never

The thought of harming myself has occurred to me.

3  Yes, quite often
2  Sometimes
1  Hardly
0  Never

<table>
<thead>
<tr>
<th>Column Total: _______</th>
<th>Column Total: _______</th>
<th>Total: _______</th>
</tr>
</thead>
</table>

(Scoring may be eliminated when tool is reproduced for use)

• Validation studies have utilized various threshold scores in determining which women were positive and in need of referral.
• Cut-off scores ranged from 9-13 points. Therefore, to err on safety’s side, a woman scoring 9 or more points or indicating any suicidal ideation should be referred immediately for follow-up.
• The EPDS is only a screening tool, it does not diagnose depression.


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04/19/13

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