8. DEPRESSION

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We relied on the following sources to construct quality indicators for depression in adult women: the AHCPR Clinical Practice Guideline Depression in Primary Care (Volumes 1 and 2): Treatment of Major Depression (Depression Guideline Panel, 1993a and 1993b), as well as selected review and journal articles. We conducted a MEDLINE search of review articles published in English between the years 1985 and 1995.

IMPORTANCE

Major depression is a common condition, affecting more than 10 percent of adults between the ages of 14 and 55 annually (Kessler, 1994). Major depressive disorder is characterized by one or more episodes of major depression without episodes of mania or hypomania. By definition, major depressive episodes last at least two weeks, and typically much longer. Up to one in eight individuals may require treatment for depression during their lifetime (Depression Guideline Panel, 1993b). The common age of onset is from 20 to 40; however, depression can start at any age.

Approximately 11 million people in the United States suffered from depression in 1990; a disproportionate share (7.7 million) were women (Greenberg et al., 1993). The point prevalence for major depressive disorder in Western industrialized nations is 2.3 to 3.2 percent for men and 4.5 to 9.3 percent for women (Depression Guideline Panel, 1993a).\(^3\) Katon and Schulberg (1992) report that among general medical outpatients, the prevalence rate for major depression is between 5 and 9 percent and 6 percent for the less severe diagnosis of dysthymia. Consistent with these findings, Feldman et al. (1987) found that the point prevalence of major depressive disorder in primary care outpatient settings ranged from 4.8 to 8.6 percent. The lifetime risk for developing depression is between 20 and 25 percent for women.

\(^3\)For a summary of the prevalence literature, refer to pg. 25, Volume 1, Depression Guidelines.
Depression is associated with severe deterioration of a person’s ability to function in social, occupational, and interpersonal settings (Broadhead et al., 1990; Wells et al., 1989a). Broadhead et al. (1990) found that patients with major depressive disorder reported 11 disability days per 90-day interval compared to 2.2 disability days for the general population. Roughly one-quarter of all persons with major depressive disorder reported restricted activity or bed days in the past two weeks (Wells et al., 1988). The functioning of depressed patients is comparable with or worse than that of patients with other major chronic medical conditions, such as congestive heart failure (Hays et al., 1995).

The direct costs associated with treating major depressive disorder combined with the indirect costs from lost productivity account for about $16 billion per year in 1980 dollars (Depression Guideline Panel, 1993a). Greenberg et al. (1993) estimate that the total costs of affective disorders are $12.4 billion for direct treatment, $7.5 billion for mortality costs due to suicide, and $23.8 billion in morbidity costs due to reduction in productivity ($11.7 billion from excess absenteeism and $12.1 billion while at work).

Sturm and Wells (1994) recently demonstrated the cost-effectiveness of treatment for depression. They found that treatment consistent with standards/guidelines lowers the average cost per quality-adjusted life-year when compared to no treatment or ineffective treatment (e.g., subtherapeutic doses of antidepressants). To achieve this gain, however, total costs of care are higher.

**EFFICACY AND/OR EFFECTIVENESS OF INTERVENTIONS**

**Screening/Detection**

The under-diagnosis of depression seriously impedes interventional efforts. The Depression Guidelines report that only one-third to one-half of all cases of major depressive disorders are properly recognized by primary care and non-psychiatric practitioners (Depression Guideline Panel, 1993a; Wells et al., 1989b). The Medical Outcomes Study (MOS) revealed that approximately 50 percent of patients with depression were detected by general medical clinicians, and among patients in prepaid
health plans the rates of detection were much lower than those observed for patients in fee-for-service plans (Wells et al., 1989b).

No definitive screening method exists to detect major depression. Patient self-report questionnaires are available but are non-specific. These questionnaires can be used to supplement the results of direct interview by a clinician (Depression Guideline Panel, 1993a). Burnam et al. (1988) used an eight-item screen in the MOS; however, no standard screen currently exists for clinical work.

A clinical interview is the most effective method for detecting depression (Depression Guideline Panel, 1993a). Clinicians should especially look for symptoms in patients who are at high risk. Risk factors for depression include (Depression Guideline Panel, 1993a):

1) Prior episodes of depression (one major depressive episode is associated with a 50 percent chance of a subsequent episode; two episodes with a 70 percent chance and three or more with a 90 percent chance of recurrent depression over a lifetime (NIMH Consensus Development Conference, 1985);
2) Family history of depressive disorder;
3) Prior suicide attempts;
4) Female gender;
5) Age of onset under 40;
6) Postpartum period;
7) Medical comorbidity;
8) Lack of social support;
9) Stressful life events; and,
10) Current alcohol or substance abuse.

Laboratory testing for depression is effective only in identifying underlying physiologic reasons for depression (e.g., hypothyroidism). No laboratory screening test exists for depression per se and thus, laboratory tests should be tailored to the patient, when indicated, as part of a diagnostic work-up. Laboratory testing should especially be considered as part of the general evaluation if:

1) the medical review of systems reveals signs or symptoms that are rarely encountered in depression;
2) the patient is older; 
3) the depressive episode first occurs after the age of 40-45; or 
4) the depression does not respond fully to routine treatment  
(Depression Guideline Panel, 1993a).

**Diagnosis**

The diagnosis of depression is based primarily on DSM-IV criteria. The criteria state that at least five of the following symptoms must be present during the same period to receive a diagnosis of major depression (American Psychiatric Association, 1994).

1) depressed mood; 
2) markedly diminished interest or pleasure in almost all activities; 
3) significant weight loss/gain; 
4) insomnia/hypersomnia; 
5) psychomotor agitation/retardation; 
6) fatigue; 
7) feelings of worthlessness (guilt); 
8) impaired concentration; and, 
9) recurrent thoughts of death or suicide.

The symptoms should be present most of the day, nearly daily, for a minimum of two weeks.

Practitioners need to consider the presence of other comorbidities prior to making a diagnosis of major depression. Other factors that may contribute to the patient’s mental health and which the clinician may want to treat first include:

1) substance abuse; 
2) medications; 
3) general medical disorder; 
4) causal, non-mood psychiatric disorder; and/or, 
5) grief reaction (Depression Guideline Panel, 1993a).

The clinician should also consider alternative diagnoses by eliciting a proper patient history. Examples of alternative diagnoses include:
1) Bipolar disorder if the patient manifests prior manic episodes;
2) Dysthymic disorder if the patient has a chronic mood disturbance (sadness) present most of the time for at least two consecutive years (Depression Guideline Panel, 1993a).

**Treatment**

Treatment is more effective if provided earlier in the depressive episode, prior to the condition becoming chronic (Bielski and Friedel, 1976; Kupfer et al., 1989). Unless noted otherwise, the recommendations for treatment are drawn from the Depression Guidelines (Depression Guideline Panel, 1993b).

**Use of Antidepressant Medications**

Antidepressant medications are the first-line treatments for major depressive disorder. Medications have been shown to be effective in all forms of major depressive disorder (Depression Guideline Panel, 1993b). Anti-depressant medications are highly likely to be of benefit when:

1) the depression is moderate to severe;
2) there are psychotic, melancholic, or atypical symptom features;
3) the patient requests medication;
4) psychotherapy by a trained, competent psychotherapist is not available;
5) the patient has shown a prior positive response to medication; and,
6) maintenance treatment is planned.

The choice of anti-depressant is less important than use of antidepressants at appropriate dosages (Wells et al., 1994). No single antidepressant medication is clearly more effective than another and no single medication results in remission for all patients. Pharmacologic doses are recommended in the Depression Guidelines (1993b)

The specific choice of medication should be based on:

1) short- and long-term side effects;
2) prior positive/negative response to medication;
3) concurrent, nonpsychiatric medical illnesses that may make selected medications more or less risky; and/or,
4) the concomitant use of other nonpsychotropic medications that may alter the metabolism or increase the side effects of the antidepressant (Depression Guideline Panel, 1993b).

In general, anti-anxiety agents should not be used (with possible exception of alprazolam) (Depression Guideline Panel, 1993b).

Use of Psychotherapy

Maintenance medication clearly prevents recurrences, while, to date, maintenance psychotherapy does not (Depression Guideline Panel, 1993a). Clinicians should consider psychotherapy alone for major depression as a first-line treatment if the episode is mild to moderate AND the patient desires psychotherapy as the first-line therapy (Depression Guideline Panel, 1993b). If psychotherapy is completely ineffective by 6 weeks of treatment or if psychotherapy does not result in nearly a fully symptomatic remission within 12 weeks, then a switch to medications is appropriate due to the clear evidence of the efficacy of treatment with medications (Depression Guideline Panel, 1993b).

Medication Plus Psychotherapy

Clinicians should consider combined treatment initially with medications and psychotherapy if:

1) the depression is chronic or characterized by poor inter-episode recovery;
2) either treatment alone has been only partially effective;
3) the patient has a history of chronic psychosocial problems; or,
4) the patient has a history of treatment adherence difficulties.

However, there is little evidence that indicates that patients being seen in primary care practices who have major depression require initial psychotherapy in addition to medication. It is recommended that medication be added to (or substituted for) psychotherapy if:

1) there is no response to psychotherapy at 6 weeks;
2) there is only partial response at 12 weeks;
3) the patient worsens with psychotherapy; or,
4) the patient requests medications and symptoms are appropriate (Depression Guideline Panel, 1993b).

Clinicians may add psychotherapy to prescribed medications if:
1) residual symptoms are largely psychological (e.g., low self-esteem); or
2) patient has difficulty with adherence.

Follow-up

Most patients with major depressive disorder respond partially to medication within 2 to 3 weeks and full symptom remission is typically seen within 6 to 8 weeks (Depression Guideline Panel, 1993a). Most patients who receive time-limited psychotherapy respond partially by 5 to 6 weeks and fully by 10 to 12 weeks. Office visits or telephone contacts to manage indications should occur weekly for the first 3 to 4 weeks following initial diagnosis to ensure adherence to medication regimen, adjust dosage, and detect and manage side effects. The depression panel recommends that patients with severe depression be seen weekly for the first 6 to 8 weeks (Depression Guideline Panel, 1993a). Once the depression has resolved, visits every 4 to 12 weeks are reasonable (Depression Guideline Panel, 1993a). The Depression Guideline Panel recommended the following guidelines for evaluating patients at each subsequent visit.

Failure to Respond to Medications

If the patient shows no response to the current medication by six weeks, then the clinician should both reassess adequacy of the diagnosis and reassess adequacy of treatment. Change in diagnosis or treatment plan (e.g., change of medication, referral to mental health specialist) is indicated (Depression Guideline Panel, 1993b).

If the patient exhibits a partial response by six weeks, but cognitive symptoms remain, then the clinician should:
• continue treatment;
• reassess response to treatment in six more weeks;
• increase the dose of the current medication or change the medication entirely if reevaluation reveals only a partial response. Alternately, referral to a mental health specialist for addition of psychotherapy may be warranted;
• consult a psychiatrist if two attempts at acute-phase medication have failed to resolve symptoms (Depression Guideline Panel, 1993b).

Continuation of Treatment

Unless maintenance treatment is planned, anti-depressant medication should be discontinued at four to nine months (Depression Guideline Panel, 1993b, pg. 109). Patients should be followed for the next several months to ensure that a new depressive episode does not occur. We recommend follow-up visits at 16-week intervals; the Depression Guideline Panel recommended 12-week intervals, but did not have any evidence about optimal timing. It is unclear from the literature when the optimal time is to discontinue psychotherapy.

Maintenance

Maintenance treatment is designed to prevent new episodes of depression. Patients should be considered for maintenance treatment if they have had:

a) Three or more episodes of major depressive disorder; or
b) Two episodes of major depressive disorder and other circumstance (i.e., family history of bipolar disorder, history of recurrence within one year after previously effective medication was discontinued, family history of recurrent major depression, early onset (prior to age 20) of the first depressive episode, both episodes were severe, sudden, or life-threatening in the past three years) (Depression Guideline Panel, 1993b).
## RECOMMENDED QUALITY INDICATORS FOR DEPRESSION

The following indications apply to women ages 18-50.

**Diagnosis/Detection**

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<thead>
<tr>
<th>Indicator</th>
<th>Quality of evidence</th>
<th>Literature</th>
<th>Benefits</th>
<th>Comments</th>
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<tbody>
<tr>
<td>1. Clinicians should ask about the presence or absence of depression or depressive symptoms* in any person with any of the following risk factors for depression: a. divorce in past six months, b. unemployment, c. history of depression, d. death in family in past six months, or e. alcohol or other drug abuse.</td>
<td>III</td>
<td>USPSTF, 1989</td>
<td>Alleviate symptoms of depression.*</td>
<td>Risk factors for depression have been relatively well-defined in cross-sectional studies.</td>
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<td>2. If the diagnosis of depression is made, specific co-morbidities should be elicited and documented in the chart: a. presence or absence of substance abuse; b. medication use; and c. general medical disorder(s).</td>
<td>III</td>
<td>Depression Guideline Panel, 1993a &amp; 1993b</td>
<td>Alleviate symptoms of depression.* Prevent complications of substance abuse.**</td>
<td>Certain co-morbidities may contribute to or cause depression. The practitioner should be aware of these co-morbidities when making a treatment plan for depression. Documentation may have occurred on previous visits.</td>
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<td>3. If co-morbidity (substance abuse, contributing medication) is present that contributes to depression, the initial treatment objective should be to remove the comorbidity or treat the medical disorder.</td>
<td>III</td>
<td>Depression Guideline Panel, 1993a &amp; 1993b (meta-analysis)</td>
<td>Alleviate symptoms of depression.* Prevent complications of substance abuse.**</td>
<td>Depression may be treated by addressing the co-morbidity. For example, alcoholism should be treated and patients should be taken off of medications that may have CNS depressant properties.</td>
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<td>4. Once diagnosis of major depression has been made, treatment with anti-depressant medication and/or psychotherapy should begin within 2 weeks.</td>
<td>I, II-1, II-2</td>
<td>Depression Guideline Panel, 1993a &amp; 1993b</td>
<td>Alleviate symptoms of depression.* Reduce disability days.</td>
<td>Randomized controlled trials cited in the guidelines (not individually reviewed) substantiate the usefulness of medication and psychotherapy for the treatment of depression. Antidepressant medication therapy is probably the more effective sole modality. The guidelines recommend &quot;prompt&quot; treatment, but no definition of prompt is given. We suggest two weeks are a reasonable time interval.</td>
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<td>5. Presence or absence of suicidal ideation should be documented during the first or second diagnostic visit.</td>
<td>II-2, III</td>
<td>Depression Guideline Panel, 1993a &amp; 1993b</td>
<td>Prevent death from suicide. Prevent morbidity from suicide attempts.</td>
<td>Presence of suicidality is a marker for severe depression and would argue for instituting therapy with anti-depressants and against psychotherapy alone. Suicidality with psychosis, drug abuse, and/or plan of action warrants hospitalization.</td>
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<td>6. Medication treatment visits or telephone contacts should occur weekly for a minimum of 4 weeks.</td>
<td>III</td>
<td>Depression Guideline Panel, 1993a &amp; 1993b</td>
<td>Alleviate symptoms of depression.* Reduce disability days.</td>
<td>Once treatment is started, the practitioner needs to document improvement. Most patients improve at least partially within 3 weeks. The guidelines advocate weekly follow-up by phone or in person for 4-6 weeks. Our indicator specifies the lower end of the recommendations.</td>
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<td>7. At least one of the following should occur if there is no or incomplete response to therapy for depression at 6 weeks: • Referral to psychotherapist, if not already seeing one; • Change or increase in dose of medication, if on medication; • Addition of medication, if only using psychotherapy; • Change in diagnosis documented in chart</td>
<td>III</td>
<td>Depression Guideline Panel, 1993a &amp; 1993b</td>
<td>Alleviate symptoms of depression.* Reduce disability days.</td>
<td>Almost all clinical depression responds at least partially by 6 weeks. If response is incomplete, the diagnosis needs to be re-evaluated and/or treatment plan changed/augmented.</td>
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<td>8.</td>
<td>Anti-depressants should be prescribed at appropriate dosages.</td>
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<td>Depression Guideline Panel, 1993b; Wells, 1994</td>
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<td>Alleviate symptoms of depression.* Reduce disability days.</td>
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<td>Only appropriate doses of anti-depressants will be effective in treatment, yet subtherapeutic doses are often used. For example, a patient on 25 mg of amitriptyline at bedtime is not on a therapeutic antidepressant dose. Since these indicators only apply to women under age 50, we will not need to adjust for change in dose requirements in the elderly. We will exclude those with renal and hepatic dysfunction from this indicator.</td>
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<td>9.</td>
<td>Anti-anxiety agents should generally NOT be used (except alprazolam).</td>
<td>I</td>
<td>Depression Guideline Panel, 1993b</td>
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<td>Alleviate symptoms of depression.* Reduce disability days. Avoid dependence on anti-anxiety agents.</td>
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<td>With the possible exception of alprazolam, anti-anxiety agents have not shown to be of benefit and may be of harm. Foregoing antidepressants in favor of anxiolytics deprives patients of potential benefits of antidepressant treatment.</td>
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<td>10.</td>
<td>Persons who have suicidality should be asked if they have specific plans to carry out suicide.</td>
<td>III</td>
<td>Depression Guideline Panel, 1993b</td>
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<td>Prevent death from suicide. Prevent morbidity from suicide attempts.</td>
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<td>If a person has a plan to carry out suicide, the risk of success increases. These persons should be hospitalized.</td>
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<td>11.</td>
<td>Persons who have suicidality and have any of the following risk factors should be hospitalized: • psychosis • current alcohol or drug abuse • specific plans to carry out suicide (e.g., obtaining a weapon, putting affairs in order, making a suicide note).</td>
<td>III</td>
<td>Depression Guideline Panel, 1993b</td>
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<td>Prevent death from suicide. Prevent morbidity from suicide attempts.</td>
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<td>Presence of risk factors for successful suicide in a person who admits to suicidality warrants hospitalization.</td>
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## Follow-up

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<td>12. Once depression has resolved, follow-up visits should occur every 16 weeks at a minimum, while patient is still on medication, for the first year of treatment.</td>
<td>III</td>
<td>Depression Guideline Panel, 1993b</td>
<td>Alleviate symptoms of depression.* Reduce disability days. Reduce remissions.</td>
<td>The guidelines recommend visit intervals every 12 weeks for the duration of treatment. Occasionally, patients may be on indefinite treatment. In order to allow variation in follow-up times given patient preferences and long-term duration of treatment, we recommend 16-week interval visits during the first year of treatment. Even so, it may be difficult to penalize a practitioner whose patients are seeing a psychotherapist in addition to him/herself for not seeing a patient on a frequent basis.</td>
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<td>13. At each visit during which depression is discussed, degree of response/remission and side effects of medication should be assessed and documented during the first year of treatment.</td>
<td>III</td>
<td>Depression Guideline Panel, 1993b</td>
<td>Alleviate symptoms of depression.* Reduce toxicities of medication. Reduce remission.</td>
<td>Even effectively treated patients may relapse or develop toxicities to medications. While most persons will be off of medications after one year, the optimal time to remove medications is still not well established.</td>
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<td>14. Persons hospitalized for depression should have follow-up with a mental health specialist or their primary care doctor within two weeks of discharge.</td>
<td>III</td>
<td>Depression Guideline Panel, 1993b</td>
<td>Alleviate symptoms of depression.* Reduce disability days. Prevent death from suicide. Prevent morbidity from suicide attempts.</td>
<td>The guidelines do not specifically address time-interval between discharge and follow-up. However, given severity of disease, more than two weeks should probably not pass before re-evaluation. If the patient is also seeing a mental health specialist, the two week interval can apply to that specialist instead of the primary care provider.</td>
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*Symptoms of depression include: depressed mood, diminished interest or pleasure in activities, weight loss/gain, impaired concentration, suicidality, fatigue, feelings of worthlessness and guilt, and psychomotor agitation/retardation.

**Medical complications of substance abuse are numerous and include: for alcohol, blackouts, seizures, delerium, liver failure; for IV drugs of any kind, local infection, endocarditis, hepatitis and HIV, death from overdose; for cocaine and amphetamines, seizures, myocardial infarction, and hypertensive crises.

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**Quality of Evidence Codes:**

I: RCT
II-1: Nonrandomized controlled trials
II-2: Cohort or case analysis
II-3: Multiple time series
III: Opinions or descriptive studies

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