

Clinical
Guideline
for the
Treatment of Depression
in the
Primary
Care
Setting

Introduction

Tufts Health Plan is providing this guideline to aid in the detection and treatment of depression in the primary care setting. The content has been primarily derived from the AHCPR Guideline, "Depression in Primary Care: Detection, Diagnosis, and Treatment" (published in 1993), and updated with information from more recent evidence-based guidelines, review articles and primary literature.¹ A multidisciplinary team prepared and reviewed this guideline.²

This guideline is not expected to apply to all patients or situations. Practitioners must use their own judgement in adapting guidelines to any particular patient and circumstance.

Background

Depression, as opposed to sadness or bereavement, is a serious medical condition which impacts patients, families, employers, and health care systems. The World Health Organization predicts that within the next twenty years depression will become the second most burdensome disorder in the world (behind ischemic heart disease.)

While twenty percent of the general population may suffer from a major depressive disorder during their lifetime, fewer than one third of these individuals will be accurately diagnosed and treated. Depression also worsens the prognosis for a number of other medical conditions. The worst outcome of untreated depression is suicide.

Unfortunately, people sometimes view depression as evidence of character weakness or lack of self-control. Thus, it is important for the primary care physician to educate patients and their families that depression is a **biological disorder that is very treatable**.

Detection and Diagnosis

Approximately one tenth of patients seen in a primary care setting suffer from a depressive disorder. Women are at a particularly high risk for depression. One half of

¹ Sources include: The Texas Medication Algorithm Project for Depression (TMAP) (1998), the British Association for Psychopharmacology (BAP) Guideline for treating Depressive Disorders with Antidepressants (2000), the American Psychiatric Association (APA) Practice Guideline for Treatment of Patients with Major Depressive Disorder-Revised (2000), and the VHA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder in Adults in the Primary Care Setting, Module A (2000).

² Including: psychiatry, primary care, pharmacy, psychology, and social work

depressed patients present with somatic complaints rather than typical depressive symptoms. **The primary somatic complaints include insomnia, fatigue, headache, and weight change. The common emotional complaints include anxiety, irritability, and apathy.**

Patients with specific medical co-morbidities are at higher risk of having or developing a depressive disorder. The most common of these include diabetes, congestive heart failure, dementia, chronic pain and cancer. Patients who have had a cerebral vascular accident or myocardial infarction are also at higher risk for developing depression than the general population.

A clinical interview is suggested to detect depressive disorders. Some clinicians find it useful to give the patient a list of the diagnostic criteria (elucidated below) for self-report of symptoms. In addition, family members may help to clarify the duration of presenting symptoms or history of prior mood disturbances.

Major Depression

The diagnosis of a major depressive disorder is made if a patient has at least five of the following symptoms and at least one of the first two symptoms is present. Symptoms must be present nearly every day for two consecutive weeks.

- **Depressed mood most of the day, nearly every day**
- **Markedly diminished interest or pleasure in all, or almost all, activities**
- Significant weight loss or weight gain
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feelings of worthlessness or excessive or inappropriate guilt
- Diminished ability to think or concentrate, or indecisiveness
- Recurrent thoughts of death, or suicidal thoughts or suicide attempt or plan³

Assessment for Suicide

All patients presenting with depression should be assessed for suicidality by direct questioning about:

³ APA Diagnostics and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, 2000.

- Current suicidal ideation or plan
- Past history of suicide attempts and level of remorse about unsuccessful attempts
- Access to a means for suicide (pills, firearms, etc.)
- Presence of substance use disorder
- Disruption of important relationships

These questions about suicidality can be put into perspective for the patient by explaining that thoughts about suicide are a common symptom of depression. Table 1 lists the risk factors associated with completed suicide.

Table 1: Suicide Risk Factors

<u>Psychosocial and Clinical</u>	<u>History</u>	<u>Diagnostic</u>
Hopelessness Caucasian race Male gender Advanced age Living alone	Prior suicide attempts Family history of suicide attempts Family history of substance abuse	General medical illnesses Psychosis Substance abuse

If suicide is a distinct risk, consult a mental health specialist immediately or refer the patient to an Emergency Department for immediate evaluation.

Dysthymia

Dysthymia is a depressive disorder that occurs in approximately six percent of the general population. It is characterized by the same symptoms as a major depressive disorder but is less severe and more chronic (having symptoms more days than not for two years.) It is equally responsive to antidepressant treatment as major depression.

Bereavement

When a patient presents with a mood disorder following the loss of a loved one, sadness should be considered a normal response to the loss. If the patient presents with symptoms that meet the criteria for a major depressive disorder two months or more after the loss, or if there is significant functional impairment associated with mood problems, a diagnosis of major depression should be considered and treated if appropriate. In addition, the following symptoms are **not** part of the normal grieving reaction:

- Obsessional thoughts about death or worthlessness
- Excessive guilt about actions not taken by the survivor at the time of death of the loved one
- Marked psychomotor retardation
- Hallucinatory experiences

Bipolar Disorder

If a patient meets the criteria for a major depressive disorder, screening for bipolar disorder should be considered part of a complete evaluation. Patients with bipolar disorder differ from those with major depressive disorder in that they have experienced a manic or hypomanic episode in addition to depression. These patients will require pharmacotherapy with a mood stabilizer (e.g. lithium).

A manic episode is defined as at least four of the following symptoms, including the first symptom below, present for at least one week. These symptoms are severe enough to cause marked impairment in social or occupational functioning:

- **A distinct period of abnormally and persistently elevated, expansive or irritable mood**
- Inflated self-esteem or grandiosity
- Decreased need for sleep
- Hypertalkative or pressure to keep talking
- Flight of ideas or the feeling that thoughts are racing
- Easily distracted
- Increase in goal directed behavior (either socially, at work or school or sexually) or psychomotor agitation
- Excessive involvement in pleasurable activities which have a high potential for painful consequences (buying sprees, sexual indiscretions or foolish business investments)⁴

Hypomania

Hypomania includes the same symptoms as mania but symptoms are **not** severe enough to cause **marked** impairment in social or occupational functioning.

Psychosis

Patients with severe symptoms may also have psychotic features such as hallucinations or delusions. These patients may be at very high risk for suicide or violence. They usually require specific pharmacotherapy and are candidates for a referral to a specialist.

⁴ APA Diagnosical and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, 2000.

When to Refer to a Specialist

Consultation or referral to a mental health specialist should be considered in the following situations:

- The clinical complexity of the case is beyond the scope of these guidelines
- The patient fails to respond fully to two medication trials
- The patient is actively suicidal
- The patient is psychotic or appears to meet the criteria for bipolar disorder
- Psychiatric hospitalization is a consideration
- The patient may benefit from formal psychotherapy
- Specialized treatments such as ECT or light therapy are being considered
- The patient shows chronic psychosocial problems
- The patient or clinician wishes a second opinion

For assistance in selecting a mental health provider you may call the Tufts Health Plan Mental Health/Substance Abuse Department at **(800) 208-9565**.

Depressive Symptoms and General Medical Disorders

A complete medical history and physical examination should be performed as part of the evaluation because medications and medical conditions can induce depressive symptoms. Table 2 lists common medications that can induce depressive symptoms. Table 3 lists medical conditions that can mimic depression. These tables are not all-inclusive.

Table 2: Medications That May Lead to Depressive Symptoms:		Table 3: Medical Conditions That May Lead to Depressive Symptoms:
Baclofen	Interferon	Chronic Pain
Barbituates	Levodopa	Dementia (e.g. neurodegenerative disorders)
Benzodiazepines	Methyldopa	Drug toxicities and withdrawal
Cimetidine	Metoclopramide	Endocrine disorders (e.g. thyroid dysfunction - hyper and hypo)
ranitidine	Opiates	Metabolic disorders (e.g. anemia, malnutrition, electrolyte disturbances)
Clonidine	Oral contraceptives	Neoplasms
Cycloserine	Propranolol	
Digoxin	Reserpine	
Gonadotropin-releasing agonists	Steroids	
	Verapamil	

Other Psychiatric Disorders

Substance Use Disorders

Substance use disorders can cause depressive symptoms, complicate an ongoing depressive disorder, or present as a co-morbid condition to the depressive disorder. If a substance abuse disorder is suspected, that condition should be addressed first and often the mood symptoms will abate.

The CAGE questionnaire is a quick screener that can help assess the risk of an alcohol problem. (Table 4)

Table 4 : C A G E Q u e s t i o n n a i r e ⁵

If the patient answers “yes” to at least two of these questions, further investigation of a substance use disorder is warranted.

Have you tried to *cut* down your drinking but couldn’t?

Do you get *annoyed* when people say you drink too much?

Do you feel *guilty* about your drinking?

Do you need a drink in the morning when you wake up (an *eye-opener*)?

If depression persists during sobriety then consider treatment for a depressive disorder.

Anxiety and Panic Disorders

Approximately forty percent of depressed patients also have co-morbid anxiety disorders such as general anxiety disorder or panic disorder. Assessment of anxiety symptoms is important since it will impact pharmacotherapeutic strategies. Typically, patients with anxiety symptoms will require a slower dose titration of certain antidepressants or the addition of adjunctive anxiolytic therapy.

Treatment

Step 1: DEVELOP A TREATMENT PLAN

Once a diagnosis of depression is made, a treatment plan should be formulated with the patient (and family if appropriate.)

⁵ Mayfield, D, McLeod, G, Hall, P. The CAGE questionnaire: Validation of a new alcoholism instrument. American Journal of Psychiatry 1974; 131:1121-1123. *Reprinted with permission from the American Journal of Psychiatry. Copyright 1974 American Psychiatric Association*

Treatment of depression consists of three phases: 1) acute treatment, 2) continuation treatment and 3) maintenance treatment. Table 5 describes the duration and goal of each phase.

Table 5: Three Phases of the Treatment of Depression

Phase	Duration	Goal
Acute Phase	8-12 weeks	Eliminate symptoms or approach baseline
Continuation Phase	16-20 weeks beyond acute phase	Prevention of relapse
Maintenance Phase	As needed	Prevention of future episodes

The objective of treatment is for the patient to reach a sustained level of improvement. The essential features of treatment include:

- Patient education prior to initiation of treatment (see table 6)
- Regular monitoring of side effects
- Regular monitoring of depressive symptoms
- Adjustment of treatment plan if the response is not adequate

Step 2: SELECT THE MOST APPROPRIATE ACUTE PHASE TREATMENT

The goal of the acute phase of treatment is symptom remission. Treatment of depression in the primary care setting may include: medication, psychotherapy, or a combination of both.

The choice of treatment should be based upon the history of illness and the severity of the depressive episode. Depression can be ranked from mild to severe. These rankings are determined by the number of symptoms and level of impairment.

Medication

Research has demonstrated that 55-65% of depressed individuals treated with an anti-depressant will have substantial improvement or a complete remission of symptoms. Table 9 presents a flow chart for the treatment of depression with medication.

Education is a critical element that helps ensure patient compliance. **Approximately fifty percent of patients will be non-compliant within the first three months of treatment.** Specific statements to patients have shown to increase compliance and enhance outcomes (Table 6). This education should take place in the first visit or as early as possible in the course of treatment.

Table 6: Educational Message

Patients should take the antidepressant daily (or as prescribed)

Antidepressants need to be taken 2-4 weeks before noticeable effects will occur

Patients need to continue taking the antidepressant even if they start to feel better

Patients should not stop taking the antidepressant without talking with the clinician

Patients should be given specific instructions on how to resolve questions regarding their treatment (i.e. identify contact person who patient should call)

Psychotherapy

Cognitive behavioral therapy and interpersonal therapy have been shown to be as effective as antidepressant treatment for depression in individuals with mild to moderate forms of the disorder. For the purposes of this guideline, it is important to note that psychotherapy is not simply unstructured and brief support commonly offered in the context of a primary care office visit. Cognitive behavioral therapy and interpersonal therapy are specifically structured psychotherapeutic interventions. Please see Table 7 for medication and psychotherapy considerations during the acute phase of treatment.

Table 7: Considerations for Acute Phase

Consider Medications Alone Under the Following Circumstances:

- More severe symptoms
- Recurrent episodes of depression
- Presence of psychotic features
- Family history of depression
- Prior response to antidepressant treatment
- Incomplete response to psychotherapy alone
- Patient preference

Consider Psychotherapy Alone Under the Following Circumstances:

- Less severe depression
- Absence of psychotic features
- Positive prior response to psychotherapy
- Incomplete response to medication alone
- Medication contraindicated or refused
- Patient preference

Consider Combined Medication and Psychotherapy Treatments Under the Following Circumstances:

- More severe depression
- Recurrent depression with poor recovery between episodes
- Incomplete response to medication or psychotherapy alone
- Complex psychosocial problems
- Poor compliance with treatment
- Patient preference

Step 3: SELECTION OF MEDICATION

Once a decision is made to initiate pharmacotherapy, selection of the most appropriate medication is important. All antidepressants are equally effective. The choice of antidepressant should be individualized to each patient based upon the following considerations:

- Side effect profile of the antidepressant
- History of response or non-response to previously tried antidepressants
- Drug/drug and drug/disease interactions
- Patient age
- Cost of medications

Patients with co-morbid medical conditions may be at risk for more severe adverse drug interactions. Geriatric patients may require lower doses of antidepressants or a slower titration of dosing. In both of these populations initiation and continued medication treatment should be done with caution. (See Table 10)

Step 4: EVALUATE TREATMENT RESPONSE

Regardless of the type of treatment modality chosen, response should be assessed on a regular basis.

Medication

Although the efficacy of medication is usually not apparent until the fourth week of therapy, patients should be evaluated prior to that time. **The frequency of patient contact is dependent on the patient's severity, although contact weekly or every two weeks is recommended.** During these contacts the clinician should address the following issues and provide an opportunity for the patient to raise any other concerns regarding treatment:

- Adherence to medication
- Monitoring of adverse effects and adjustment of medications if necessary
- Assessment of mood and/or vegetative symptoms
- Assessment of suicidality or other at risk behavior

~Four Week Evaluation: Partial or Non-Responders to Medication~

Medication response should be assessed at four weeks. If the response to antidepressant treatment is inadequate consider the following:

- Review the evidence to ensure the diagnosis is correct
- Evaluate for compliance with the medications
- Determine the need for increased dosing (See Table 10)
- Change medications -- often a patient will be idiosyncratically non-responsive to one

SSRI and have a robust response to another, or the patient may benefit from a different class of antidepressant

- If the patient has had two adequate medication trials⁶ without a good response then referral to a psychopharmacologist is strongly suggested
- Add psychotherapy to the treatment

Once the patient has responded, continue current treatment for four more weeks. After this the patient will enter the continuation phase.

Psychotherapy

Up to fifty percent of patients with mild to moderate depression will gain substantial improvement from psychotherapy alone. Again, full remission is the object of treatment.

~Four to Six Week Evaluation: Partial or Non-Responders to Psychotherapy~

If there is no symptom improvement by four to six weeks, the choice of treatment modality should be reevaluated. **For patients who are only partially improved by twelve weeks, treatment with medication should be strongly considered.**

Step 5: PROCEED TO CONTINUATION PHASE

The continuation phase consists of maintaining the antidepressant at acute phase doses, monitoring for adherence and monitoring for continued efficacy.

Patients with significant symptom reduction that approaches baseline can transition into the continuation phase of treatment. This phase continues treatment that was successful in the acute phase although monitoring may be less frequent. The continuation phase should last for four to six months. For medication management, acute phase plus continuation phase should last a minimum of six months.

Medication

During the continuation phase the dose of medication should remain the same. Visits can be extended to every four to eight weeks.

Psychotherapy

Although there has been less study on the use of psychotherapy in the continuation phase to prevent relapse, there is growing evidence to support the use of a specific structured therapy.

⁶ At usual therapeutic doses for at least four weeks each.

Step 6: EVALUATE THE NEED FOR MAINTENANCE PHASE TREATMENT

Following the continuation phase, the maintenance phase is the next treatment consideration. (See table 8) Recurrence rates for major depressive episodes are 50% after one episode, 70% after two episodes and 90% after three episodes. Patients who have had three or more episodes of major depression should be considered a candidate for lifetime antidepressant prophylaxis against recurrent episodes of depression. Medications would be continued at the same dose as in the continuation phase.

**Table 8:
Characteristics of Patients Likely to Need Maintenance Phase Treatment**

<p>Prior major depressive episodes</p> <p>Presence of co-morbid conditions (psychiatric or chronic general medical condition)</p> <p>Residual symptoms between episodes</p> <p>Severe symptoms during episodes such as suicidality, psychosis, severe functional impairment</p>

Table 9 : Treatment of Depression

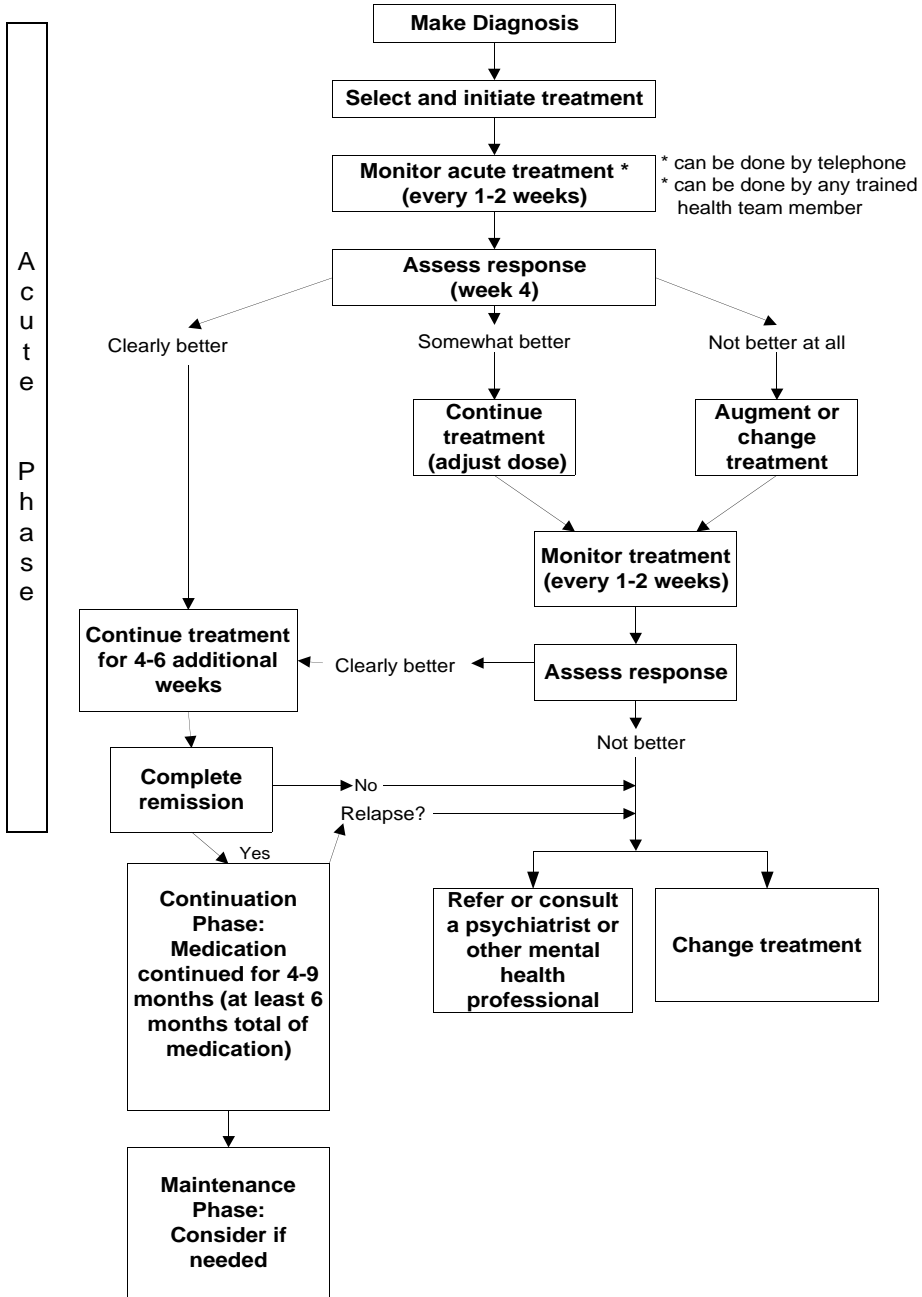


Table 10: Antidepressant Medication List*

Medication Brand // generic name	Adult Target Dose**	Adult Maximum Dose**	Adult Dosing Schedule**
Selective Serotonin Reuptake Inhibitors-SSRIs			
Prozac // fluoxetine	20 mg	80 mg	QD
Paxil // paroxetine	20-30 mg	60 mg	QD
Zoloft // sertraline	50-100 mg	200 mg	QD
Celexa // citalopram	40-60 mg	60 mg	QD
Tricyclic Antidepressants-TCAs			
Elavil // amitriptyline	150-200 mg	300 mg	QD
Pamelor // nortriptyline	75-100 mg	150 mg	QD
Tofranil // imipramine	150 mg	300 mg	QD
Norpramin // desipramine	150 mg	300 mg	QD
Anafranil // clomipramine	100-150 mg	250 mg	QD
Other Classes			
Wellbutrin // bupropion	225-300 mg	450 mg	BID-TID : Not to exceed 150 mg/dose
WellbutrinSR // bupropion SR	200-300 mg	400 mg	BID : Not to exceed 200 mg/dose
Remeron // mirtazapine	30 mg	45 mg	QD
Serzone // nefazodone	200-400 mg	600 mg	BID
Effexor // venlafaxine	150-225 mg	375 mg	BID-TID
Effexor XR // venlafaxine XR	75-150 mg	300 mg	QD-BID
Desyrel // trazodone	200-300 mg	600 mg	QD

* This table represents commonly used antidepressants. Dosing strategies are suggestions only. Clinical judgment should dictate specific patient dosing needs. A baseline medical exam and lab tests as well as the appropriate monitoring parameters are recommended.

**Pediatric and geriatric doses may vary.

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Addendum: Geriatric Depression Guideline

Many people consider depression to be part of the normal aging process – it is not. Seniors are at increased risk for depression from a variety of factors, including:

- complications of medical illness and drugs used to treat these illnesses
- occult substance use/abuse
- grief and/or social isolation due to loss of loved ones
- loss of employment, and/or loss of physical and mental functioning.

In general, seniors do not recognize their own depression and therefore might not admit to depression if asked directly about it. More likely, they will become more preoccupied with bodily function and report symptoms such as anxiety, somatic, or memory complaints.

There is an increased risk of completed suicide in this population; in fact, elderly white male widowers are the demographic group at highest risk of completed suicide. **It is important to remember that seniors are unlikely to contact a hotline or crisis intervention program for help with this issue. It is more likely they will make an appointment to see a physician.**

“Start low and go slow.” Because of multiple physical changes in this population, adverse drug effects are quite common. This is due, in part, to:

- decreased body mass and decreased proteins for drug binding
- frequent impairment in renal, hepatic, or cardiac function
- polypharmacy with medications used to treat medical illnesses

Thus, it is suggested to be careful about the selection of the antidepressant, dosing guidelines and length of therapeutic drug trials. It is prudent to avoid drugs with high anticholinergic side effects such as tricyclic antidepressants, as well as sedating antidepressants, which may increase risk of falling.

According to expert consensus, the following are good candidates for the treatment of depression in this population, primarily because these drugs avoid many of the problematic interactions listed above:

- Citalopram (Celexa)
- Sertaline (Zoloft)
- Bupropion-SR (Wellbutrin-SR)
- Venlafaxine-XR (Effexor-XR)

We suggest you review an on-line database or a PDA-based system to review both drug/drug interactions and dosing guidelines.

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DEPRESSION SCREENING

A 2002 report from the U.S. Preventive Services Task Force indicates there is sufficient evidence to recommend that PCPs routinely screen adult patients for depression and that screening has been shown to be cost-effective. While many depression screeners are available, two common, brief, and well-established screeners used in the primary care setting are the **Whooley Two Question Screener** and the **Geriatric Depression Scale (GDS)**. They are included for your reference. Please note that the GDS is a two-sided handout. One side is the form that you may copy and ask your patients to complete. The reverse side provides the questions with instructions on scoring the results.

Patients with a Positive Depression Screening Result:

- If a positive screening is obtained, we recommend the patient be interviewed to assess if they meet diagnostic criteria. Both diagnostic criteria and a step-by-step guide to treatment are included in our clinical guideline.
 - The MacArthur Initiative on Depression and Primary Care at Dartmouth and Duke provides clinicians with depression resources and a tool kit (including the PHQ-9 PRIME-MD). Their Web address is: www.depression-primarycare.org.
 - If you need assistance in referring a Tufts Health Plan patient for mental health services, you or your patient may contact the Tufts Health Plan Mental Health Department at (800) 208-9565 or www.tuftshealthplan.com. Our Web site includes educational materials for members and resources for physicians.
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Two Question Screen

During the past month, have you often been bothered by:

1. Little interest or pleasure in doing things? Yes No
 2. Feeling down, depressed or hopeless? Yes No
- If the patient's response to both questions is "no," the screen is negative
 - If the patient responded yes to either question, consider asking more detailed questions or using another screening instrument, such as the PHQ-9 (PRIME-MD PHQ)

Whooley et al. (1997) compared the 2-question screen to the Quick Diagnostic Interview Schedule (QDIS-III) and reported a sensitivity and specificity of 96% and 57% respectively.

Whooley MA, Avins AI, et al. Case finding instruments for depression. Two questions are as good as many. Journal of General Internal Medicine. 1997 July; 12(7): 439-445.

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Updated 2005

****For Physician Use****

Physician: The following are the questions from the **Geriatric Depression Scale** along with instructions on how to score this form. The reverse side is the actual screening instrument to give to your patients to complete. It may be reproduced.

Score one point for each bold answer. For clinical purposes a score > 5 points is suggestive of depression and warrants a follow-up interview. Scores > 10 are highly indicative of depression. (Note: Please see references for further information on scoring sensitivities.)

MOOD SCALE

Choose the best answer for how you have felt over the past week:

1. Are you basically satisfied with your life? **YES** / NO
2. Have you dropped many of your activities and interests? **YES** / NO
3. Do you feel that your life is empty? **YES** / NO
4. Do you often get bored? **YES** / NO
5. Are you in good spirits most of the time? YES / **NO**
6. Are you afraid that something bad is going to happen to you? **YES** / NO
7. Do you feel happy most of the time? YES / **NO**
8. Do you often feel helpless? **YES** / NO
9. Do you prefer to stay at home, rather than going out and doing new things? **YES** / NO
10. Do you feel you have more problems with memory than most? **YES** / NO
11. Do you think it is wonderful to be alive now? YES / **NO**
12. Do you feel pretty worthless the way you are now? **YES** / NO
13. Do you feel full of energy? YES / **NO**
14. Do you feel that your situation is hopeless? **YES** / NO
15. Do you think that most people are better off than you are? **YES** / NO

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(Physician: This patient form may be copied and given to your patient for completion.)

MOOD SCALE

Choose the best answer for how you have felt over the past week:

1. Are you basically satisfied with your life? YES / NO
2. Have you dropped many of your activities and interests? YES / NO
3. Do you feel that your life is empty? YES / NO
4. Do you often get bored? YES / NO
5. Are you in good spirits most of the time? YES / NO
6. Are you afraid that something bad is going to happen to you? YES / NO
7. Do you feel happy most of the time? YES / NO
8. Do you often feel helpless? YES / NO
9. Do you prefer to stay at home, rather than going out and doing new things? YES / NO
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13. Do you feel full of energy? YES / NO
14. Do you feel that your situation is hopeless? YES / NO
15. Do you think that most people are better off than you are? YES / NO

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Medication Addendum to Depression Clinical Guideline			
Medication Brand // generic name	Adult Target Dose*	Adult Maximum Dose*	Adult Dosing Schedule*
Antidepressants new to market since publication (2002)			
Lexapro//escitalopram	10-20 mg	20 mg	QD
Paxil CR(Controlled Release)// paroxetine HCL	25-35.7 mg	62.5 mg	QD
Wellbutrin XL// bupropion XL	300 mg	450 mg	QD
Cymbalta//duloxetine	40 -60 mg	60 mg	QD-BID

Schatzberg, A, Nemeroff, C. American Psychiatric Publishing Textbook of Psychopharmacology, Third Edition. American Psychiatric Publishing; 2004.

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