



## Complete Summary

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### GUIDELINE TITLE

VHA/DOD clinical practice guideline for the management of major depressive disorder in adults.

### BIBLIOGRAPHIC SOURCE(S)

VHA/DOD clinical practice guideline for the management of major depressive disorder in adults. Washington (DC): Department of Veterans Affairs (U.S.); 2000. Various p.

## COMPLETE SUMMARY CONTENT

SCOPE  
METHODOLOGY - including Rating Scheme and Cost Analysis  
RECOMMENDATIONS  
EVIDENCE SUPPORTING THE RECOMMENDATIONS  
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS  
CONTRAINDICATIONS  
IMPLEMENTATION OF THE GUIDELINE  
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT  
CATEGORIES  
IDENTIFYING INFORMATION AND AVAILABILITY

## SCOPE

### DISEASE/CONDITION(S)

- Major depressive disorder (MDD)

### GUIDELINE CATEGORY

Diagnosis  
Evaluation  
Management  
Treatment

### CLINICAL SPECIALTY

Geriatrics  
Psychiatry  
Psychology

### INTENDED USERS

Advanced Practice Nurses  
Nurses  
Physician Assistants  
Physicians  
Social Workers

#### GUIDELINE OBJECTIVE(S)

- To assist administrators at each of the federal agencies and care access sites to develop innovative plans to break down the barriers preventing primary care providers, subspecialists and allied health professionals from working together, and from preventing patients from having prompt access to preventive care
- To improve local management of patients with major depressive disorder and thereby improve patient outcomes

#### TARGET POPULATION

Veterans with major depressive disorder.

#### INTERVENTIONS AND PRACTICES CONSIDERED

Major Depressive Disorder (MDD) - Outline:

- Primary Care Setting
- Outpatient Mental Health Setting
- Inpatient Mental Health Setting

Primary Care Setting

##### Assessment

1. Screen for depression using validated screening tools such as Primary Care Evaluation of Mental Disorders depression questions (PRIME-MD), Center of Epidemiological Studies-Depression Scale (CES-D), Zung Depression Rating Scale, Beck Depression Inventory (BDI), Medical Outcomes Study Depression Scale (MOS), Hamilton Depression Scale (HAM-D)
2. Assess for dangerousness and identify unstable conditions that require immediate attention including delirium, marked psychotic symptoms, severe depressive symptoms/depression, suicidality, potential for violence, and unstable urgent medical conditions
3. Brief medical assessment, brief mental status exam, suicidal/violent behavior assessment
4. History (psychiatric, marital, past physical or sexual abuse, family, military, and medication or substance use), physical examination, laboratory tests
5. Mental status examination (MSE) and drug inventory (including over-the-counter [OTC] drugs and herbals)
6. Screen for substance abuse using instruments such as CAGE, PRIME-MD, AUDIT (Alcohol Use Disorders Identification Test), or DAST (Drug Abuse Screening Test)
7. Screen for co-morbid psychiatric conditions

8. DSM-IV [Diagnostic and Statistical Manual of Mental Disorders] criteria for major depressive disorder (MDD)

### Treatment

1. Assess appropriateness of treatment in primary care setting and need for consultation with a specialist
2. Psychosocial interventions, such as cognitive, behavioral, interpersonal, brief dynamic, and marital psychotherapy; spiritual counseling, family therapy and grief therapy as well as vocational therapy, financial/money management or other tangible socioeconomic assistance, and contact with a relevant special interest national association/organization for connection to local support resources.
3. Pharmacologic management:
  - Assess patient's willingness to take medications
  - Selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine, sertraline, paroxetine, citalopram
  - Tricyclic antidepressants (TCAs), such as nortriptyline, desipramine, amitriptyline, imipramine, doxepin, protriptyline, trimipramine
  - Dual mechanism antidepressants, such as bupropion, nefazodone, venlafaxine, mirtazepine
  - Monoamine oxidase inhibitors (MAOIs), such as phenelzine, tranylcypromine, isocarboxazid
  - Other antidepressants, such as amoxapine, maprotiline, trazodone
4. Combined pharmacologic and psychotherapy
5. Electroconvulsive therapy (ECT)
6. Patient and family education

### Management

1. Monitor treatment adherence and side effects
2. Assess response; adjust, augment or change treatment
3. Assess remission status with a standardized rating scale such as the Hamilton Depression Scale (HAM-D)
4. Follow-up maintenance and prevention of recurrence
5. Patient and family education

### Outpatient Mental Health Setting

#### Assessment

1. Assess signs and symptoms of depression
2. Assess for dangerousness and identify unstable conditions that require immediate attention including delirium, marked psychotic symptoms, severe depressive symptoms/depression, suicidality, potential for violence, and unstable urgent medical condition
3. Confirm MDD (DSM-IV criteria)
4. Determine appropriate level of care; review criteria for hospitalization [SAIC (Sciences Allocations International Corporation) Standards]
5. History (psychiatric, marital, past physical or sexual abuse, family, military, and medication or substance use), physical examination, laboratory tests
6. Screen for substance abuse using instruments such as CAGE

7. Assess use of other medications that may cause depression
8. Assess other medical conditions that may contribute to depressed symptoms
9. Assess patient's support system (housing and transportation needs to obtain outpatient care)
10. Assessment for current or past mania, hypomania, or mixed state, or psychosis

### Treatment

1. Identify patients with non-MDD disorders and those in need of more specialized treatment, and refer as appropriate
2. Modify, maintain, or initiate interdisciplinary treatment plan
3. Patient and family education
4. Primary and secondary electroconvulsive therapy (ECT)
5. Psychosocial interventions (see primary care above)
6. Pharmacologic management with antidepressant (see primary care above) and/or antipsychotic
7. Combined pharmacologic and psychotherapy
8. Medication-resistant depression:
  - Review diagnosis and exclude possibility of a coexisting medical or psychiatric problem
  - Addition of adjunct to an antidepressant, such as lithium or thyroid hormone
  - Simultaneous use of multiple non-MAO antidepressants (SSRIs, bupropion) or anticonvulsants (carbamazepine)

### Management

1. Monitor treatment for adherence and side effects
2. Assess response
3. Assess remission status with a standardized rating scale such as the Hamilton Depression Scale (HAM-D)
4. Review criteria for hospitalization using assessment instruments such as the SAIC Criteria for Hospitalization
5. Follow-up maintenance and prevention of recurrence
6. Patient and family education

### Inpatient Mental Health Setting

#### Assessment

1. Assess for unstable medical conditions and for those at high risk for suicide or violence
2. Confirm MDD (DSM-IV criteria)
3. Obtain history including psychiatric, family, psychosocial, military stress, past physical or sexual abuse, and substance abuse. Perform MSE and GAF, or Axis V of DSM-IV
4. Assess use of other medications that may cause depression
5. Assess other medical conditions that may contribute to depressed symptoms
6. Physical examination, laboratory evaluation (CBC, UA, LFTs, other labs and studies as indicated)
7. On or before admission: discharge planning and patient/family education

## Treatment

1. Interdisciplinary treatment plan addressing medication (see primary care), appropriate psychotherapy (see primary care), other psychosocial interventions (see primary care), co-morbidity, if applicable, and patient preferences
2. Management or consultation with medical service to manage concurrent medical disorders
3. Electroconvulsive therapy

## Management

1. Assess need for continued hospitalization using the GAF scale and suicide/violent behavior risks
2. Assess response to treatment; adjust treatment as necessary. Perform assessments and make adjustments working toward discharge
3. Discharge to the appropriate mental health level of outpatient care (including partial hospitalization or supervised living). Schedule follow-up appointment within 2 weeks

## MAJOR OUTCOMES CONSIDERED

### Assessment

- Validity and reliability (specificity, sensitivity, correlation) of screening and diagnostic instruments

### Treatment

- Risk of suicidal/violent behavior
- Symptom control
- Occupational and psychosocial functioning
- Risk of symptom/episode recurrence

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

#### Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The search was limited to publication dates between 1997 and 1999 in the English language only since the previous version contained references and rating through 1998. The literature search was carried out using the National Library of Medicine's (NLM) MEDLINE database. To find candidate titles, the term Depressive Disorder was used as the first medical subject heading (MeSH). As a result the following entries were used to frame the query:

- Psychiatry and Psychology (MeSH Category)

- Mental Disorders
- Mood Disorders
- Depressive Disorder
  - Depression

In addition, the following Boolean expressions and terms were used concomitantly with the above approaches: cognitive therapy, criteria efficacy, primary care, protocols, psychosocial, screening instruments, therapy (all types), treatment.

Each search was conducted using the above parameters plus a qualifier dealing with specific types of publication such as clinical trial, meta-analysis, practice guideline and random control trial.

Other articles were selected for review and inclusion as possible evidence based upon a clinical review through Pub Med and Grateful Med, yielding many more articles that provided evidence to support or not support the efficacy of a given treatment or diagnostic or follow-up modality that related to specific aspects of the already defined questions.

#### NUMBER OF SOURCE DOCUMENTS

Not stated

#### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

#### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

##### Quality of Evidence

I - Evidence obtained from at least one properly randomized controlled trial.

II-1 - Evidence obtained from well-designed controlled trials without randomization.

II-2 - Evidence obtained from well-designed cohort or case-control analytical studies, preferably from more than one center or research group.

II-3 - Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III - Opinions of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

The quality of the evidence is related to study design, such as large randomized control trials.

## METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not applicable

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The recommendations are the product of fifteen months of consensus building among experts in the treatment of major depression and professionals from all aspects of the Veterans Health Administration care continuum.

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of Recommendation

- A. There is good evidence to support the recommendation that the condition be specifically considered in a periodic health examination.
- B. There is fair evidence to support the recommendation that the condition be specifically considered in a periodic health examination.
- C. There is insufficient evidence to recommend for or against the inclusion of the condition in a periodic health exam, but recommendations may be made on other grounds.
- D. There is fair evidence to support the recommendation that the condition be excluded from consideration in a periodic health examination.
- E. There is good evidence to support the recommendation that the condition be excluded from consideration in a periodic health examination.

The strength of recommendation uses evidence that supports (or does not support) the suggested intervention.

## COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

### MAJOR RECOMMENDATIONS

The recommendations for major depressive disorder are organized into 3 major algorithms. Each algorithm, the annotations that accompany it, and the evidence supporting the recommendations are presented below. The strength of recommendation grading (A-E) and level of evidence grading (I-III) are defined following the "Major Recommendations."

Note: A list of all abbreviations is provided at the end of the "Major Recommendations" field.

[Algorithm A1 - Initial Assessment](#)

[Algorithm A2 - Establish Diagnosis](#)

[Algorithm A3 - Initial Assessment and Treatment](#)

[Algorithm A4 - Follow-up Treatment](#)

#### Module A: Management of Major Depressive Disorder in Adults in the Primary Care Setting

##### A. Patient Age > 18 with Suspected Depression Presenting to Primary Care

###### Definition

All patients older than 18 who have a positive screen for depression.

###### Discussion

Depression is known to be under-diagnosed in primary care settings. There is some controversy regarding the value of screening patients in primary care settings. Since recent studies suggest screening is feasible in primary care, the working group decided screening should be recommended.

In recognition of the evolving nature of the literature, other published validated scales can be used. Care should be taken to assure scale validation with similar patient populations as those seen in the Veterans Administration (VA) and Department of Defense (DoD) settings. There are several available screening tools, each with its own strengths and problems. Appendix 1, Assessment Instruments, of the original guideline document offers descriptions of a number of screening instruments that may also be used to quantify symptom severity and samples of these tools. Some of the validated screening tools available are listed:

1. PRIME MD - Primary care Evaluations of Mental Disorders - depression questions

2. CES-D - Center of Epidemiological Studies-Depression Scale
3. Zung - Zung Depression Rating Scale
4. BDI - Beck Depression Inventory
5. MOS - Medical Outcomes Study Depression Scale
6. Ham-D - Hamilton Depression Scale

In all settings, a validated screening tool should be filled out before the patient sees the primary care provider, and results of the screening should be made available to the provider. Each setting should determine which screener will be adopted, at what point in the check-in process the screener will be utilized, and who will administer the screener (e.g., clerk, nurse who takes vital signs).

## B. Assess for Dangerousness

### Objective

To identify patients that are at high risk of harm to self or others and with any medical or psychiatric conditions requiring immediate attention.

### Annotation

Unstable conditions, whether physiological or psychiatric, represent situations that require immediate attention. They include the following:

1. Delirium - Delirium (also known as organic brain syndrome, organic psychosis, acute confusional state, acute brain syndrome and various other names) is a very common disorder of cognition and consciousness of abrupt onset that is commonly unrecognized. This is especially true in the elderly and chronically ill.
2. Marked psychotic symptoms - "Psychosis," in and of itself, is not a disorder. Rather, it is a symptom which may present in a variety of conditions. Psychotic patients have an impaired sense of reality, which may manifest in several ways (hallucinations, delusions, mental confusion or disorganization).
3. Severe depressive symptoms/depression (e.g., catatonia, malnourishment, severe disability) - The clinical presentation of depressed patients is marked by considerable variation, not only in the expression of various neurovegetative symptoms themselves, but also in the magnitude of severity of these symptoms. While many mild to moderate illnesses may not necessarily present situations requiring immediate attention, the presence of severe depressive symptoms may represent an urgent condition, even in the absence of suicidal ideation.
4. Suicidality - Suicidal behavior is best assessed with the following criteria: current suicidal ideas or plans, presence of active mental illness (severe depression or psychosis), presence of substance use disorder, past history of suicidal acts, formulation of plan, availability of means for suicide (firearms, pills, etc.), disruption of important personal relationship, or failure at important personal endeavors. If some or all of these criteria are present, a referral or consultation with a mental health professional is indicated.

5. Potential for violence - Violence often emerges as a response to perceived threat or marked frustration resulting from the inability to meet goals by nonviolent means. The specific factors which contribute to violent behavior include psychiatric, medical, environmental and situational/social. Whatever the cause, the following situations may serve as warning signs of violence:
- Ideas about or intent to harm others
  - History of violent behavior
  - Severe agitation or hostility
  - Active psychosis

Immediate attention and intervention may be required in order to stave off the potential for escalation of agitation or violent impulses.

6. Unstable urgent medical conditions - Any condition immediately threatening to life, limb, or eye sight or requiring emergency medical care. These may include acute myocardial infarction, respiratory failure, hypertensive crisis, diabetic ketoacidosis, crushing radiating chest pain, etc.

For more information on these conditions see Appendix 2, Unstable and High Risk Conditions and Appendix 3, Suicidality, of the original guideline document.

#### Evidence

Specific factors that contribute to violent behavior include psychiatric, medical, environmental and situational/social. (Hasting, 1997; Thienhaus, 1998; U.S. Preventive Services Task Force [USPSTF], 1996) Quality of the evidence: II-1, Strength of recommendation: B

Insufficient evidence to support routine screening of depression, suicide risk, child abuse or domestic violence. (USPSTF, 1996) Quality of the evidence: II-2, Strength of recommendation: B

Clinicians should maintain a high index of suspicion for depressive symptoms in persons at increased risk of depression, suicide risk, child abuse or domestic violence. (USPSTF, 1996) Quality of the evidence: III, Strength of recommendation: B

- C. Provide Appropriate Care or Refer to Stabilize and Follow Legal Mandates

#### Objective

To assure appropriate care and protocols are followed during diagnosis and stabilization.

#### Annotation

If a patient represents a risk to self or others, providers should follow local, state, and federal guidelines which should be already well established. For VA patients, these procedures should also reflect the opinion and guidance of the Veterans Health Administration (VHA) District Council. For DoD patients, these procedures are directed by DoD Directive 6490.1, "Mental Health Evaluation of Members of the Armed Forces," DoD Instruction 6490.4, "Requirements for Mental Health Evaluations of Members of the Armed Forces," and related Service regulations/instructions. These regulations/instructions may require a number of notifications (e.g., commanders) which would not be made in a civilian practice. Primary care and administrative staff should be familiar with the applicable policies and procedures. Mental health staff should be prepared not only to manage patients who pose a risk, but should also be prepared to consult with primary care and other medical specialties concerning patients who may be encountered in their clinics. Patient care management plans must reflect the realities of local resources, staffing, and transportation.

If patients represent a risk to others, additional notifications may be required by state or federal laws and/or regulations. When making notifications, it is wise to consult a peer and/or medical law consultant on the legal and ethical requirements.

- D. Obtain History (including Psychiatric, Marital, Family, Military, Past Physical or Sexual Abuse, and Medication or Substance Use), Physical Examination and Laboratory Tests. Perform Mental Status Examination (MSE), Drug Inventory (Including Over-the-Counter [OTC] Drugs and Herbals).

#### Objective

To develop an appropriate clinical understanding of the patient that will inform subsequent provider decisions.

#### Annotation

In primary care and long-term care settings, depression is often undiagnosed and untreated because patients with significant symptoms of depression rarely identify depression as a chief complaint. Depression may be suspected based entirely on a history of the present illness that reveals recent depressive symptoms. In some cases, the patient may not relate current depressive symptoms, but a screening psychiatric history may reveal one or more past depressive episodes. In other cases, a history of the present illness and the past psychiatric history are unrevealing, but certain medical and psychosocial risk factors suggest that a high index of suspicion is appropriate. For example, multiple unexplained physical symptoms suggest a high likelihood of depression.

After determining that the patient is stable, the priorities are now:

1. Recognizing current signs and symptoms of depression
2. Obtaining a careful psychiatric history, looking for past depressive episodes

3. Remaining attentive to "red flags" suggesting that a higher than usual index of suspicion is necessary

Obtain a psychiatric history - Key elements of the past history of depression include: prior antidepressant use, past hospitalization for depression or suicidality, and inability to function in usual life roles. Substance use and misuse can cause and/or exacerbate depression. Use of screening tools (such as the CAGE [a screening mnemonic for determining drunkenness], the Alcohol Use Disorders Identification Test [AUDIT], the Michigan Alcoholism Screening Test [MAST] or the Drug Abuse/dependence Screening Test [DAST] - see the Veterans Health Administration [Substance Use Disorders Guideline](#), for substance use assessment tools) can improve detection of substance use disorders.

There is a high likelihood of depression among individuals with past or present physical or sexual abuse history or a history of substance use disorders. Primary care physicians should respectfully ask each patient direct and specific questions about physical or sexual abuse during the history.

"Red Flags" suggesting need for a higher than usual index of suspicion - Certain physiological and psychological conditions or life events may contribute to the development or exacerbation of depression symptoms. These may include, but are not limited to:

- Medically unexplained physical symptoms
- Chronic, debilitating medical condition
- Current substance abuse/use
- Decrease in sensory, physical, or cognitive function
- Victim of current or past physical or sexual abuse or emotional neglect
- Family history of major depression
- Loss of significant relationship, primary support system, or economic status
- Neurological disorder (e.g., Multiple Sclerosis, Parkinson's disease, stroke) or history of closed head injury
- Protracted care-giving role for a family member with a chronic, disabling condition
- Spousal bereavement and widowhood
- Symptoms or signs of post traumatic stress disorder (PTSD)

Physical Examination - A brief, screening physical examination may uncover endocrine, cardiac, cerebrovascular, or neurologic disease that may be exacerbating or causing depressive symptoms. Particularly in the elderly patient, a full Mental Status Examination (MSE) includes cognitive screening assessment that may consist of a standardized instrument such as the Folstein Mini-Mental State Examination (MMSE). If screening is suggestive of cognitive impairment and the patient is not delirious, then a laboratory evaluation to assess for reversible causes of dementia is appropriate. The depression assessment should be continued. If delirium is present, consider it an emergency and stabilize the patient before proceeding, then return to the algorithm and continue with depressive assessment Box 4 of the algorithm. Other MSE findings of importance in depression include slow speech, sighing, psychomotor retardation or agitation, downcast eyes, and little or no smiling.

Laboratory Evaluation - Use the history and physical examination findings to direct a conservative laboratory evaluation. There is no test for depression, so testing is directed toward detection of associated general medical conditions. Appropriate laboratory studies to rule out medical disorders that may cause symptoms of depression include complete blood count (CBC), chemistry profile, thyroid studies, and toxicology screen. For patients over the age of 40, an electrocardiogram (ECG) may be useful.

Diagnostic imaging and neuropsychological or psychological testing is not a part of the standard laboratory evaluation for depression. Proceed with the algorithm while awaiting the completion of the laboratory evaluation.

#### Evidence

Brief Screening may be useful in identifying depression. (Rost et al., 1993; USPSTF, 1996) Quality of the evidence: II-2, Strength of recommendation: B

### E. Assess Signs and Symptoms of Depression

#### Objective

To identify core signs and symptoms that may lead to a diagnosis of depression versus other conditions.

#### Annotation

Core symptoms and signs of depression include:

0. Depressed mood
  1. Loss of pleasure in normally pleasurable activities (anhedonia)
  2. Feelings of guilt, hopelessness, and helplessness
  3. Fatigue or energy loss
  4. Poor concentration or memory problems
  5. Persistent appetite changes and weight loss or gain
  6. Psychomotor slowing or agitation
  7. Morbid thinking to include suicidal ideation and behaviors
  8. Significant altered sleep (too much or not enough) (see the Diagnostic and Statistical Manual for Mental Disorders, fourth edition [DSM-IV])

### F. Assess Functional Disability

#### Objective

To ensure that patient has no other mental health concerns before discharge from the clinic.

#### Annotation

Prior to concluding the interview and examination, the clinician should inquire about the patient's ability to carry out personal and daily activities not covered by either the chief complaint or the depression screening questions. This may be elicited in the following manner:

0. "During the past few weeks, have any physical or emotional problems interfered with your typical daily activities?"
1. "Has it been more difficult to do things on your own or with your (family, friends, neighbors, church, etc.)?"  
If positive, areas for brief inquiry include: job, pleasurable hobbies, social activities, and important personal relationships.
2. "Are there any other problems that we have not discussed?"

If any patient responses are affirmative, the clinician should define any impediments to optimal daily functioning, recognizing that the patient may have already denied depression and substance abuse. One should be alert for alternative ways of expressing discouragement, distress, or demoralization, especially in those individuals who tend to avoid emotional words for describing themselves.

#### G. Is Patient a Threat to Self or Others?

##### Objective

To identify patients who pose active risk for dangerousness and who should be assessed further in mental health.

##### Annotation

Eliciting Suicidal Ideation or Intent - Direct and nonjudgmental questioning regarding suicidal ideation/intent is indicated in all cases where depression is suspected. A significant number of patients who contemplate suicide are seen by a physician in the month prior to their attempt. Direct assessment of suicidal ideation and intent does not increase the risk of suicide. Consider gathering collateral information from a third party, if possible.

One recommended line of questioning uses the following:

- "Have you had thoughts about death or about killing yourself?"
- "Tell me about your hopes for the future?"
- "Do you have a plan for how you would kill yourself?"
- "Are there means available (e.g., pills, a gun and bullets, or poison)?"
- "Have you actually rehearsed or practiced how you would kill yourself?"
- "Do you tend to be impulsive?"
- "How strong is your intent to do this?"
- "Can you resist the impulse to do this?"
- "Have you heard voices telling you to hurt or kill yourself?"
- Ask about previous attempts, especially the degree of intent.
- Ask about suicide of family members or significant others.

Homicidal Ideation - Homicidal ideation and suicidal ideation may co-occur. Risk of violence towards others should be assessed by asking directly whether or not the patient has thoughts of harming anyone.

- Assess whether the patient has an active plan and method/means (i.e., weapons in the home)
- Assess whom the patient wishes to harm
- Assess whether the patient has ever lost control and acted violently
- Assess seriousness/severity of past violent behavior

If some or all of these are present, a referral or consultation with a mental health professional is indicated. In the event of expressed dangerousness to self or others, steps must be taken to insure patient safety until further evaluation.

#### Evidence

Suicide Risk Factors and related conditions:

Psychiatric illness. (USPSTF, 1996) Quality of the evidence: I, Strength of recommendation: B

Serious medical illness. (USPSTF, 1996) Quality of the evidence: I, Strength of recommendation: B

Persons with social adjustment problems. (USPSTF, 1996) Quality of the evidence: I, Strength of recommendation: B

Living alone. (USPSTF, 1996) Quality of the evidence: I, Strength of recommendation: B

Recent bereavement. (USPSTF, 1996) Quality of the evidence: I, Strength of recommendation: B

Personal or family history of suicide attempt. (USPSTF, 1996) Quality of the evidence: I, Strength of recommendation: B

Family history of completed suicide. (USPSTF, 1996) Quality of the evidence: I, Strength of recommendation: B

Divorce or separation. (USPSTF, 1996) Quality of the evidence: I, Strength of recommendation: B

Unemployment. (USPSTF, 1996) Quality of the evidence: I, Strength of recommendation: B

Caucasian race, male gender. (USPSTF, 1996) Quality of the evidence: I, Strength of recommendation: B

Advanced age. (USPSTF, 1996) Quality of the evidence: I, Strength of recommendation: B

Family history of substance abuse. (USPSTF, 1996) Quality of the evidence: I, Strength of recommendation: B

Substance abuse. (USPSTF, 1996) Quality of the evidence: I, Strength of recommendation: B

#### H. Is There Evidence of Psychosis?

##### Objective

To identify patients with acute or chronic psychosis who may require treatment in mental health.

##### Annotation

Psychosis is defined as a mental state in which the patient is significantly out of touch with reality to the extent that it impairs functioning.

Patients with psychotic symptoms may present in an acutely agitated state with a fairly recent onset of disturbed and/or disturbing symptoms. Patients may also present with enduring, chronic symptoms which are long-standing and to which patients have made a reasonably comfortable adaptation. Examples of acute psychotic symptoms that are inappropriate to treat in a primary care setting include:

0. Serious delusions (e.g., fixed false beliefs)
1. Visual or (typically) auditory hallucinations
2. Incoherence
3. Confusion
4. Catatonic behavior (e.g., motoric immobility or excessive agitation)
5. Extreme negativism or mutism, peculiar voluntary movement
6. Inappropriate affect of a bizarre or odd quality

In particular, paranoid concerns that others wish to harm the patient and voices (especially command hallucinations) telling the patient to hurt him or herself or someone else, are indications for an immediate mental health consultation or referral. Patients who have longstanding psychotic illness and who are able to attend to present circumstances without responding to their psychosis may be evaluated and treated for a co-morbid depression in the primary care setting.

It is important to bear in mind that psychotic symptoms may be the direct result of an underlying medical condition, toxic state, alcohol or substance use disorder, or may be associated with a mental health condition such as schizophrenia or affective illness.

#### I. Is There Evidence of Substance Use Disorder?

##### Objective

To identify patients who require evaluation and treatment according to the guideline for substance use disorder.

##### Annotation

All patients should be asked about any current or recent use of nicotine, alcohol, or other psychoactive substances.

Screening can be based on:

0. Brief self-report screening instruments for alcohol problems (AUDIT, CAGE, PRIME-MD), nicotine, or other drug problems (DAST, Drug Abuse/Dependence Screening Tool)
1. Reports from responsible others
2. Laboratory tests (e.g., blood or breath alcohol tests, breath carbon monoxide for smoking, urine toxicology elevated carbohydrate deficient transferrin, increased mean corpuscular volume (MCV) or gamma glutamic transferase (GGT))

Laboratory tests are not recommended for routine screening of asymptomatic persons. Patients who screen positive should receive a more thorough assessment for substance use disorder and the relationship of substance use to depression.

See the Veterans Health Administration [Substance Use Disorders Guideline](#) for further diagnosis and treatment. The CAGE is a beneficial mnemonic consisting of questions about alcohol use. One or more positive responses to the following questions can be considered a positive result to the CAGE test:  
Scoring:

C Have you ever attempted to cut down on your drinking?

A Have you ever been annoyed by other people criticizing your drinking?

G Have you ever felt guilty about your drinking?

E Have you ever taken a morning eye-opener?

If the CAGE score is 2 or higher, further investigation of substance use is warranted.

Evidence

Brief self-report screening instruments for alcohol problems may help identify drug problems. (American Society of Addiction Medicine [ASAM], 1996; USPSTF, 1996) Quality of the evidence: II-3, Strength of recommendation: B

#### J. Do Medications Cause or Contribute to Symptoms?

Objective

To identify patients who may be experiencing depressed symptoms as a side effect of medication.

Annotation

Many prescription or over-the-counter (OTC) drugs contribute to depression. Although there is little published information on alternative medicines causing depression, consideration should also be given to herbal, nutritional, vitamins and body building supplements, particularly when consumed in large doses. The table below "Compounds that Commonly Cause Depression" provides supportive evidence.

Table. Compounds that Commonly Cause Depression

Drug/Drug Class	QE	SR
ACE inhibitors	II-2	C
Amphetamine withdrawal	I	B
Anabolic Steroids	I	B
Antihyperlipidemics	II-2	C
Benzodiazepines	II-2	C
Cimetidine, Ranitidine	II-2	C
Clonidine	II-2	C
Cocaine withdrawal	I	C
Cycloserine	II-2	C
Digitalis	I	B
Glucocorticoids	I	B
Gonadotropin-releasing agonists	II-2	A
Interferons	II-2	C
Levodopa	II-2	C
Methyldopa	II-2	C
Metoclopramide	II-2	C
Oral contraceptives	II-2	C
Pimozide	II-2	A
Propranolol (Beta Blockers)	II-2	B
Reserpine	II-1	C
Topiramate	II-2	C
Verapamil (Calcium channel Blockers)	II-2	C

#### K. Do Medical Conditions Contribute to Symptoms?

##### Objective

To identify patients who may be experiencing depressed symptoms as a result of an underlying medical condition.

##### Annotation

The table titled "Pathobiologies Related to Depression" (below) includes many of the pathobiologies associated with depression. Simultaneous treatment is often required for both the medical problem and psychiatric symptoms. Additionally, there is often a strong association between the level of disability from the medical condition and the depressive symptom requiring treatment.

A useful mnemonic for remembering these is [TIC]<sup>2</sup>p<sup>2</sup>m<sup>2</sup>d<sup>3</sup>. The mnemonic stands for:

0. Trauma
1. Tumor
2. Infection - immune and autoimmune
3. Cardiac/vascular
4. Congenital/hereditary
5. Physiologic - seizure
6. Metabolic malignancy
7. Degenerative
8. Drug toxicity
9. Demyelinating

Patients with chronic pain may also have associated mood disturbance. This may be encountered among individuals suffering conditions such as chronic obstructive pulmonary disease (COPD), or asthma, or more commonly, bone pain with cancer.

Table. Pathobiologies Related to Depression

Pathology	Disease
Cardio/vascular	Coronary artery disease Congestive heart failure Uncontrolled hypertension Anemia Stroke Vascular dementias
Chronic Pain Syndrome	Fibromyalgia Reflex sympathetic dystrophy Low back pain (LBP) Chronic pelvic pain Bone or disease related pain
Degenerative	Presbyopia Presbycusis Alzheimer's disease Parkinson's disease Huntington's disease Other neurodegenerative diseases

Immune	HIV (both primary and infection-related) Multiple Sclerosis Systemic Lupus Erythematosus (SLE) Sarcoidosis
Infection	Systemic Inflammatory Response Syndrome (SIRS) Meningitis
Metabolic/Endocrine Conditions (include renal and pulmonary)	Malnutrition, Vitamin deficiencies Hypo/hyperthyroidism Addison's Disease Diabetes mellitus Hepatic disease (cirrhosis) Electrolyte disturbances Acid-base disturbances Chronic Obstructive Pulmonary Disease (COPD) or Asthma Hypoxia
Neoplasm	Of any kind, especially pancreatic or central nervous system (CNS)

L. Determine and Document DSM-IV Criteria for MDD

Objective

To identify patients with a major depressive disorder.

Annotation

The essential feature of MDD is a clinical course characterized by one or more major depressive episodes without a history of manic, mixed, or hypomanic episodes, or without being better accounted for by other medical or mental disorders. At least five of the DSM IV symptoms have been present during the same 2-week period, nearly every day, and represent a change from previous functioning. At least one of the symptoms must be either (1) depressed mood or (2) loss of interest or pleasure. See Appendix 1, Assessment Instruments, of the original guideline document for the formal criteria including four additional required symptoms for a diagnosis of major depressive episode.

The criteria for a major depressive episode are set at a fairly high threshold. At least five symptoms must occur simultaneously, and the symptoms must be present for most of the day, nearly every day and for at least two weeks.

Symptoms can be indicated by either subjective account of the patient or the observation of others. Contacts with family members may help make an accurate diagnosis.

## M. Is There Evidence of Psychotic Features, Past Mania or Hypomania?

### Objective

To differentiate unipolar from bipolar depression.

### Annotation

Some depressed patients manifest periods of mania. According to DSM-IV, a manic episode is a distinct period of persistently elevated, expansive, or irritable mood, lasting at least four days, that is clearly different from the usual nondepressed mood and is observable by others. During this period of abnormal mood at least three of the following symptoms are present to a significant degree and have persisted:

0. Inflated self esteem or grandiosity
  1. Decreased need for sleep
  2. Pressure to keep talking
  3. Flight of ideas or subjective experience that thoughts are racing
  4. Distractibility
  5. Increase in goal-directed activity or psychomotor agitation
  6. Excessive involvement in pleasurable activities that have a high potential for painful consequences

These symptoms are severe enough to cause marked impairment in social or occupational functioning or require hospitalization. Symptoms are not secondary to a substance use or general medical condition. Hypomania is characterized by a manic episode without accompanying impairment or psychosis. A past history of mania or hypomania excludes a patient from a diagnosis of MDD. These patients may require referral to a mental health professional. These patients often need specialist's treatment and follow-up, since initiating or titrating routine antidepressant medication can precipitate a manic episode.

## N. Are There Signs of Co-morbid Psychiatric Conditions?

### Objective

To determine whether other psychiatric conditions are present in addition to MDD that may complicate treatment.

### Annotation

Patients with evidence of psychiatric disorders in addition to MDD may require referral to a specialist. Evidence of co-morbid disorders that should prompt the primary care provider to consider referral include:

0. Extensive history of childhood abuse, unstable or broken relationships, or criminal behavior starting before or during adolescence suggestive of a personality disorder
  1. Extreme weight loss suggestive of anorexia nervosa

2. A pattern of "binging" (rapid and excessive consumption of food) and/or "purging" (use of self-induced vomiting, laxatives, or diuretics) to control weight that may suggest bulimia nervosa
3. Frequent and disabling nightmares or flashbacks suggestive of post traumatic stress disorder
4. Other major mental disorders (e.g., schizophrenia or bipolar disorder) likely to significantly complicate the primary care management of depression symptoms

Patients with medically unexplained physical symptoms suggestive of a somatoform disorder may sometimes require referral to a mental health specialist. However, patients with unexplained physical symptoms often resent psychiatric referral and fail to follow through. Primary care providers should initiate MDD treatment if possible by building a trusting relationship with the patient. The practitioner should carefully explain the reason for referral before and after it is recommended, and set a follow-up appointment after the referral. These measures will help to allay patient concerns that their physical symptoms are being addressed, yet they require more specialized attention to their state of well being and, therefore, are being referred for consultation.

O. Discuss Treatment Options and Patient's Preferences. Provide Patient and Family education

Objective

To provide the patient and significant others an understanding of the available treatment options.

Annotation

There are four broad treatment options for patients with MDD.

0. Pharmacotherapy including other somatic therapies, including Electroconvulsive Therapy (ECT)
  1. Empirically Supported psychoTherapies (EST)
  2. Combined psychotherapy and pharmacotherapy
  3. Clinical evaluation of one to three visits

Patients should be educated about the potential consequences of untreated MDD, and encouraged to return.

Pharmacotherapy - There is a wide range of available antidepressant medications for patients to select from (see Appendix 5 of the original guideline document, Pharmacological Therapy of MDD). The specific medication choice is generally based on side effect profiles, safety in overdose, history of prior response, concomitant medical conditions, family history of response, and type of depression.

Benefits of pharmacotherapy include:

4. Potential of a more rapid initial treatment response
5. Patient's preference for medications over talk therapies

Risks or drawbacks of pharmacotherapy include:

6. Need to take medications consistently and exactly as prescribed
7. Potential for medication side-effects or interactions with other medications or medical problems
8. Potential for need to take medication for an indefinite or extended period

Psychotherapy - This is the use of one of the ESTs, offered in either one-on-one or group format. See Appendix 4, Empirically Supported Psychotherapy (EST), of the original guideline document for a full list of the ESTs and supporting evidence. Generally these approaches aim to help depressed individuals thoughtfully examine their behavior, beliefs, emotions, stressors, and personal relationships in an effort to lead to lasting change in factors that may have contributed to the development of depression. For the purposes of this guideline, psychotherapy is NOT simply unstructured and brief support commonly offered in the context of a primary care office visit.

Benefits of psychotherapy include:

9. Effects may persist beyond the duration of treatment
10. The need to take antidepressant medications or experience medication side-effects may be reduced
11. An opportunity for the patient to make meaningful self-improvements or life changes

Risks or drawbacks of psychotherapy include:

12. Patients need to come consistently for therapy appointments on a frequent basis for several months at a time
13. A therapist trained in an empirically supported psychotherapy may not be available in every care setting

Clinical Evaluation - For patients that do not meet criteria for complexity, an extended (two to three visits) can often identify those patients whose depressive symptoms are transient. Some individuals will have spontaneous remission of symptoms, particularly when symptoms have been precipitated by a life crisis. The main risk of extended clinical evaluation is that MDD may not respond and may worsen without active treatment.

Evidence

Neither pharmacotherapy nor empirically supported psychotherapy have been shown to be consistently superior in the immediate or long term outcomes. (Rush & Hollon, 1991; Reynolds et al., 1999) Quality of the evidence: I, Strength of recommendation: A

Medication treatment may lead to faster response, whereas psychotherapy (particularly cognitive behavioral therapy) may reduce risk of relapse. (Fava et al., 1994; Rush & Hollon, 1991) Quality of the evidence: I, Strength of recommendation: A

Combination of an empirically supported psychotherapy with medication has not been shown to produce consistently better outcomes for most patients than use of one of these approaches on its own, although there may be exceptions with some subtypes. (Reynolds et al., 1999) Quality of the evidence: I, Strength of recommendation: C

Severity of depression among psychiatric outpatients is not a reliable discriminator of short term response to either medication or empirically supported psychotherapies. (DeRubeis et al., 1999) Quality of the evidence: II-2, Strength of recommendation: B

#### P. Unable to Treat Patient in the Primary Care Setting

##### Objective

To assure appropriate level of care based on local resources available.

##### Annotation

Many patients with major depressive disorder can be effectively treated in primary care settings. Primary care providers are strongly urged to aim for full symptom remission and to refer without unnecessary delay those patients whose symptoms are not remitting.

Primary care providers vary significantly in skill, comfort, and motivation to treat major depression. Before initiating treatment, the primary care provider should weigh the need for referral to a mental health care specialist. The more specific the referring provider's consultation questions, the more successful the referral/ consultation. Reasons for referral to a specialist include the following:

- Patient request for mental health care specialist referral/consultation
- Provider request for diagnostic consultation
- Complicating general medical problems
- Complicating mental disorders ("co-morbidity")
- Severe, recurrent, or psychotic depression
- Suspected need for hospitalization
- Suspected need for involuntary commitment
- Need or patient request for psychotherapy
- Need for light therapy
- Need for electro-convulsive therapy (ECT)
- Questions regarding medication selection, initiation, interactions, or administration
- Provider concerns about patient adherence to treatment
- Symptom breakthrough after a positive acute phase treatment response

- History of poor or partial treatment response

When weighing the need for consultation, the primary care provider should take into account the common barriers to effective mental health consultation. Potential barriers may include:

- Patient reluctance to see a mental health care specialist
- Feasibility for the patient
- Geographical distance from consultants
- Length of time to consultant availability

Q. Is Psychotherapy Preferred, Appropriate, and Available?

Objective

To determine the best treatment option for the patient.

Annotation

0. Psychotherapy for depression is generally appropriate for all forms of depression managed in the primary care setting. Because there are no demonstrated differences in outcome between patients treated with psychotherapy or pharmacotherapy, patient choice should be strongly considered in treatment planning.
1. Collaborative management of depressed patients with a mental health specialist, especially those with persistent symptoms, can increase the cost effectiveness of care and may be useful for patients who refuse off-site mental health and consultation.
2. Utilization of mental health specialists affiliated with a primary care center will facilitate communication, joint management, and more convenience for the patient.
3. Availability of a competent psychotherapist is a prerequisite for the psychotherapy option. It has been shown, for example, that the competency of the psychotherapist affects treatment effectiveness. Variability in the quality of administration of all treatments affects the patient's outcome for both medication and psychotherapy.
4. Combination of an empirically-supported psychotherapy with medication has not been shown to produce consistently better outcomes for most patients than use of one of these approaches on its own. However, addition of cognitive-behavioral therapy to medication has been shown to reduce risk of relapse.

See Appendix 4 of the original guideline document, Empirically Supported psychoTherapies of MDD.

Evidence

Cognitive-Behavioral Therapy is efficacious for reducing residual symptoms of depression and relapse rates among patients successfully treated with antidepressant drugs. (Fava et al., 1994; Rush & Hollon, 1991) Quality of the evidence: I; Strength of recommendation: A

Competency of the psychotherapist affects treatment effectiveness. (Jacobson & Hollon, 1996) Quality of the evidence: I; Strength of recommendation: A

Collaborative management of MDD improves symptoms of depression and treatment adherence. (Katon et al., 1995) Quality of the evidence: I; Strength of recommendation: B

Collaborative Care of MDD increased depression treatment costs but improved the cost-effectiveness of treatment for patients with major depression. (von Korff et al., 1998) Quality of the evidence: I; Strength of recommendation: B

Stepped collaborative care improved adherence to antidepressants, satisfaction with care, and depressive outcomes compared with usual care among patients whose depressive symptoms persisted after initiation of antidepressant medication. (Katon et al., 1999) Quality of the evidence: I; Strength of recommendation: B

#### R. Is Pharmacotherapy Appropriate and Is Patient Willing to Take Medications?

##### Objective

To determine whether the patient should receive a pharmacological intervention.

##### Annotation

Generally patients should receive antidepressant medications for the following indications:

- Moderate or severe symptoms of depression
- Significant impairment in social or occupational functioning due to depression
- Suicidal ideation

Strong indications for antidepressant medication include:

- Past history of a positive response to medications
- Negative response to psychotherapeutic interventions
- Recurrent depressive episodes
- Family history of depression
- Patient preference for drug therapy

When determining treatment modality, patient preference should be taken into consideration. However, if the patient does not elect to start antidepressant medications and this is deemed detrimental to the patient's welfare, the clinician should continue discussing all treatment options and monitor the patient for worsening of the symptoms. Educational materials may be helpful for persuading the patient that antidepressant medications can be beneficial.

## S. Initiate Pharmacotherapy

### Objective

To determine and initiate the preferred pharmacological treatment.

### Annotation

No antidepressant medication is clearly more effective than another. No single medication results in remission for all patients. Patient factors and drug side effect profiles may favor one class of antidepressants over another for a given individual, but there are no clear differences in efficacy between or within classes. The clinician should consider the medical condition of the patient. In some instances, particularly certain gastrointestinal disorders (chronic diarrhea or peptic ulcer disease) the tricyclic class of antidepressants may be a better first choice. The clinician should determine which medications have been efficacious in the past and at what dosages. Generally medications with favorable side effects profiles should be used. Previously efficacious medications, regardless of class, should be considered as a first choice if medications with favorable side-effects profiles do not help.

Selective Serotonin Reuptake Inhibitors (SSRIs) or venlafaxine are generally first line antidepressants for patients in the primary care setting because of their low toxicity and ease of administration relative to other antidepressants. There is insufficient evidence to recommend one antidepressant over another for all patients.

Prior to declaring treatment failure with any antidepressant, it is important to ensure that an appropriate dose titration and target dose range has been achieved and an adequate response period allowed. Doses should be titrated in order to improve the chance of tolerating the drug. Before assessing the efficacy of an antidepressant, a patient should remain on any given drug for a minimum of four to six weeks. In general, initial doses used for the elderly should be lower than in healthy adults. Adequate treatment response may require titration to a full maintenance dose.

### General Considerations

0. The choice of medication is based on side effect profiles (see Appendix 5, Pharmacological Therapy of MDD, Table 2 of the original guideline document), history of prior response, family history of response, type of depression, concurrent medical illnesses, concurrently prescribed medications, and cost of medication.
1. Rates of response to antidepressants are reported as high as 60 to 70 percent. However the rate of complete remission may be substantially lower.
2. Some depressive target symptoms (e.g. sleep, anxiety, insomnia, decreased appetite, decreased energy, libido) may respond to therapy sooner than the depressed mood resolves.
3. Patient and family education about the course and nature of depressive illness, treatment and potential side effects, time course to see symptomatic improvement, and importance of treatment

compliance helps to improve treatment adherence and the likelihood of success.

4. Antidepressants may precipitate manic episodes in bipolar patients, and may activate latent psychosis in some susceptible patients. Close monitoring for such symptoms may be necessary. Abrupt discontinuation of any antidepressant may result in adverse withdrawal symptoms or return of original depressive symptoms. Discontinuation of antidepressant maintenance therapy should be done with a slow taper. Tapering of the antidepressant should be guided by the elimination half-life of the parent compound and metabolites, and close monitoring of depressive symptoms. For discussion of dosing see Appendix 5 of the original guideline document, Pharmacological Therapy of MDD.

#### Evidence

Neither pharmacotherapy nor empirically supported psychotherapy have been shown to be consistently superior in the immediate or long term outcomes. (Rush & Hollon, 1991; Reynolds et al., 1999) Quality of the evidence: I, Strength of recommendation: A

Medication treatment may lead to faster response, whereas psychotherapy (particularly cognitive behavioral therapy) may reduce risk of relapse. (Fava et al., 1994; Rush & Hollon, 1991) Quality of the evidence: I, Strength of recommendation: A

Combination of an empirically supported psychotherapy with medication has not been shown to produce consistently better outcomes for most patients than use of one of these approaches on its own, although there may be exceptions with some subtypes. (Reynolds et al., 1999) Quality of the evidence: I, Strength of recommendation: C

Severity of depression among psychiatric outpatients is not a reliable discriminator of short-term response to either medication or empirically supported psychotherapies. (DeRubeis et al., 1999) Quality of the evidence: II-2, Strength of recommendation: B

Fluoxetine treatment for MDD is not associated with an increased likelihood of suicidal behavior. (Leon et al., 1999; Warshaw, 1996) Quality of the evidence: II-3, Strength of recommendation: B

Clinical characteristics can help target patients with MDD at high risk for relapse. Risk factors identified included persistent subthreshold depressive symptoms, chronic mood symptoms, or history of two or more major depressive episodes. (Lin et al., 1998) Quality of the evidence: II-1, Strength of recommendation: B

Patients with atypical depression features are less responsive to TCAs. (Stewart et al., 1998) Quality of the evidence: II-2; Strength of recommendation: C (unreplicated)

Sertraline maintenance therapy is well tolerated and prevents recurrence or reemergence of depression in chronically depressed patients. (Keller et al., 1998) Quality of the evidence: I, Strength of recommendation: B

Cognitive therapy is an effective acute phase treatment alternative to MAOI antidepressant medications for patients with MDD and atypical features. (Jarrett et al., 1999) Quality of the evidence: I, Strength of recommendation: C (unreplicated)

Analyses of coroners' data suggest that TCAs are associated with elevated death rates in overdose compared with SSRIs. (Montgomery, 1997) Quality of the evidence: III, Strength of recommendation: C

Presence of personality disorders has generally been linked to poorer outcomes for treatment of MDD. (Thase, 1996) Quality of the evidence: II-1, Strength of recommendation: B

T. Concern About Patient's Mental Health Persists?

Objective

To determine if further mental health care is indicated.

Annotation

Other disorders that present with depressive features may warrant treatment in primary care, but are outside the scope of the original guideline document. Information on some of the most common of these disorders appears in Appendix 6 of the original guideline document, Non-MDD Conditions Potentially Requiring Specialty Consultation. Of these disorders, only some are likely to be deemed appropriate for treatment in the primary care setting; the most likely are bereavement and adjustment disorder with depressed mood.

U. Monitor Treatment Every 1 to 2 Weeks. Assess Adherence and Side Effects

Objective

To ensure patient is responding to treatment.

Annotation

Patients who are early in a course of treatment or patients who have recently undergone a treatment change require subsequent evaluation of response to the new treatment. Although it is too early to expect a full remission of symptoms, many patients will experience an early improvement in depression symptoms. More importantly, the clinician should assess common antidepressant side effects and discuss the patient's overall treatment adherence and satisfaction. During the visit, the patient may ask questions

regarding their condition, symptoms, or care. Providers should seize this opportunity to build rapport, convey hope and encouragement.

Patients may refuse psychotherapy and antidepressant medications for a variety of reasons. Some patients with untreated major depression will recover spontaneously, but a significant number require active intervention to achieve full remission of symptoms and functioning. The functional impairment from depression is comparable to impairment from a number of other chronic medical conditions. Depressed patients also tend to use more medical services and are at an increased risk of suicide.

Side effects - Common short-term side effects affecting adherence to the SSRIs include insomnia, agitation or anxiety, appetite reduction, head pain, nausea, and loose stool. Initiating medication regimens at low doses (e.g., 10 mg of fluoxetine qd, 25 mg of sertraline, or 10 mg of paroxetine) may reduce severity of these side effects, and a qam regimen may ease complaints of insomnia. SSRIs may be augmented with trazodone, generally in doses of 25 to 100 mg, hs, to manage insomnia. It should be noted that of the SSRIs, paroxetine may be more likely to cause drowsiness or asthenia, and for this reason it is frequently administered at bedtime (qhs). Nefazodone and mirtazapine have also been associated with complaints of fatigue or insomnia, and administration at bedtime may be more appropriate for these agents as well.

Sexual dysfunction (reduced libido, delayed orgasm, or decreased vaginal lubrication in women) is the most frequent long-term side effect associated with the SSRIs. Some have suggested that Bupropion or other agents (cyproheptadine, yohimbine, and others) may counteract these side effects although there is little evidence for their efficacy.

Use caution in tapering one medication when substituting another. A discontinuation syndrome when stopping SSRIs and venlafaxine has been observed. Commonly reported symptoms are dizziness, nausea or vomiting, fatigue, aches, chills, anxiety, irritability and crying spells. Rebound depression may occur. Symptoms generally occur within one to three days of discontinuation. Discontinuation syndrome has not been described for fluoxetine, perhaps because of its very long half-life.

Another caution is the very rare but potentially grave possibility of a "central serotonin syndrome" (sweating, fever, tachycardia, hypertension, altered mental status; more severely hyperpyrexia, cardiovascular collapse, and death) during the transition from one medication to another. The risk of this may be increased when two serotonergic agents are administered together or in close proximity. Some authors recommend waiting for at least five times the half-life of a drug (or its metabolites), before initiating treatment with a second agent.

#### V. Assess Response in 4 to 6 Weeks

##### Objective

To ensure patient remains on treatment with desired outcome.

## Annotation

A large body of literature studying the effectiveness of either pharmacotherapy or psychotherapy or both typically report at least a partial remission (50 percent symptom reduction) within four to six weeks of treatment. Full response, defined as minimal or no symptoms, often requires a longer duration of treatment, and full restoration of psychosocial functioning may take several months.

Patients may discontinue treatment at the four to six week interval if either the symptoms are not improving or the symptoms have remitted somewhat despite the natural course of the illness. The four to six week patient visit is an important time to reinforce the need for continued treatment, possible treatment modification, patient education and assessment of adherence.

## Evidence

AHCPR and American Psychiatric Association Practice Guidelines for Depression recommend a four to six week reassessment for treatment response. (Schulberg et al., 1998; Shelton, 1999) Quality of the evidence: I, Strength of recommendation: B

Rate of response for individuals with MDD who show no improvement by week four will be very low and no better than placebo, and a change in treatment regimen is indicated. (Quitkin, 1996) Quality of the evidence: II-2, Strength of recommendation: A

## W. Adjust Treatment as Indicated

### Objective

To manage treatment collaboratively with the patient.

### Annotation

When changing treatment, it is most appropriate to engage the patient in the decision and to reconsider available alternatives. Some alternative treatments may include medication (if started on psychotherapy), other medications or psychotherapy (if started on medication), and/or combination therapy. Combination treatment may benefit patients unresponsive to psychotherapy or pharmacotherapy alone.

Problems with adherence leading to modification of treatment - Adherence to medications may be lower to drugs requiring bid or tid dosing. Utilization of sustained release preparations enhances compliance with these agents. In general, medications that can be taken on a qd schedule are preferred when adherence to a dosing schedule is an issue. Because of its long half-life, fluoxetine may be the best choice for patients who have trouble adhering to a dosing schedule.

Adherence to psychotherapy appointments and assignments is an important predictor of improvement in the empirically supported psychotherapies. If the patient is not compliant, changes in the therapist or the therapy approach should be considered. Combination therapy may also be considered.

For patients who show particularly poor adherence to initial treatment with medication, psychotherapy should be discussed as an alternate treatment option. Likewise, for patients who show particularly poor adherence to psychotherapy, medication should be discussed as an alternative treatment approach.

#### Evidence

Combination treatment may benefit patients unresponsive to psychotherapy or pharmacotherapy alone. (Schulberg et al., 1998) Quality of the evidence: I, Strength of recommendation: C

### X. Remission?

#### Objective

To assess whether the patient with MDD achieves a full remission of symptoms.

#### Annotation

Remission is defined as a return to full pre-morbid functioning accompanied by a substantial reduction of depressive symptoms. For research studies, experts typically define remission and improvement as a change in score on standardized rating scales such as the Hamilton Depression Scale (HAM-D). Many efficacy studies cite a 50 percent response rate to define improvement, but a more complete symptom and functional status response is necessary to achieve remission. Expert consensus supports a fairly complete symptom and functional status response before declaring a remission of symptoms.

The use of rating instruments is one approach to looking for symptom remission. Measures of use include the Hamilton Depression Rating Scale, PRIME-MD Patient Health Questionnaire (PHQ), the Beck Depression Inventory, and the Zung Depression Rating Scale (See Appendix 1 of the original guideline document, Assessment Instruments). In primary care settings, however, often a review of "SIG-E-CAPS" depression symptoms (see below) will suffice. At least one group has presented data suggesting that measuring symptom response based on clinician's global impression may be adequate.

S Sleep disturbance (insomnia or hypersomnia)

I Interests (anhedonia or loss of interest in usually pleasurable activities)

G Guilt and/or low self-esteem

- E Energy (loss of energy, low energy, or fatigue)
- C Concentration (poor concentration, forgetful)
- A Appetite changes (loss of appetite or increased appetite)
- P Psychomotor changes (agitation or slowing/retardation)
- S Suicide (morbid or suicidal ideation)

#### Evidence

Remission defined as the patient no longer meeting the DSM III-R criteria for major depression and having Hamilton Depression Scale scores less than seven for up to three consecutive weeks. (Reimherr et al., 1998) Quality of the evidence: II-2, Strength of recommendation: B

Texas Medication Algorithm Project Report defined remission as equal to or greater than 75 percent global improvement in symptoms. Emphasized goal of symptomatic remission and normalization of function rather than only symptom improvement. (Crismon et al., 1999) Quality of the evidence: III, Strength of recommendation: B

Remission defined as the total final Hamilton Depression Scale 24 item score equal to or less than seven. (Hirschfeld et al., 1998) Quality of the evidence: III, Strength of recommendation: B

Danish University Antidepressant Group defined full remission as seven or less on the 17 item HAM-D. (Fuglum et al., 1996) Quality of the evidence: III, Strength of recommendation: B

#### Y. Institute Continuation and Maintenance Phase Treatment. Follow-up Including Prevention of Recurrence and Patient/Family Education

##### Objective

To prevent relapse or recurrence of future major depressive episodes.

##### Annotation

MDD is best conceptualized as a chronic illness resulting in a continuum of outcomes ranging from excellent to poor. Increased rates of recurrence were found in fifty percent of the patients with a single episode of MDD, and the greater the number of episodes the more likely are future depressive episodes. A high percentage of individuals with recurrent major depressive disorder will require indefinite prophylactic antidepressant treatment. Factors increasing the risk of future recurrence include:

0. A strong family history of mood disorders
1. A history of recurrence within one year after discontinuation of a previously efficacious medication

2. One or more suicide attempts
3. Onset of the first episode before age 20
4. Two or more episodes of major depression in the past two years
5. Concurrent dysthymia

Continuation phase of antidepressant treatment follows the acute phase and begins when the patient has complete remission of depressive symptoms. Continuation phase treatment usually lasts up to nine months and is followed by maintenance phase treatment, an indefinite period of prophylaxis against future depressive episodes.

Continuation Phase Treatment - Priorities of the continuation phase include sustaining the dose of medication resulting in acute phase symptom remission; preventing relapse or recurrence of depressive symptoms; monitoring depressive symptoms and functional status; and building a constructive therapeutic alliance.

In psychotherapy, a maintenance plan should be developed during the course of therapy. The plan should include a summary of learning that occurred during therapy; ways the patient will continue to use lessons from the therapy; a prediction of times of high recurrence risk (e.g., death of a significant other); and coping approaches for such crisis periods. Use of booster sessions and occasional reassessment of depressive symptoms should be considered.

Maintenance Phase Treatment - Following the continuation phase, decisions regarding extended maintenance phase treatment are implemented. Patients who have had three or more episodes of major depression or two or more episodes in combination with another risk factor for recurrence (see list above) should remain on prophylactic antidepressant medication for one or more years after remission of the acute episode at the continuation phase dosage.

Patient/Family Education - Education is important for patients and families concerning risk of relapse and ways to reduce risk and sustain remission status. Information about recurrence risk factors, medications, and early recognition of recurrence should be included.

### [Algorithm B - Outpatient Mental Health Specialty](#)

#### Module B: Management of Major Depressive Disorder in Adults in the Outpatient Mental Health Setting

##### A. Patient with Suspected Depression Presenting to Outpatient Mental Health Specialty Care

###### Definition

This module targets a large population and aims to provide guidance related to the many ways to access care. The common feature in all presentations is that the patient has reported signs or symptoms of depression, either by a

screening instrument or in an interview situation. The patient may or may not have a previously confirmed diagnosis of MDD and may already be receiving treatment for MDD. Entry points include the following:

1. Patients referred from primary care who were diverted to outpatient specialty care at one of various points in the algorithm are noted below:

#### MODULE A

- Box 9 - concerns about mental health persist, although depression symptoms were not elicited by primary care provider
  - Box 12 - positive screen and threat to self or others
  - Box 13 - positive screen and symptom reports of depression, with evidence of psychosis
  - Box 24 - meets DSM-IV criteria for MDD, but case is too complex
  - Box 26 - unable or unwilling to treat patient in primary care
  - Box 33 - positive screen for depression and some symptoms reported, but patient does not meet criteria for MDD; concerns about mental health persist
  - Box 44 - patient has been treated for over 12 weeks without remission and primary care chooses to refer to mental health rather than revising treatment in their setting
2. Patients coming through mental health walk-in clinic
  3. Patients referred from within mental health setting as a result of new emergence of complaints of depression
  4. Patients followed up after discharge from inpatient care:

#### MODULE C

- Box 21 (MDD confirmed and treated; GAF and/or lethality improved and now insufficient to justify continued hospitalization, but patient not clearly in remission)
- Box 28 (MDD confirmed and treated, with at least a second course of treatment needed after initial non-response); GAF and/or lethality improved and now insufficient to justify continued hospitalization, but patient not clearly in remission)

#### B. Assess for Dangerousness

##### Objective

To identify patients that are at high risk to self or others or who have any medical or psychiatric conditions requiring immediate attention.

##### Annotation

Unstable conditions, whether physiological or psychiatric, represent situations that mandate immediate attention. These include the following:

1. Delirium - Delirium (also known as organic brain syndrome, organic psychosis, acute confusional state, acute brain syndrome and various other names) is a disorder of cognition and consciousness with abrupt onset that is frequently overlooked. This is common in the elderly and medically ill.
2. Acute or marked psychosis - "Psychosis" in and of itself, is not a disorder. Rather, psychosis is a symptom which may present in a variety of conditions. Psychotic patients have an impaired sense of reality, which may manifest in several forms (hallucinations, delusions, mental confusion or disorganization). Acute psychosis represents a medical emergency.
3. Severe debilitating depression (e.g., catatonia, malnourishment, severe disability) - While many mild to moderate illnesses may not necessarily present situations mandating immediate attention, the presence of severe depressive symptoms may represent a medical emergency-even in the absence of suicidal ideation.
4. Suicidality - Suicidal behavior is best assessed with the following criteria: presence of active depression or psychosis, presence of substance abuse, past history of suicidal acts, formulation of plan, a stated intent to carry out the plan, feeling that the world would be better off if the patient were dead, availability of means for suicide (firearms, pills, etc.), disruption of an important personal relationship, failure at an important personal endeavor. The presence of these factors often constitutes a psychiatric emergency and must always be taken seriously. See Appendix 3 of the original guideline document, Suicidality.
5. Potential for violence - Violence often emerges as a response to perceived threat or marked frustration by the patient from their inability to meet goals by nonviolent means. The specific factors which contribute to violent behavior may include psychiatric, medical, environmental and situational/social engagements. Often, it is a combination of these factors which precipitates and aggravates potential for violence, which may quickly escalate to frank agitation or the carrying out of violent impulses. Whatever the cause, the following situations may serve as warning signs pointing towards a very real threat of violence:
  - Ideation and/or intent to harm others
  - Past history of violent behaviors
  - Severely agitated or hostile
  - Actively psychotic

Immediate attention and intervention may be required in order to ward off the potential for escalation of agitation or violent impulses.

6. Unstable urgent medical conditions - Any condition immediately threatening to life, limb, eye sight, or requiring of emergency medical care. Conditions include acute myocardial infarction, respiratory failure, hypertensive crisis, diabetic ketoacidosis, crushing radiating chest pain, etc.

See Appendix 2, Unstable and High Risk Conditions and Appendix 3, Suicidality, of the original guideline document.

## Evidence

Specific factors that contribute to violent behavior include psychiatric, medical, environmental and situational/social. (Hasting, 1997; Thienhaus, 1998; USPSTF, 1996) Quality of the evidence: II-1, Strength of recommendation: B

Insufficient evidence to support routine screening of depression, suicide risk, child abuse or domestic violence. (USPSTF, 1996) Quality of the evidence: II-2, Strength of recommendation: B

Clinicians should maintain a high index of suspicion for depressive symptoms in persons at increased risk of depression, suicide risk, child abuse or domestic violence. (USPSTF, 1996) Quality of the evidence: III, Strength of recommendation: B

## C. Does Patient Require Hospitalization?

### Objective

To determine if the patient meets criteria for appropriate psychiatric hospitalization.

### Annotation

Usual reasons for urgent hospitalization include acute suicide risk; acute violence risk due to mental illness; delirium; and acute unstable medical condition.

Specialized treatment only available or often best provided in a hospital include:

1. Electro-convulsive therapy (ECT)
2. Close monitoring and daily titration of medication with disabling side effects or toxicity
3. Constant staff observation as part of an intensive behavioral modification program
4. Close monitoring of behavior in an episodic disorder
5. Close monitoring of vital signs or need for multiple daily laboratory or electrophysiological testing

Specific admission criteria must be determined at each setting reflecting local circumstances. However, national uniform standards, such as the Science Allocations International Corporation (SAIC) standards, are strongly recommended. Review of all admissions using standardized utilization review criteria, such as those available from InterQual Medical Necessity Criteria or Science Allocations International Corporation (SAIC) Inpatient Criteria has been recommended by VHA's Under Secretary for Health. The Department of Defense has adopted the use of SAIC admission criteria for CHAMPUS contracts. Thus any facility (VHA or DoD) providing CHAMPUS care is expected to use SAIC criteria for its utilization reviews in accordance with the

specifications of its contract. See Appendix 1, Assessment Instruments, of the original guideline document for SAIC Criteria for Hospitalization.

D. Refer to Inpatient Mental Health, Module C. Follow Legal Mandates

Objective

To ensure patient's safety is maintained during stabilization.

Annotation

If a patient represents a risk to self or others, providers must follow established local, state, and federal guidelines. For VA patients, these procedures should reflect the opinion and guidance of the VA district Council. For DoD patients, these procedures are directed by DoD Directive 6490.1, "Mental Health Evaluation of Members of the Armed Forces", DoD Instruction 6490.4, "Requirements for Mental Health Evaluations of Members of the Armed Forces", and related service regulations/instructions. Regulations/instructions may require a number of notifications (e.g., commanders) which would not be required in a civilian practice. Mental health staff should be prepared not only to manage patients who pose a risk but also be prepared to consult with primary care and other medical specialties on patients who may be encountered in their clinics. Plans for management must reflect the realities of local resources, staffing, and transportation.

If patients represent a risk to others, state or federal laws and/or regulations may require additional notifications. When making notifications, it may be useful to consult a peer and/or medical law consultant for questions on the legal and ethical requirements.

E. Obtain History (Psychiatric, Marital, Family, Military, Past Physical or Sexual Abuse, and Medication or Substance Use), Physical Examination, Laboratory Tests. Perform Mental Status Examination (MSE), Drug Inventory (Including Over-the-Counter Drugs and Herbals)

Objective

To develop an appropriate clinical understanding of the patient that can inform subsequent provider decisions.

Annotation

After determining that the patient is stable, the priorities are:

1. Recognizing current symptoms and signs of depression
2. Obtaining a careful psychiatric history looking for past depressive episodes
3. Performing complete physical examination and directed laboratory assessment

4. Remaining attentive to "red flags" that suggest a higher than usual index of suspicion is necessary
  5. Estimating anticipated length of treatment
  6. Initiating discharge planning
- F. Assess Current Signs and Symptoms of Depression

Objective

To determine the presence or absence of the cardinal signs and symptoms of major depressive disorder.

Annotation

Core symptoms and signs of depression include:

1. Depressed mood
2. Loss of enjoyment in normally pleasurable activities (anhedonia)
3. Feelings of guilt, hopelessness, and helplessness
4. Fatigue or energy loss
5. Poor concentration or memory problems
6. Persistent appetite changes and weight loss or gain
7. Psychomotor slowing or agitation
8. Morbid thinking to include suicidal ideation and behaviors
9. Significantly altered sleep (too much or not enough) (DSM-IV)

See Appendix 1, Assessment Instruments, of the original guideline document for the DSM-IV Diagnostic Criteria for MDD.

- G. Does the Patient Have a Support System Available (Stable Housing, Transportation, Other Axis IV Needs)?

Objective

To determine the adequacy of patient's social supports.

Annotation

Without a reasonably stable living situation and a means of transportation to the treatment program, the patient is unlikely to attend treatment and/or comply with a treatment regimen.

Concerns to be addressed may include:

1. Need for case management
2. Housing
3. Transportation
4. Any guidelines specific to the delivery system
5. Need to refer to VHA homeless program (VA beneficiaries only)

Housing is usually not a barrier to outpatient treatment for active duty service members. However, if they are in transit and require outpatient treatment,

housing may be arranged on a local military facility. Transportation to a treatment facility is the responsibility of the active duty member unless he or she is in a basic training or deployed status and then it becomes the responsibility of the command to provide transportation to an outpatient facility.

If there are problems with housing and transportation for other DoD or VA Medical Beneficiaries, information and assistance is supplied to these patients by the Social Work Service for the purpose of securing adequate services. Case management may be a helpful tool to coordinate services and identify barriers.

#### H. Is There Evidence of Substance Use Disorder?

##### Objective

To identify patients who require evaluation and treatment according to guidelines for substance use disorder.

##### Annotation

All patients should be asked about any current or recent use of nicotine, alcohol, or other psychoactive substances. Screening for alcohol may be accomplished using the "CAGE" questions:

C Have you ever attempted to cut down on your drinking?

A Have you ever been annoyed by other people criticizing your drinking?

G Have you ever felt guilty about your drinking?

E Have you ever taken a morning eye-opener?

The CAGE is a beneficial mnemonic consisting of questions about alcohol use. One or more positive responses can be considered a positive result to the CAGE test. If the CAGE score is two or more, then more focused assessment for alcohol problems is indicated.

See the Veterans Health Administration [Substance Use Disorders Guideline](#) for further diagnosis and treatment.

It is useful to start the questioning with the family history of alcohol or drug use, then to follow with a question about the patient's own substance use (e.g., "Have you ever had a problem with drugs or alcohol?"). Note that substance histories relying on quantity of use (e.g., "How much would you say you drink each day?") are notoriously inaccurate. Other systematic screening instruments are available and useful. Descriptions of these instruments may be found in the Guideline on Substance Use Disorders.

Corroboration of the history from significant others is useful, as many problem substance users will convincingly deny their drug use.

Laboratory tests are not recommended for routine screening of asymptomatic persons. Patients who screen positive for substance use should be carefully evaluated in accordance with the Substance Use Guideline.

Evidence

Brief self-report screening instruments for alcohol problems may help identify drug problems. (ASAM, 1996; USPSTF, 1996) Quality of the evidence: II-3, Strength of recommendation: B

I. Do Medications Cause or Contribute to Symptoms?

Objective

To identify patients who may be experiencing depressed symptoms from a medication side effect.

Annotation

Many prescriptions or over-the-counter drugs may possibly contribute to depression.

Below is an alphabetical table of medications and evidence ratings linking various medications to increased risk of depression. Although there is little published information on alternative medicines and their relationship to depression, consideration should be given to herbal, nutritional, vitamin and body building supplements, particularly when consumed in large doses.

Table. Compounds That Commonly Cause Depression

Drug/Drug Class	QE	SR
ACE inhibitors	II-2	C
Amphetamine withdrawal	I	B
Anabolic Steroids	I	B
Antihyperlipidemics	II-2	C
Benzodiazepines	II-2	C
Cimetidine, Ranitidine	II-2	C
Clonidine	II-2	C
Cocaine withdrawal	I	C
Cycloserine	II-2	C
Digitalis	I	B
Glucocorticoids	I	B
Gonadotropin-releasing agonists	II-2	A
Interferons	II-2	C
Levodopa	II-2	C
Methyldopa	II-2	C

Metoclopramide	II-2	C
Oral contraceptives	II-2	C
Pimozide	II-2	A
Propranolol (Beta Blockers)	II-2	B
Reserpine	II-1	C
Topiramate	II-2	C
Verapamil (Calcium channel Blockers)	II-2	C

J. Do Medical Conditions Contribute to Symptoms?

Objective

To identify patients who may be experiencing depressed symptoms as a result of an underlying medical condition.

Annotation

The table below includes many of the pathobiologies associated with depression. Simultaneous treatment is often required for both the medical problem and psychiatric symptoms. Additionally there is often a strong association between the level of disability from the medical condition and the depressive symptom requiring treatment.

A useful mnemonic for remembering these is [TIC]<sup>2</sup>p<sup>2</sup>m<sup>2</sup>d<sup>3</sup>. The mnemonic stands for:

1. Trauma
2. Tumor
3. Infection - immune and autoimmune
4. Cardiac/vascular
5. Congenital/hereditary
6. Physiologic - seizure
7. Metabolic malignancy
8. Degenerative
9. Drug toxicity
10. Demyelinating

Patients with chronic pain may also have associated mood disturbance. This may be encountered among individuals suffering conditions such as Chronic Obstructive Pulmonary Disease (COPD) or Asthma or more commonly bone pain with cancer.

Table. Pathobiologies Related to Depression

Pathology	Disease
-----------	---------

Cardio/vascular	Coronary artery disease Congestive heart failure Uncontrolled hypertension Anemia Stroke Vascular Dementia
Chronic Pain Syndrome	Fibromyalgia Reflex sympathetic dystrophy Low back pain (LBP) Chronic pelvic pain Bone or disease related pain
Degenerative	Presbyopia Presbycusis Alzheimer's disease Parkinson's disease Huntington's disease Other Neurodegenerative diseases
Immune	HIV (both primary and infection-related) Multiple Sclerosis Systemic Lupus Erythematosus (SLE) Sarcoidosis
Infection	Systemic Inflammatory Response Syndrome (SIRS) Meningitis
Metabolic/Endocrine Conditions (include renal and pulmonary)	Malnutrition, vitamin deficiencies Hypo/hyperthyroidism Addison's Disease Diabetes mellitus Hepatic disease (cirrhosis) Electrolyte disturbances Acid-base disturbances Chronic obstructive pulmonary disease (COPD) or asthma Hypoxia
Neoplasm	Of any kind, especially pancreatic or central nervous system (CNS)

K. Meets DSM-IV Criteria for Major Depressive Disorder (MDD)?

Objective

To identify patients with the diagnosis of Major Depressive Disorder.

## Annotation

At least five symptoms of depression must occur simultaneously, and the symptoms must be present for most of the day, nearly every day, for at least two weeks. To meet formal diagnostic criteria, one of the symptoms present must be either depressed mood or anhedonia (loss of interest). When evaluating a patient for a major depressive episode, the symptoms of depressed mood, loss of interest, psychomotor agitation or retardation, and diminished ability to concentrate can be indicated by either the patient's subjective account or by evidence that the symptoms are apparent to others. Contacts with family members may be necessary to make an accurate diagnosis.

Note that past manic, mixed manic, or hypomanic episodes must be excluded before the diagnosis is confirmed. In addition, the depressive episode must not be due to Schizoaffective Disorder, Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder not otherwise specified.

See Appendix 1, Assessment Instruments, of the original guideline document for the DSM-IV Criteria for MDD.

## L. Treat Non-MDD Disorder in an Appropriate Setting

### Objective

To differentiate patients with other psychiatric disorders requiring specialty mental health care.

### Annotation

Other disorders that present with depressive features deserve serious consideration in mental health outpatient settings, but are outside the scope of this guideline. Information on some of the most common of these disorders appears in Appendix 6 of the original guideline document, Non-MDD Conditions Requiring Specialty Treatment. For information on the treatment of Psychosis and related psychiatric disorders, see Psychoses Guideline.

## M. Is This a Complex Patient Already in Treatment for Depression?

### Objective

To identify those patients who require more involved or specialized management.

### Annotation

Complicating factors that may influence treatment decisions include:

1. Current treatment - Any patient currently receiving treatment for depression

2. Provider responsible for coordinating current treatment - Any patient for whom you are not the provider that initiated the current treatment
  3. Prior treatment response - Any patient with a history of failed depression treatment or otherwise complicating treatment
  4. Comorbid mental health problems - Any patient with a co-existing mental health disorder in need of treatment or otherwise complicating treatment
  5. Co-morbid medical problems - Any patient with a co-existing medical condition that has significant impact on the course or treatment of depression
  6. Atypical depressive features - Any patient with some combination of depressive symptoms that include hypersomnia, hyperphagia, and/or rejection sensitivity
  7. Family or patient history of suicidality - Any patient with either a personal or family history of suicide attempts or suicidal ideas necessitating psychiatric hospitalization
  8. Recurrent depressive episodes - Any patient with more than one past depressive episode or a past depressive episode involving severe loss of functioning or other life consequences
- N. For the Patient Who Has Had Previous Episodes of Depression, Consider Partial Hospitalization

#### Objective

To provide the appropriate level of care to the patient.

#### Annotation

1. If there is a history of successful MDD treatment, consider reinstating the previously successful approach
2. If patient requires greater assistance or a higher intensity of care, consider partial hospitalization:
  - a. Partial hospitalization, or primary day hospitals are appropriate for patients with a depressive disorder when more support, observation, and intensive efforts than is available through clinic appointments is needed. Day hospitals, where they are available, may run in conjunction with residential care and are available for patients for up to eight hours a day, as an alternative to or an extension of acute hospitalization.
  - b. Common indications for partial hospitalization are:
    1. The patient has a DSM-IV disorder with decompensation severe enough to impair daily social, vocational, or educational functioning.
    2. The patient is not an imminent risk for harm to self or others and has sufficient impulse control to be maintained outside of an acute inpatient setting.
    3. The patient has sufficient community-based support to be maintained outside of an acute inpatient setting.
    4. The patient is able to participate in and cooperate with partial hospitalization treatment.
    5. One of the following criteria have been met:

- The patient has not improved after an adequate trial of outpatient treatment
- The patient is unlikely to improve with an adequate trial of outpatient treatment
- The patient is being discharged from an acute inpatient setting but continues to need daily monitoring, support, and therapeutic intervention

O. Modify, Maintain, or Initiate Interdisciplinary Treatment Plan

Objective

To describe a course of clinical action for the various types of complex patients with MDD.

Annotation

The patient should be assigned to a consistent interdisciplinary mental health care team, including members who represent both biomedical and psychosocial perspectives. The interdisciplinary team may include members of the following disciplines depending on the patient's unique health care needs:

1. Psychiatry - management of psychiatric disorders
2. Primary care provider - coordination of the patient's overall health and preventive care
3. Medical specialists other than psychiatry - as indicated by medical comorbidities
4. Psychology - for behavioral and emotional aspects of care to include psychotherapy, biofeedback, and similar modalities
5. Social work - for coordination of community resources, counseling, and support groups
6. Nursing - health education and training such as for home health care and routine follow-up health care
7. Pharmacist - for the patient on pharmacotherapy, especially those on multiple medications, co-morbid medical conditions requiring pharmacotherapy or interacting with the patient receiving antidepressant therapies
8. Dietary - for education pertaining to nutritional status and dietary aspects of pharmacotherapy (e.g., MAOIs)
9. Occupational therapy - assistance for the patient in need of life skills training
10. Recreational therapy - assistance for the patient in need of employment and/or benefits counseling
11. Vocational rehabilitation - assistance for the patient in need of employment and /or benefits counseling
12. Chaplaincy - assistance for the patient with religious or spiritual concerns or requests

The interdisciplinary team will discuss the patient's diagnosis, etiological factors, and potential treatment options. Treatment options will also be discussed with the patient. Patient preference will play a major role in deciding what treatment(s) to initiate.

After decisions are made, it is preferable that a specific provider individualizes and coordinates the patient's care. If the patient is hospitalized, the current provider will either continue the care or arrange timely follow-up with another practitioner. The practitioner will establish a close working alliance with the patient, characterized by caring, shared decision-making, and respect for patient privacy. The practitioner will continue to consult with the interdisciplinary team, particularly if the patient does not improve during the first planned course of treatment.

#### Evidence

Fluoxetine treatment for MDD is not associated with an increased likelihood of suicidal behavior. (Leon et al., 1999; Warshaw, 1996) Quality of the evidence: II-3, Strength of recommendation: B

Clinical characteristics can help target patients with MDD at high risk for relapse. Risk factors identified included persistent subthreshold depressive symptoms, chronic mood symptoms, or history of two or more major depressive episodes. (Lin et al., 1998) Quality of the evidence: II-1, Strength of recommendation: B

Patients with atypical depression features are less responsive to TCAs (unreplicated). (Stewart et al., 1998) Quality of the evidence: II-2; Strength of recommendation: C

Sertraline maintenance therapy is well tolerated and prevents recurrence or reemergence of depression in chronically depressed patients. (Keller et al., 1998) Quality of the evidence: I, Strength of recommendation: B

Cognitive therapy is an effective acute phase treatment alternative to MAOI antidepressant medications for patients with MDD and atypical features (unreplicated). (Jarrett et al., 1999) Quality of the evidence: I, Strength of recommendation: C

Analyses of coroners' data suggest that TCAs are associated with elevated death rates in overdose compared with SSRIs. (Montgomery, 1997) Quality of the evidence: III, Strength of recommendation: C

Presence of personality disorders has generally been linked to poorer outcomes for treatment of MDD. (Thase, 1996) Quality of the evidence: II-1, Strength of recommendation: B

#### P. Discuss Treatment Options and Patient's Preferences

##### Objective

To guide informed decisions about treatment options.

##### Annotation

Before initiating any specific treatment(s), the clinician should discuss with the patient (and family, where appropriate) the nature of the disorder. The following treatment options should be discussed and offered, including risks and benefits of each (AHCPR Depression Guideline, Vol. 2, p. 38). Patients should be encouraged to engage in treatment.

There are four broad treatment options for patients with MDD. These are:

1. Pharmacotherapy including other somatic therapies [e.g., electroconvulsive therapy (ECT)]
2. Empirically Supported psychoTherapies (EST)
3. Combined psychotherapy and pharmacotherapy
4. Clinical evaluation of one to three visits

Patients should be educated about the potential consequences of untreated MDD, and encouraged to return.

Pharmacotherapy - There is a wide range of available antidepressant medications for patients to select from (see Appendix 5 of the original guideline document, Pharmacological Therapy of MDD). The specific medication choice is generally based on side effect profiles, safety in overdose, history of prior response, concomitant medical conditions, family history of response, and type of depression.

Benefits of pharmacotherapy include:

5. Potential of a more rapid initial treatment response
6. Patient's preference for medications over talk therapies

Risks or drawbacks of pharmacotherapy include:

7. Need to take medications consistently and exactly as prescribed
8. Potential for medication side-effects or interactions with other medications or medical problems
9. Potential for need to take medication for an indefinite or extended period

Psychotherapy - This is the use of one of the ESTs, offered in either one-on-one or group format. See Appendix 4, Empirically Supported psychoTherapy (EST), of the original guideline document for a full list of the ESTs and supporting evidence. Generally these approaches aim to help depressed individuals thoughtfully examine their behavior, beliefs, emotions, stressors, and personal relationships in an effort to lead to lasting change in factors that may have contributed to the development of depression. For the purposes of this guideline, psychotherapy is NOT simply unstructured and brief support commonly offered in the context of a primary care office visit.

Benefits of psychotherapy include:

10. Effects may persist beyond the duration of treatment

11. The need to take antidepressant medications or experience medication side-effects may be reduced
12. An opportunity for the patient to make meaningful self-improvements or life changes

Risks or drawbacks of psychotherapy include:

13. Patients need to come consistently for therapy appointments on a frequent basis for several months at a time
14. A therapist trained in an empirically supported psychotherapy may not be available in every care setting

Clinical Evaluation - For patients that do not meet criteria for complexity, an extended (two to three visits) can often identify those patients whose depressive symptoms are transient. Some individuals will have spontaneous remission of symptoms, particularly when symptoms have been precipitated by a life crisis. The main risk of extended clinical evaluation is that MDD may not respond and may worsen without active treatment.

Evidence

Neither pharmacotherapy nor empirically supported psychotherapy have been shown to be consistently superior in the immediate or long term outcomes. (Rush & Hollon, 1991; Reynolds et al., 1999) Quality of the evidence: I, Strength of recommendation: A

Medication treatment may lead to faster response, whereas psychotherapy (particularly cognitive behavioral therapy) may reduce risk of relapse. (Fava et al., 1994; Rush & Hollon, 1991) Quality of the evidence: I, Strength of recommendation: A

Combination of an empirically supported psychotherapy with medication has not been shown to produce consistently better outcomes for most patients than use of. (Reynolds et al., 1999) Quality of the evidence: I, Strength of recommendation: C

Severity of depression among psychiatric outpatients is not a reliable discriminator of short term response to either medication or empirically supported psychotherapies. (DeRubeis et al., 1999) Quality of the evidence: II-B, Strength of recommendation: B

#### Q. Provide Patient/Family Education

Objective

To assist the patient/family in making informed decisions by providing the patient and family information about the disease process, treatment options, and expectations so they may make an informed decision.

Annotation

See Appendix 7 of the original guideline document, Patient Education.

#### R. Can the Patient be Followed in the Primary Care Setting?

##### Objective

To state general considerations for determining the extent that the MDD patient can be appropriately managed in the primary care setting.

##### Annotation

1. The patient, primary care provider, and the remainder of the interdisciplinary team are to collaborate in all decisions regarding the appropriate intensity and setting for follow-up MDD care.
2. Facilitation of primary care-based MDD treatment should involve a detailed plan with parameters for return to specialty mental health care as appropriate for questions, concerns, or intensified need.

There is broad range of training, experience, and comfort with the provision of mental health care among primary care clinicians. All members of the interdisciplinary team, including the patient, must be comfortable with the patient's management in the primary care setting. Examples of MDD patients often amenable to primary care manager (PCM) treatment include:

3. Those with their first episode of MDD
4. Those well controlled on medication or psychotherapy (maintenance or remission)
5. Those with co-morbid medical conditions requiring frequent primary care visits

##### Evidence

Clinical characteristics can help target patients with MDD at high risk for relapse. Risk factors identified included persistent subthreshold depressive symptoms, chronic mood symptoms, or history of two or more major depressive episodes. (Lin et al., 1998) Quality of the evidence: II-1, Strength of recommendation: B

A substantial proportion of PCPs report diagnostic and treatment approaches that are consistent with high-quality depression care. (Williams et al., 1999) Quality of the evidence: II-2, Strength of recommendation: B

#### S. Monitor Treatment Every 1 to 2 Weeks. Assess Adherence and Side Effects

##### Objective

To assess response to therapy.

##### Annotation

1. Assess treatment response - If the patient is responding to current treatment, but the response is only partial, or if the patient is not responding to current treatment, then assess treatment adherence and side effects.
2. Assess treatment adherence - Is the patient attending therapy sessions regularly? If not, why? Is the patient taking prescribed antidepressants or other medicines as directed? If not, why? The patient's answers to these questions will suggest whether a modification of treatment is necessary to achieve a therapeutic response.
3. Assess treatment side effects - Side effects are a common reason for poor adherence to therapy. Undesirable side effects of psychotherapy may include the need to miss work or other important activities and unanticipated effects on important relationships or increases in symptoms.

The following problems may be noted during follow-up:

4. Patient is not taking medication as prescribed (e.g., does not obtain refills of medication at appropriate intervals)
5. Patient is not attending psychotherapy appointments consistently
6. Patient expresses dissatisfaction with treatment due to side effects of medications, difficulty following psychotherapy protocol, perceived problems with the assigned therapist, and/or a request for change

T. Response in 4 to 6 weeks?

Objective

To assess and manage response to therapy.

Annotation

Research studying the effectiveness of pharmacotherapy, psychotherapy, or both suggests a partial remission (50 percent symptom reduction) is common within four to six weeks of treatment. Full response, defined as minimal or no symptoms, often requires a longer duration of treatment; full restoration of psychosocial function may take several months.

Evidence

Four to six weeks allows titration to adequate antidepressant therapy and time for response to therapy. (AHCPR Guideline for Depression in the Primary Care Setting, 1993; American Psychiatric Guideline for Major Depression, 1993; Schulberg et al., 1998) Quality of the evidence: II-3, Strength of recommendation: B

The rate of response for those showing no improvement by week four will be very low and no better than placebo. (Quitkin et al., 1996) Quality of the evidence: II-1, Strength of recommendation: B

U. Remission?

## Objective

To assess whether the patient with MDD achieves a full remission of symptoms.

## Annotation

Remission is defined as a return to full pre-morbid functioning accompanied by a substantial reduction of depressive symptoms. For research studies, experts typically define remission and improvement as a change in score on standardized rating scales such as the HAM-D. Many efficacy studies cite a 50 percent response rate to define improvement, but a more complete symptom and functional status response is necessary to achieve remission. Expert consensus supports a fairly complete symptom and functional status response before declaring a remission of symptoms.

The use of rating instruments is one approach to looking for symptom remission. Measures of use include the Hamilton Depression Rating Scale, PRIME-MD Patient Health Questionnaire (PHQ), the Beck Depression Inventory, and the Zung Depression Rating Scale (See Appendix 1 of the original guideline document, Assessment Instruments). In specialty mental health care settings, use of a valid, reliable, and systematic assessment of depression symptoms is recommended.

## Evidence

Remission defined as the patient no longer meeting the DSM III-R criteria for major depression and having Hamilton Depression Scale scores less than seven for up to three consecutive weeks. (Reimherr et al., 1998) Quality of the evidence: II-2, Strength of recommendation: B

Texas Medication Algorithm Project Report defined remission as equal to or greater than 75 percent global improvement in symptoms. Emphasized goal of symptomatic remission and normalization of function rather than only symptom improvement. (Crismon et al., 1999) Quality of the evidence: III, Strength of recommendation: B

Remission defined as the total final Hamilton Depression Scale 24 item score equal to or less than seven. (Hirschfeld et al., 1998) Quality of the evidence: III, Strength of recommendation: B

Danish University Antidepressant Group defined full remission as seven or less on the 17 item HAM-D. (Fuglum et al., 1996) Quality of the evidence: III, Strength of recommendation: B

## V. Institute Continuation and Maintenance Phase Treatment. Follow-up Including Prevention and Patient/Family Education.

### Objective

To prevent relapse or recurrence of future major depressive episodes.

## Annotation

MDD is best conceptualized as a chronic illness resulting in a continuum of outcomes ranging from excellent to poor. Increased rates of recurrence were found in fifty percent of the patients with a single episode of MDD, and the greater the number of episodes the more likely are future depressive episodes. A high percentage of individuals with recurrent major depressive disorder will require indefinite prophylactic antidepressant treatment. Factors increasing the risk of future recurrence include:

1. A strong family history of mood disorders
2. A history of recurrence within one year after discontinuation of a previously efficacious medication
3. One or more suicide attempts
4. Onset of the first episode before age 20
5. Two or more episodes of major depression in the past two years
6. Concurrent dysthymia

Continuation phase of antidepressant treatment follows the acute phase and begins when the patient has complete remission of depressive symptoms. Continuation phase treatment usually lasts up to nine months and is followed by maintenance phase treatment, an indefinite period of prophylaxis against future depressive episodes.

Continuation Phase Treatment - Priorities of the continuation phase include sustaining the dose of medication resulting in acute phase symptom remission; preventing relapse or recurrence of depressive symptoms; monitoring depressive symptoms and functional status; and building a constructive therapeutic alliance.

In psychotherapy, a maintenance plan should be developed as during the course of therapy. The plan should include a summary of learning that occurred during therapy; ways the patient will continue to use lessons from the therapy; a prediction of times of high recurrence risk (e.g., death of a significant other); and coping approaches for such crisis periods. Use of booster sessions and occasional re-assessment of depressive symptoms should be considered.

Maintenance Phase Treatment - Following the continuation phase, decisions regarding extended maintenance phase treatment are implemented. Patients who have had three or more episodes of major depression or two or more episodes in combination with another risk factor for recurrence (see list above) should remain on prophylactic antidepressant medication for one or more years after remission of the acute episode at the continuation phase dosage.

Patient/Family Education - It is important for patients and families concerning risk of relapse and ways to reduce risk and sustain remission status. Information about recurrence risk factors, medications, and early recognition of recurrence should be included.

W. Does Patient Meet Criteria for Hospitalization?

## Objective

To decide whether the patient requires inpatient psychiatric hospitalization.

## Annotation

Usual reasons for inpatient hospitalization include acute suicide risk; acute violence risk due to mental illness; or grave disablement due to mental illness (e.g., loss of ability to provide basic personal hygiene, shelter, clothing, or food). See Appendix 1 of the original guideline document, Assessment Instruments, for SAIC Criteria for Hospitalization.

Sometimes specialized treatment is only available or best provided in a hospital. Examples include:

1. Electroconvulsive therapy (ECT)
2. Close monitoring and daily titration of medication with disabling side effects or toxicity
3. Constant staff observation as part of an intensive behavioral modification program
4. Close monitoring of behavior in an episodic disorder
5. Close monitoring of vital signs or need for multiple daily laboratory or electrophysiological test

Specific admission criteria must be determined at each setting reflecting local circumstances. Use of a national uniform standard, such as the SAIC standards (See Appendix 1 of the original guideline document, Assessment Instruments). VHA's Under Secretary for Health has recommended review of all admissions using standardized utilization review criteria (e.g., InterQual Medical Necessity Criteria or SAIC Inpatient Criteria). Department of Defense has adopted the use of SAIC admission criteria for CHAMPUS contracts, such that any facility (including VHA or DoD) providing CHAMPUS care is expected to use SAIC criteria for utilization review in accordance with the specifications of its contract.

## X. Were There Prior Episodes of Treatment Resistance?

### Objective

To assess for the presence of treatment resistant MDD.

### Annotation

Treatment-resistant MDD is present if there has been an inadequate response to two or more adequate trials of depression treatment. An adequate trial of antidepressant medication must be at least six weeks of treatment at an adequate daily dosage. The diagnosis of MDD should be reconsidered/reverified and the possibility of a coexisting medical or psychiatric problem should be excluded. The following treatment modalities may be considered for individuals with treatment resistant MDD:

1. Psychotherapy is a useful augmentation strategy for treatment refractory MDD.
2. The clinician should attempt to augment treatment if there has been a partial response to one antidepressant. This can be accomplished by adding tri-iodothyronine (T3), 25 to 50 micrograms in one daily dose to the existing medication regimen. Baseline thyroid function tests (T4, TSH) are not predictive of response but provide a means of ensuring that TSH levels are no more than partially suppressed during T3 therapy.
3. An alternative strategy is to add lithium carbonate, 600 to 900 mg per day, to the existing medication regimen. The dosage is titrated to therapeutic serum levels. Lithium augmentation may be less efficacious for patients with multiple depressive episodes in a year compared to individuals with less frequent episodes.
4. Trazodone, 50 to 100 mg at night, is sometimes used to improve sleep among depressed patients, particularly those on an SSRI. Sometimes this allows higher doses of SSRI when insomnia is a dose-limiting side effect. Trazodone is preferable to benzodiazepines or other sedative-hypnotics for chronic sleep disturbance accompanying depression.
5. Bupropion may be used with SSRIs, particularly among patients complaining of fatigue or sexual dysfunction.
6. Anticonvulsants (e.g., carbamazepine) may be useful with conventional antidepressants, particularly among patients with patients with multiple depressive episodes in a year or those with prominent impulsivity, irritability, and/or anxiety.
7. Changing the class of antidepressant may help. Patients with atypical depression characterized by unrelenting mood reactivity, rejection sensitivity, hypersomnia, 'leaden paralysis', or increased appetite respond well to MAOI inhibitors. Combination MAOI-TCA therapy is risky and requires an experienced psychopharmacologist. If response is achieved, consideration should be given to tapering and discontinuing the TCA.
8. ECT is useful for treatment-refractory MDD. If ECT is successful, it should be followed by maintenance therapy using an antidepressant or maintenance ECT.

#### Evidence

Patients with atypical MDD are preferentially responsive to MAOIs. (Liebowitz et al., 1988) Quality of the evidence: I, Strength of recommendation: B

T3 increases the rapidity of TCA response by approximately 25 percent. (Nemeroff, 1991) Quality of the evidence: I, Strength of recommendation: C

A significant percentage of patients with antidepressant treatment resistant MDD respond to ECT. (Prudic, Sackeim, & Rifas, 1994) Quality of the evidence: II-2, Strength of recommendation: C

#### Y. Re-evaluate/Consider Consultation

#### Objective

To monitor patient response to treatment and manage any needed adjustments.

#### Annotation

AHCPR Clinical Practice Guidelines for treating depression in primary care recommend consultation when the clinician feels they lack sufficient knowledge or experience to manage a patient's medication or if two or more attempts at acute phase medication treatment have failed or resulted in partial response. Consultation options in the mental health specialty setting include a local clinical case conference, psychological testing, specialized psychopharmacology clinic or pharmacist, or referral to a specialized mood disorders program.

Failure to display at least a partial remission (25 to 50 percent symptom reduction) at this point should evoke concern regarding:

1. Adherence - poor adherence is commonly due to adverse effects of treatment, patient misunderstanding about treatment, or other causes.
2. Concurrent medical illness - this may impede clinical response, especially if the medical condition is poorly controlled or compensated.
3. Co-morbid psychiatric disorders
4. Co-morbid substance use disorder
5. Exacerbating psychosocial stressors
6. Error in diagnosis

### [Algorithm C - Inpatient Mental Health Specialty](#)

#### Module C: Management of Major Depressive Disorder in Adults in the Inpatient Mental Health Setting

##### A. Patient Admitted to Inpatient Unit with Presumptive Diagnosis of MDD

###### Definition

This module applies to any patient newly admitted to inpatient psychiatric care for purposes of intensifying care or providing a more restrictive management setting. This is generally a relatively high-risk patient for whom effective psychiatric care is essentially unmanageable in a lower level of care.

##### B. Initial Assessment for Risk and Unstable Medical Condition

###### Objective

To assess the newly admitted inpatient for factors that may acutely alter the required treatment setting or intensity.

###### Annotation

Newly admitted psychiatric patients should be considered unstable until an initial assessment can be obtained. The patient should first be assessed for psychiatric or medical instability. Assessment of dangerousness includes acute risk of harming self or others. Assessment of medical instability should focus on medical conditions that will necessitate rapid consultation with either a medical or surgical consultant and/or precipitate transfer to a medical or surgical inpatient service.

Refer to Appendix 2, Unstable and High Risk Conditions, of the original guideline document for information about potential dangerousness and/or urgent medical conditions.

C. High Risk for Suicide, Violence, or Other Precautions Are Required?

Objective

To implement the least restrictive strategies that will ensure patient safety.

Annotation

Assess treatment setting and patient for factors related to maintaining patient safety. Patients are to be admitted to the least restrictive treatment setting, indiscriminate use of "closed admitting wards" is discouraged. Potential for self-harm and harm to others must be reassessed upon admission even if a very recent pre-admission assessment was completed.

Special observation is a common nursing activity in psychiatric units and may employ intensified observation and assessment of high-risk patients. The indication, intensity and duration of special observation should be based upon the individual needs of the patient within parameters established by local facility policy, national hospital guidelines, and medical and legal standards.

D. Obtain History Including (Psychiatric, Family, Psychosocial, Military, Stress, Past Physical or Sexual Abuse, and Substance Use). Perform MSE and GAF or Axis V of DSM-IV, Physical Examination, Laboratory Tests, and Other Studies as Indicated

See Annotation E from Module B. Functional Status Assessment Instruments such as the GAF and SF-36 provide a means of determining the patient's ability to perform certain activities and/or respond to therapy at the time. These instruments also provide a baseline from which to measure improvement in functionality.

E. Is Medical Condition Contributing to Symptoms?

Objective

To identify patients who may be experiencing depressed symptoms as a result of an underlying medical condition.

Annotation

Many prescription or over-the-counter medicines can cause or compound symptoms of depression. Many pathobiologies may cause or compound symptoms of depression. For more detail see Module B Annotation J.

Table. Compounds That Commonly Cause Depression

Drug/Drug Class	QE	SR
ACE inhibitors	II-2	C
Amphetamine withdrawal	I	B
Anabolic Steroids	I	B
Antihyperlipidemics	II-2	C
Benzodiazepines	II-2	C
Cimetidine, Ranitidine	II-2	C
Clonidine	II-2	C
Cocaine withdrawal	I	C
Cycloserine	II-2	C
Digitalis	I	B
Glucocorticoids	I	B
Gonadotropin-releasing agonists	II-2	A
Interferons	II-2	C
Levodopa	II-2	C
Methyldopa	II-2	C
Metoclopramide	II-2	C
Oral contraceptives	II-2	C
Pimozide	II-2	A
Propranolol (Beta Blockers)	II-2	B
Reserpine	II-1	C
Topiramate	II-2	C
Verapamil (Calcium channel blockers)	II-2	C

F. Meets DSM-IV Criteria for Major Depressive Disorder (MDD)?

See Appendix 1, Assessment Instruments, of the original guideline document for the DSM-IV Criteria for MDD.

G. Identify and Treat Depression While Treating Other Co-morbid Conditions

Objective

To determine treatment for depressed patient with co-morbid conditions.

Annotation

Depression may appear in conjunction with other DSM-IV, Axis 1, 2, or 3 diagnoses.

See Appendix 6, Non-MDD Conditions Potentially Requiring Specialty Consultation, of the original guideline document for some examples of co-morbid disorders. Also consider other DSM-IV and ICD-10 conditions in conjunction with depression and related disorders.

- H. Complete Interdisciplinary Treatment Plan Addressing: Medication, Appropriate Psychotherapy, Other Psychosocial Interventions. Consider Co-morbidity if it exists, and Patient Preferences.

#### Objective

To describe a course of clinical action for the various types of complex patients with MDD.

#### Annotation

The patient should be assigned to a consistent interdisciplinary mental health care team, including members who represent both biomedical and psychosocial perspectives. The interdisciplinary team may include members of the following disciplines depending on the patient's unique health care needs:

1. Psychiatry - management of psychiatric disorders
2. Primary care provider - coordination of the patient's overall health and preventive care
3. Medical specialists other than psychiatry - as indicated by medical co-morbidities
4. Psychology - for behavioral and emotional aspects of care to include psychotherapy, biofeedback, and similar modalities
5. Social work - for coordination of community resources, counseling, and support groups
6. Nursing - health education and training such as for home health care and routine follow-up health care
7. Pharmacist - for the patient on pharmacotherapy, especially those on multiple medications, co-morbid medical conditions requiring pharmacotherapy or interacting with the patient antidepressant therapies
8. Dietary - for education pertaining to nutritional status and dietary aspects of pharmacotherapy (e.g., MAOIs)
9. Occupational therapy - assistance for the patient in need of life skills training
10. Recreational therapy - assistance for the patient in need of employment and/or benefits counseling
11. Vocational rehabilitation - assistance for the patient in need of employment and /or benefits counseling
12. Chaplaincy - assistance for the patient with religious or spiritual concerns or requests

The interdisciplinary team will discuss the patient's diagnosis, etiological factors, and potential treatment options. Treatment options will also be

discussed with the patient. Patient preference will play a major role in deciding what treatment(s) to initiate.

After decisions are made, it is preferable that a specific provider individualizes and coordinates the patient's care. If the patient is hospitalized, the current provider will either continue the care or arrange timely follow-up with another practitioner. The practitioner will establish a close working alliance with the patient, characterized by caring, shared decision-making, and respect for patient privacy. The practitioner will continue to consult with the interdisciplinary team, particularly if the patient does not improve during the first planned course of treatment.

#### Evidence

Fluoxetine treatment for MDD is not associated with an increased likelihood of suicidal behavior. (Leon et al., 1999; Warshaw, 1996) Quality of the evidence: II-3, Strength of recommendation: B

Clinical characteristics can help target patients with MDD at high risk for relapse. Risk factors identified included persistent subthreshold depressive symptoms, chronic mood symptoms, or history of two or more major depressive episodes. (Lin et al., 1998) Quality of the evidence: II-1, Strength of recommendation: B

Patients with atypical depression features are less responsive to TCAs (unreplicated). (Stewart et al., 1998) Quality of the evidence: II-2; Strength of recommendation: C

Sertraline maintenance therapy is well tolerated and prevents recurrence or reemergence of depression in chronically depressed patients. (Keller et al., 1998) Quality of the evidence: I, Strength of recommendation: B

Cognitive therapy is an effective acute phase treatment alternative to MAOI antidepressant medications for patients with MDD and atypical features (unreplicated). (Jarrett et al., 1999) Quality of the evidence: I, Strength of recommendation: C

Analyses of coroners' data suggest that TCAs are associated with elevated death rates in overdose compared with SSRIs. (Montgomery, 1997) Quality of the evidence: III, Strength of recommendation: C

Presence of personality disorders has generally been linked to poorer outcomes for treatment of MDD. (Thase, 1996) Quality of the evidence: II-1, Strength of recommendation: B

#### I. Initiate Discharge Planning and Patient/Family Education

See Appendix 7 of the original guideline document, Patient Education

#### J. Global Assessment of Function (GAF) or Lethality Sufficient to Justify Continued Hospitalization?

## Objective

To determine if the patient is safe to discharge to a less restrictive level of care.

## Annotation

The clinician should reassess whether the patient meets all of the following criteria for discharge to a less restrictive environment:

1. Stabilization and/or improvement of symptoms
2. Level of functioning allowing maintenance care in a less restrictive setting
3. No acute manifestations of intent to harm self or others
4. Support level allows active participation in aftercare

See Appendix 1, Assessment Instruments, and Appendix 2, Unstable and High Risk Conditions, of the original guideline document for more information.

## K. Discharge to the Appropriate Mental Health Level of Outpatient Care. Schedule Follow-up Appointment.

### Objective

To ensure appropriate level and continuity of care following discharge from the inpatient psychiatric setting.

### Annotation

Discharge planning serves as a vehicle to guide the patient/family to a successful termination of inpatient care, constructive re-integration into the community and staging for the implementation of a plan of continued recovery. Patient and family participation and education as well as continuity of care are the cornerstones of its effective application. The plan is interdisciplinary in nature (physician, psychologist, nurse, social worker, nutritionist, etc.) and identifies specific criteria for successful completion of inpatient care. Criteria will vary based on the goals of the setting, age and level of impairment. This critical activity proceeds throughout the hospitalization and requires timely and thoughtful preparation.

Discharge planning focuses on meeting the patient's assessed needs in critical domains of care. The plan is developed with the patient and family and should address the continuing physical, social, emotional, and psychological care requirements. It also attends to aspects of care that include:

- Patient and family education on aspects of all health care and high risk behaviors
- Substance abuse
- Functional status for self care, independent living and its compatibility with living arrangements
- Safe, decent, affordable, stable, and secure a domicile

- Family support for patient's recovery
- Constructive social activity that is consistent with continuing care goals
- Viable source of income that supports community re-entry
- Venue for continued or future employment that utilizes patient's skills
- Capacity to locate and access needed services as disruptive events impact on patient's stability

In preparation for the patient's discharge, the patient and family should be provided education on the following:

- The course, prognosis, and causes of depression
- Factors that will exacerbate depression
- Strategies for adaptive coping
- Techniques for relapse prevention
- Medical and psychosocial follow-up plans
- Instructions regarding discharge medications and their risks and benefits

Whenever a patient is discharged from the inpatient setting, appropriate patient information is communicated as a formulated discharge plan to ensure continuity of health care. The discharge plan consists of relevant information, including:

- The reason for treatment
- Date of admission and discharge
- Clinically significant findings
- Patient's physical and psychosocial status at admission and discharge
- Summary of care provided including progress made toward patient care goals
- Strengths, abilities, needs, and preferences of the patient
- Reason for hospital discharge
- Community resources or referrals provided or recommended to the patient and/or family
- Any specific instructions given to the patient and/or family

Instructions for care after discharge are given not only to the patient and family, but also to the clinician responsible for coordinating the patient's medical care.

#### L. Are There Indications for ECT?

##### Objective

To determine if the patient is a candidate for ECT.

##### Annotation

Primary ECT - ECT may be justified as primary therapy for MDD if any of the following are present:

0. Psychotic features

1. Catatonic stupor
2. Severe suicidality
3. Food refusal leading to nutritional compromise
4. A history of prior good response

ECT is justifiable as a first line therapy for the following indications:

5. Need for rapid, definitive treatment response on either medical or psychiatric grounds
6. Risks of other treatments outweigh the risks of ECT
7. A history of poor drug response
8. Patient preference

Secondary ECT - Secondary use of ECT may be justified for any of the following:

9. Major depression accompanied by:
  - a. Documented antidepressant treatment failure after an adequate trial (medication, dosage, and time frame must be recorded in the medical record)
  - b. Intolerable side effects of antidepressant medications (e.g., seizures, blood dyscrasia, second- and third-degree heart block, severe hypotension, severe anxiety)
10. Mania accompanied by:
  - a. Documented failure to respond to pharmacological mood stabilizers (lithium, carbamazepine, valproic acid)
  - b. Intolerable side effects to mood stabilizers (e.g., blood dyscrasia, dermatitis)
11. Psychosis with acute neuroleptic malignant syndrome
12. Schizophrenia and other functional psychoses
13. History of favorable response to ECT
14. Indications for secondary use include:
  - a. Treatment failure
  - b. Unavoidable adverse effects using alternative treatments
  - c. Deterioration of patient's condition such that first criterion is met
  - d. Informed Consent is required for all ECT.

See Appendix 8 of the original guideline document, Electro-convulsive Therapy.

#### M. Begin Pharmacotherapy or ECT as Indicated

##### Objective

To describe somatic therapies for the inpatient with MDD.

##### Annotation

See Appendix 5, Pharmacological Management of MDD; and Appendix 8, Electroconvulsive Therapy, of the original guideline document.

## Strength of Recommendation (SR)

### Strength of Recommendation

- A. There is good evidence to support the recommendation that the condition be specifically considered in a periodic health examination.
- B. There is fair evidence to support the recommendation that the condition be specifically considered in a periodic health examination.
- C. There is insufficient evidence to recommend for or against the inclusion of the condition in a periodic health exam, but recommendations may be made on other grounds.
- D. There is fair evidence to support the recommendation that the condition be excluded from consideration in a periodic health examination.
- E. There is good evidence to support the recommendation that the condition be excluded from consideration in a periodic health examination.

### Quality of Evidence

I - Evidence obtained from at least one properly randomized controlled trial.

II-1 - Evidence obtained from well-designed controlled trials without randomization.

II-2 - Evidence obtained from well-designed cohort or case-control analytical studies, preferably from more than one center or research group.

II-3 - Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III - Opinions of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

The strength of recommendation uses evidence that supports (or does not support) the suggested intervention. The quality of the evidence is related to study design, such as large randomized control trials.

### Abbreviations

ADA - American Diabetes Association

AHCPR - Agency for Health Care Policy and Research

AUDIT - Alcohol Use Disorders Identification Test

BDI - Beck Depression Inventory

BP - blood pressure

CAGE - screening mnemonic for determining drunkenness  
(Cutting down drinking; Annoyance at others for receiving criticism about drinking; feeling Guilty or bad about drinking; using alcohol as an Eye-opener in the morning)

CBC - complete blood count

CBT - cognitive behavioral therapy

CESD - Center for Epidemiological Studies - Depression Scale

CHF - congestive heart failure

CNS - central nervous system

CO<sub>2</sub> - carbon dioxide

COPD - chronic obstructive pulmonary disease

DAST - Drug Abuse/dependence Screening Test

DM - diabetes mellitus

DoD - Department of Defense

DSM-IV - Diagnostic and Statistical Manual of Mental Health Disorders

DTR - deep tendon reflex

ECG - electrocardiogram

ECDT - elevated carbohydrate deficient transferrin

ECT - electro-convulsive therapy

ESR - erythrocyte sedimentation rate

ESRD - end stage renal disease

ESTs - empirically supported psychotherapies

ETOH - ethanol

g - gram

GAF - Global Assessment of Function

GAS - Health-Sickness Rating Scale called the Global Assessment Scale: A Procedure for Measuring Overall Severity of Psychiatric Disturbance

GGTT - Gamma glutamic transferase

Ham-D - Hamilton Depression Scale

IPT - Interpersonal Therapy

LBP - low back pain

LFT - liver function tests

MAOIs - monoamine oxidase inhibitors

MAST - Michigan Alcoholism Screening Test

MCV - mean corpuscular volume

MDD - major depressive disorder

MDE - major depressive episode

MH - mental health

MMSE - mini-mental status examination-Folstein

mg/dL - milligrams per deciliter

mmols/dL - millimoles per deciliter

MSE - mental status examination

MOS - medical outcomes study

PBMMAP - Pharmacy Benefits Manual Medical Advisory Panel

PCM - primary care manager

PHQ - Patient Health Questionnaire

PRIME MD - Primary Care Evaluation of Mental Disorders

PTSD - post-traumatic stress disorder

OTC - over the counter

RCT - randomized control trial

SAIC- Science Allocations International Corporation

SAMe - s-adenosylmethionine

SDDS-PC- Symptom Driven Diagnostic System for Primary Care

SF-36 - Standard Form-36, Quality of Life

SIRS - Systemic Inflammatory Response Syndrome

SLE - Systemic Lupus Erythematosus

SMAST- Short Michigan Alcoholism Screening Test

SMBG- self-monitoring blood glucose

SSRIs - Selective Serotonin Reuptake Inhibitors

SUD - substance use disorder

T3 - Tri-iodothyronine

TCAs - Tricyclic antidepressants

TSH - thyroid stimulating hormone

UA - Urinalysis

VA - Veterans Administration

VHA - Veterans Health Administration

#### CLINICAL ALGORITHM(S)

Algorithms are provided for the management of major depressive disorder in adults in the:

1. Primary care setting:
  - [Algorithm A1 - Initial Assessment](#)
  - [Algorithm A2 - Establish Diagnosis](#)
  - [Algorithm A3 - Initial Assessment and Treatment](#)
  - [Algorithm A4 - Follow-up Treatment](#)
2. [Algorithm B - Outpatient Mental Health Specialty](#)
3. [Algorithm C - Inpatient Mental Health Specialty](#)

### EVIDENCE SUPPORTING THE RECOMMENDATIONS

#### REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

#### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Where existing literature is ambiguous or conflicting, recommendations are based on Expert Panel opinion. In the guideline you will note that the evidence grading is not valid for the content of the whole article, but about a specific criterion being recommended. These criteria have been noted in the evidence section of the guideline so that the reader and user of the guideline can know the quality of the evidence or study represented and the strength of recommendation of the specific action being recommended.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

General:

- Implementation of the guideline can assist the primary care provider in early detection of symptoms and intervention, with possible prevention of the full initial episode and/or recurrence of major depressive disorder.
- In addition, research shows that a range of cost-effective treatments is feasible and efficacious in both the primary care and specialty mental health care settings. Effective treatment can reduce and/or eliminate depression symptoms, improve health-related quality of life, and, in some research, even improve occupational performance and productivity among those with major depressive disorder (MDD). Other research has shown that guideline-driven improvements in the quality of depression care can result in improved symptoms and symptom-related quality of life for those affected.

Specific:

- Benefits of pharmacotherapy, include:
  - Potential of a more rapid initial treatment response
  - Patient's preference for medications over talk therapies
- Benefits of psychotherapy, include:
  - Effects may persist beyond the duration of treatment
  - The need to take antidepressant medications or experience medication side-effects may be reduced
  - An opportunity for the patient to make meaningful self-improvements or life changes

Subgroups Most Likely to Benefit:

Suicidal patients: Selective serotonin reuptake inhibitors have a wide therapeutic index and are significantly less lethal than other antidepressants when taken in overdose. They may be preferred in patients at risk for suicide.

### POTENTIAL HARMS

General

- Risks or drawbacks of pharmacotherapy include:
  - Need to take medications consistently and exactly as prescribed.

- Potential for medication side-effects or interactions with other medications or medical problems.
- Potential for need to take medication for an indefinite or extended period.
- Risks or drawbacks of psychotherapy include:
  - Patients need to come consistently for therapy appointments on a frequent basis for several months at a time.
  - A therapist trained in an empirically supported psychotherapy may not be available in every care setting.
  - Additional undesirable side effects of psychotherapy may include the need to miss work or other important activities and unanticipated effects on important relationships or increases in symptoms.

#### Specific adverse effects associated with pharmacotherapy

- Selective serotonin reuptake inhibitors (SSRIs)
  - The most common side effects include nausea, insomnia, sedation, headache, dizziness, fatigue, sexual dysfunction, anorexia, sweating, dry mouth, constipation (especially with paroxetine), tremor, nervousness, anxiety (especially with fluoxetine), and diarrhea and loose stools (especially sertraline).
  - A discontinuation syndrome when stopping SSRIs and venlafaxine has been observed. Commonly reported symptoms are dizziness, nausea or vomiting, fatigue, aches, chills, anxiety, irritability and crying spells. Rebound depression may occur. Symptoms generally occur within one to three days of discontinuation. Discontinuation syndrome has not been described for fluoxetine, perhaps because of its very long half-life.
  - Another caution is the very rare but potentially grave possibility of a "central serotonin syndrome" (sweating, fever, tachycardia, hypertension, altered mental status; more severely hyperpyrexia, cardiovascular collapse, and death) during the transition from one medication to another. The risk of this may be increased when two serotonergic agents are administered together or in close proximity. Some authors recommend waiting for at least five times the half-life of a drug (or its metabolites), before initiating treatment with a second agent.
- Tricyclic antidepressants (TCAs): The most common side effects include anticholinergic (dry mouth, blurred vision, increased intraocular pressure, constipation, urinary retention), cardiovascular (orthostatic hypotension, syncope, tachycardia, arrhythmias), CNS (sedation, confusion), weight gain (especially amitriptyline and doxepin) and sexual dysfunction. TCAs can decrease seizure threshold.
- Dual mechanism antidepressants
  - Bupropion: The side effects of bupropion do not include anticholinergic effects. It has little cardiovascular effects, sedation, and sexual dysfunction.
  - Nefazodone: The most common side effects associated with this agent include somnolence, dizziness, dry mouth, nausea, headache, impaired vision, and constipation.
  - Venlafaxine: The most common side effects associated with this agent include nausea, somnolence, insomnia, dizziness, abnormal

ejaculation, headache, nervousness, dry mouth, anxiety, asthenia, and sweating. Venlafaxine treatment has been associated with hypertension. The incidence of increased blood pressure was highest (13%) with doses >300 mg/day.

- Mirtazepine: Adverse effects include drowsiness, somnolence, fatigue, increased appetite, dry mouth, headache, constipation and weight gain; agranulocytosis has been reported although rare. Mirtazepine may have additive effects on cognitive and motor performance when given with alcohol and diazepam, and should be used cautiously when combining with other central nervous system antidepressants.
- Monoamine oxidase inhibitors (MAOIs): The most common side effects include orthostatic hypotension, restlessness, insomnia, sexual dysfunction, constipation, nausea, diarrhea, dry mouth, edema, anorexia, dizziness, weight gain (especially with phenelzine), headache, and vertigo. Fatal hypertensive crisis has occurred with concomitant use of tryptophan or tyramine. Serotonin syndrome has also occurred with combination tryptophan or tyramine and MAOI use, and is characterized by mental status changes (myoclonus), hyperreflexia, tachycardia, fever, diaphoresis, shivering, diarrhea, and/or constipation.
- Other antidepressants
  - Amoxapine: May cause Parkinsonian effects, tardive dyskinesia, and rarely neuroleptic malignant syndrome.
  - Maprotiline: May cause seizures.
  - Trazodone: May cause orthostasis and a high degree of sedation. It has been associated with priapism. There have been case reports of serotonin syndrome with coadministration of trazodone and paroxetine.
- Psychostimulants
  - Methylphenidate HCl: Common adverse effects include nervousness and insomnia, which may be controlled by decreasing dose and/or omitting afternoon or evening dose.

Subgroups Most Likely to be Harmed:

Pharmacotherapy

- Antidepressants may precipitate manic episodes in bipolar patients, and may activate latent psychosis in other susceptible patients.
- Selective serotonin reuptake inhibitors (SSRIs): Use cautiously in patients with hepatic and/or renal impairment where dose adjustment may be needed.
- TCAs should be used cautiously in the elderly.
- Dual mechanism antidepressants:
  - Nefazodone: Caution should be used when co-prescribing drugs that inhibit and/or are metabolized by cytochrome P450 isozymes due to potential interactions.
- Psychostimulants:
  - Methylphenidate HCl: Should be used cautiously in patients with an element of agitation or a history of substance abuse.

## CONTRAINDICATIONS

CONTRAINDICATIONS

Tricyclic antidepressants (TCAs): Contraindications include:

- hypersensitivity
- acute recovery phase following myocardial infarction (MI)
- angle-closure glaucoma or increased ocular pressure
- history of urinary retention or urethral spasm
- cardiovascular disease with ECG abnormalities, conduction abnormalities including bundle block, paroxysmal tachycardia and/or orthostatic hypotension
- patients at risk for suicide
- patients with cognitive impairment

Bupropion: Contraindicated in patients with seizure disorders or diagnosis of bulimia or anorexia nervosa.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

The Veterans Health Administration (VHA) instituted performance measures for implementation of clinical practice guidelines, including Major Depressive Disorder (MDD), Modules A (Initial Assessment and Treatment), and Module C (Inpatient Mental Health Specialty), in fiscal year (FY) 1998. These measures included screening all patients for depression in general medicine, primary care, and women's clinics as well as obtaining a Global Assessment of Functioning (GAF) rating on all discharged patients diagnosed with MDD. In FY 1999, these performance measures were expanded to include data collection on screening for alcohol use and post-traumatic stress disorder (PTSD) in the same clinics. Results for FY 1998 were an average of 44 percent nationally (ranging from 14 to 83 percent) for depression screening and an average of 97 percent (ranging from 56 to 100 percent) for GAF ratings.

With this version of the MDD Guideline, both VHA and DoD will be instituting similar performance measures developed by consensus after developing the guideline.

### RELATED NQMC MEASURES

- [Major depressive disorder: percent of patients screened for depression.](#)
- [Major depressive disorder: percent of patients with a positive screen for depression with a follow-up assessment or referral.](#)

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

VHA/DOD clinical practice guideline for the management of major depressive disorder in adults. Washington (DC): Department of Veterans Affairs (U.S.); 2000. Various p.

### ADAPTATION

Not applicable: Guideline was not adapted from another source.

The guideline developer notes that the American Psychiatric Association guideline on major depressive disorders was frequently referenced.

### DATE RELEASED

1997 (updated 2000)

### GUIDELINE DEVELOPER(S)

Department of Defense - Federal Government Agency [U.S.]  
Department of Veterans Affairs - Federal Government Agency [U.S.]  
Veterans Health Administration - Federal Government Agency [U.S.]

### SOURCE(S) OF FUNDING

United States Government

### GUIDELINE COMMITTEE

Major Depressive Disorder Working Group

### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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#### FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

#### GUIDELINE STATUS

This is the current release of the guideline.

It updates the guidelines developed in 1997 (Clinical guideline for major depressive disorder. Washington [DC]: Department of Veterans Affairs; 1997. Various pagings).

#### GUIDELINE AVAILABILITY

Electronic copies: Available from the [Veterans Health Administration \(VHA\) Web site](#).

Print copies: Available from the Office of Quality and Performance (10Q), Veterans Health Administration, Department of Veterans Affairs, 810 Vermont, NW, Washington, DC 20420.

#### AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Improving the care of Veterans who suffer from depression. Advice from Veterans and their family members. Washington, DC: Department of Veterans Affairs, 1996.

Print copies: Available from the Office of Quality and Performance (10Q), Veterans Health Administration, Department of Veterans Affairs, 810 Vermont, NW, Washington, DC 20420.

Also available:

- The pharmacologic management of major depression in the primary care setting. Supplement to the VHA/DoD clinical practice guideline for the diagnosis and management of major depressive disorder. Washington (DC): Veterans Health Administration Pharmacy Benefits Management Strategic Healthcare Group, 2000 May 35 p.

Electronic copies: Available from the [Veterans Health Administration Pharmacy Benefits Management Web site](#).

Print copies: Veterans Health Administration, Department of Veterans Affairs, 50 Irving St, SW, Washington, DC 20422.

#### PATIENT RESOURCES

None available

#### NGC STATUS

This summary was completed by ECRI on September 9, 1999. The information was verified by the guideline developer on January 10, 2000. This summary was updated by ECRI on February 28, 2001.

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