



INSTITUTE FOR CLINICAL
SYSTEMS IMPROVEMENT

Health Care Guideline

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- medical specialty and professional societies;
- researchers;
- federal, state and local government health care policy makers and specialists; and
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**Ninth Edition
May 2006**

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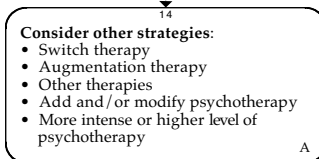
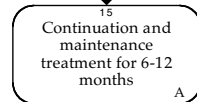
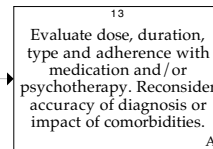
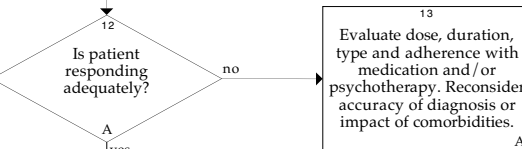
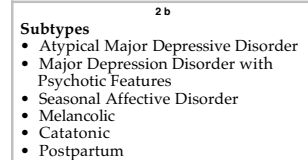
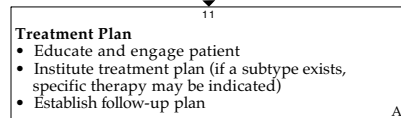
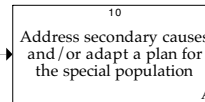
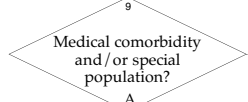
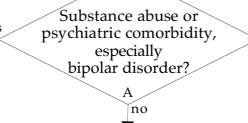
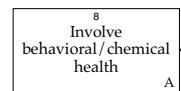
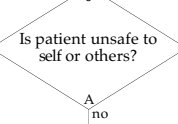
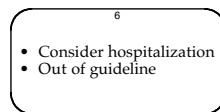
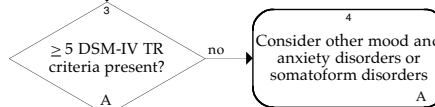
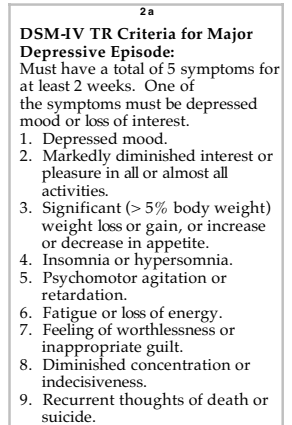
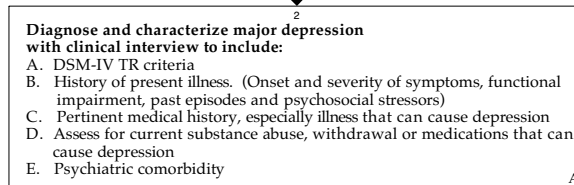
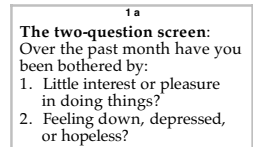
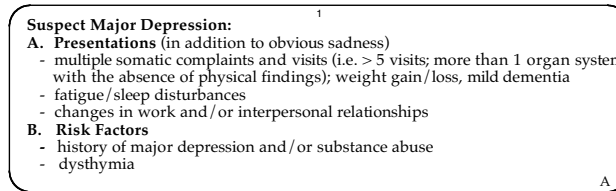
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A = Annotation

These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and are not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.

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Foreword

Scope and Target Population

All adults greater than 18 years of age.

Clinical Highlights and Recommendations

- A reasonable way to evaluate whether a system is successfully functioning in its diagnosis, treatment plan and follow-up of major depression is to consider:
 - How well the diagnosis is documented
 - How well the treatment team engages and educates patients/families
 - How well the ongoing patient contacts are documented
 - How well the outcomes are measured and documented

(Introduction)

- Patients with any chronic condition should be screened for depression, especially those with diabetes, cardiovascular disease, or chronic pain. Presentations for major depression include:
 - Multiple somatic complaints, weight gain/loss, mild dementia
 - Multiple (> 5/year) medical visits; problems in more than one organ system, with the absence of physical findings
 - Fatigue
 - Work or relationship dysfunction/changes in interpersonal relationships
 - Sleep disturbances

(Annotations #1, 9)

- Consider using a standardized instrument to document depressive symptoms. Document baseline symptoms and severity to assist in evaluating future progress, including response and remission rates. *(Annotation #2)*
- Antidepressant medications and/or referral for psychotherapy are recommended as treatment for major depression without coexisting medical conditions, substance abuse or other specific psychiatric comorbidities. Physical activity and tailored patient education are also useful tools in easing symptoms of major depression. *(Annotation #11)*
- When antidepressant therapy is prescribed, medication adherence and completion is critical. The patient should be advised of the following:
 - Most people need to be on medication at least 6 months.
 - It may take from 2-6 weeks before the patient sees improvement.
 - Take the medication as prescribed, even after the patient starts feeling better.
 - Do not stop taking the medication without calling your provider. Side effects can be managed by changes in the dosage or dose schedule.

(Annotation #11)

Foreword

- If the patient is not experiencing a significant reduction of symptoms after 4-6 weeks of treatment, other treatment strategies should be considered. (*Annotation #12, 13, 14*)
- The key objectives of treatment are:
 - To achieve remission of symptoms in the acute treatment phase for major depression.
 - To reduce patient relapse and reduction of symptoms.
 - To return to previous level of occupational and psychosocial function.

(*Annotation #13*)

Priority Aims

1. Increase the accuracy of diagnosis of major depression.
2. Improve the frequency of assessment of response to treatment in patients with major depression.
3. Improve the outcomes of treatment for major depression.
4. Increase the percent of patients with major depression who continue on antidepressants for an adequate length of time.
5. Increase the assessment for major depression of primary care patients presenting with any additional chronic condition such as diabetes, cardiovascular disease, or chronic pain.
6. Improve communication between the primary care physician and the mental health care provider (if patient is co-managed).
7. Improve the frequency of assessment of patients with major depression for the presence of substance abuse.

Related ICSI Scientific Documents

Related Guidelines

- Preventive Services
- Domestic Violence
- Prevention and Management of Obesity
- Assessment and Management of Chronic Pain
- Adult Low Back Pain
- Chronic Obstructive Pulmonary Disease
- Heart Failure in Adults
- Management of Type 2 Diabetes Mellitus
- Stable Coronary Artery Disease

Patient and Family Guidelines

- Adult Low Back Pain for Patients and Families
- Heart Failure in Adults for Patients and Families
- Major Depression in Adults in Primary Care for Patients and Families
- Management of Type 2 Diabetes Mellitus for Patients and Families
- Prevention and Management of Obesity for Patients and Families
- Stable Coronary Artery Disease for Patients and Families

Evidence Grading

Individual research reports are assigned a letter indicating the class of report based on design type: A, B, C, D, M, R, X.

A full explanation of these designators is found in the Supporting Evidence section of the guideline.

Disclosure of Potential Conflict of Interest

In the interest of full disclosure, ICSI has adopted the policy of revealing relationships work group members have with companies that sell products or services that are relevant to this guideline topic. The reader should not assume that these financial interests will have an adverse impact on the content of the guideline, but they are noted here to fully inform readers. Readers of the guideline may assume that only work group members listed below have potential conflicts of interest to disclose.

Michael Trangle, MD is a consultant for Interactive Forums, by consulting on best practices and doing focus group work.

No other work group members have potential conflicts of interest to disclose.

ICSI's conflict of interest policy and procedures are available for review on ICSI's website at <http://www.icsi.org>.

Algorithm Annotations

Introduction

A reasonable way to evaluate whether a system is successfully functioning in its diagnosis, treatment and follow-up of major depression would be to consider the following:

1. **Diagnosis:** The clinic or medical group should have a mechanism to assure that they are routinely evaluating for and documenting the presence for two weeks of at least five vegetative signs and symptoms of major depression (and that one includes sadness or loss of interest or pleasure in usual activities) in order to substantiate that the patient meets the DSM-IV TR criteria for major depression.
2. The clinic or medical group should have a systematic way to provide and document:
 - a. **Engagement Education:** The patient has received information about the nature of the disease and risks/benefits of treatment options (minimally either documentation of a discussion or that patient treatment options, handouts are routinely given.)
 - b. **Ongoing Contacts:** A documented system to assure ongoing contacts with the patient during the first 6 months of care (scheduled follow-up appointments, phone calls, and some way to react and/or reach out if the patient drops out of treatment.)
3. **Outcomes:** The system should have a way of at least periodically monitoring outcomes both individually and as a system to improve individual care and the effectiveness of the clinical practice overall.

1. Suspect Major Depression

Key Points:

- The major depression syndrome is a disorder of mood involving disturbances in emotional, cognitive, behavioral and somatic regulation.
- Some clinicians find self-administered instruments (e.g., PHQ-9 and HAM-D) useful adjuncts to the clinical interview.
- Major depression is a treatable cause of pain, suffering, disability and death, yet primary care providers detect major depression in only 1/3 to 1/2 of their patients with major depression.

The major depression syndrome is a disorder of mood involving disturbances in emotional, cognitive, behavioral and somatic regulation. The mood disorder is called secondary if it occurs in association with drug intoxication or withdrawal, as a biologic consequence of various general medical conditions, in association with other psychiatric conditions or as a consequence of selected prescription medications. The mood disorder is called primary if it does not occur in association with these conditions. Primary mood disorders are categorized into depressive (unipolar) and manic depressive (bipolar) conditions. Unipolar mood conditions are divided into major depressive disorder, dysthymic disorder and depression not otherwise specified.

Major depression can be a primary disorder or secondary to substance abuse, withdrawal from substance abuse, other psychiatric illnesses, certain medical illnesses and/or certain medications. Many patients with major depression do not initially complain of depressed mood, and providers need to suspect these diagnoses based on a profile of risk factors and common presentations.

Algorithm Annotations

Some clinicians find self-administered instruments (e.g., PHQ-9 and HAM-D) useful adjuncts to the clinical interview. They may be used to supplement but not replace the clinical interview. Additionally, this screening should only be used after one's system can reliably treat and follow-up with depressed patients.

Multiple, practical questionnaires with reasonable performance characteristics are available to help clinicians identify and diagnose patients with major depression. In case-finding studies, average questionnaire administration times ranged from less than 1 minute to 5 minutes. No significant differences regarding the accuracy of a depression diagnosis between questionnaires were found. While several questionnaires can be used to rate severity of depression and monitor response to therapy, in order to support coordination of care between providers, the following are suggested tools: Beck Depression Inventory, PHQ-9. These instruments should not be used to screen people without presentations suggestive of depression because of the low positive predictive value. Studies do not show improved outcomes when asymptomatic medical populations are screened for depression.

(Pignone, 2002; Preboth, 2000; Raine, 2002)

Supporting evidence is of classes: M, R

Importance of Major Depression

Major depression is a treatable cause of pain, suffering, disability and death, yet primary care providers detect major depression in only 1/3 to 1/2 of their patients with major depression (*Schonfeld, 1997; Williams Jr, 2002*).

Depression is common, with a lifetime risk for major depressive disorder of 7-12% for men and 20-25% for women (*U.S. Department of Health and Human Services Public Health Service, 1993*).

The estimate of the lifetime prevalence of suicide in those ever hospitalized for suicidality is 8.6%. The lifetime risk is 4% for affective disorder patients hospitalized without specification of suicidality (*Bostwick, 2000*).

Risk factors and presentations for depression are similar and providers need to suspect these conditions when multiple medical visits, multiple medically unexplained symptoms, fatigue, sleep disturbance, multiple worries and/or unexplained functional impairment, weight gain or loss, or changes in interpersonal relationships (i.e., frequent arguments, change in sexual interest, problem at work, isolation) are noted.

Supporting evidence is of classes: A, C, M, R

A. Presentations for major depression include:

- multiple (> 5/year) medical visits
- multiple unexplained symptoms
- work or relationship dysfunction
- changes in interpersonal relationships
- dampened affect
- poor behavioral follow-through with activities of daily living or prior treatment recommendations
- weight gain or loss
- sleep disturbance
- fatigue
- dementia
- irritable bowel syndrome
- volunteered complaints of stress or mood disturbance

Non-mood presentations of major depression include fatigue, pain or other somatic complaints, sleep disturbances, multiple medical visits and work or relationship dysfunction. Fatigue is the seventh most common symptom in primary care, and up to 24% of all patients surveyed in primary care clinics indicate that fatigue is a major problem (*Kroenke, 1988*).

Algorithm Annotations

See also Annotation #9, "Medical Comorbidity and/or Special Population?"

Irritable Bowel Syndrome is strongly correlated with psychiatric illness. Treatment of the underlying disease may provide more than adequate management of IBS (*Garakani, 2003*).

A mood disorder (major depression, dysthymia or bipolar) may be present in 39% of patients with a presenting complaint of chronic fatigue (fatigue present at least half the time for at least one month) (*Manu, 1988*).

Persons with major depression have a 4.8 times greater risk for work disability than asymptomatic individuals and report significantly poorer intimate relationships and less satisfying social interactions (*Broadhead, 1990; Fredman, 1988*).

Supporting evidence is of classes: B, C, D, R

B. Risk Factors for major depression include:

- family or personal history of major depression and/or substance abuse
- recent loss
- chronic medical illness
- dysthymia
- Stressful life events that include loss (death of a loved one, divorce)
- domestic abuse/violence
- traumatic events (car accident)
- major life changes (job change)
- emotional and behavioral reactions to these social stressors can include symptoms of major depression.

One previous episode of major depression is associated with a 50% chance of a subsequent episode, two episodes with a 70% chance, and three or more episodes with a 90% chance (*NIMH/NIH Consensus Development Conference Statement, 1985; U.S. Department of Health and Human Services Public Health Service, 1993a*). For women, severe obesity (body mass index greater than 40) has been strongly associated with depression (*Onyike, 2003*). Major depression is also seen in elderly patients with comorbid illnesses, such as CVA, cancer, dementia or disabilities.

Most studies indicate that in 40 to 60% of patients a major life event precedes the first episode of major depression (*Post, 1992*).

Patients with a history of mood disorders are at increased risk for postpartum depression. Several depressive conditions may follow childbirth. "Postpartum Blues" affects 50%-85% of mothers in the first two weeks after delivery. It is characterized by mood lability, tearfulness, anxiety and sleep disturbance but usually does not result in functional impairment. No specific treatment is required. If the patient remains significantly depressed 3-4 weeks following delivery, it should be considered serious and treated including eliminating medical causes of depressive symptoms such as post partum thyroid disorders or anemia. The first two to three months postpartum is the period of greatest risk for the development of major depression.

The close relationship of mind and body results in the presentation of medical illness with major depression in various forms:

- Medical illness may be a biological cause (e.g., thyroid disorder, stroke).

Algorithm Annotations

- Medical illness or patient's perception of his or her clinical condition and health related quality of life may trigger a psychological reaction to prognosis, pain or disability (e.g., in a patient with cancer).
- Medical illness may exist coincidentally in a patient with primary mood or anxiety disorder.

See also Annotation #9, "Medical Comorbidity and/or Special Population?"

Supporting evidence is of classes: D, R

2. Diagnose and Characterize Major Depression With Clinical Interview

Key Points:

- The U.S. Preventive Services Task Force (USPSTF) recommends screening adults for major depression in clinical practices that have systems in place to assure accurate diagnosis, effective treatment, and follow-up. The purpose of this guideline is to assist ICSI members to develop systems that support effective diagnosis and treatment of major depression.
- If depression is suspected on the basis of risk factors or common presentations, consider using a standardized instrument to document depressive symptoms.
- Clinicians should choose the method that best fits their personal preference, the patient population served and the practice setting.

The U.S. Preventive Services Task Force (USPSTF) recommends screening adults for major depression in clinical practices that have systems in place to assure accurate diagnosis, effective treatment, and follow-up (*U.S. Preventive Services Task Force [USPSTF], 2002*). The purpose of this guideline is to assist ICSI members to develop systems that support effective diagnosis and treatment of major depression.

- A.** Depressed mood or anhedonia (diminished interest or pleasure in activities) is necessary to diagnose major depression. If depression is suspected on the basis of risk factors or common presentations, consider using a standardized instrument to document depressive symptoms. More importantly, document baseline symptoms and severity to assist in evaluating future progress. Asking the two-question screen about mood and anhedonia may be as effective as using longer questionnaires:

Over the past month, have you been bothered by:

- Little interest or pleasure in doing things?
- Feeling down, depressed or hopeless?

If the patient answers "yes" to either one of the above questions, consider using a quantitative questionnaire to further assess whether the patient has sufficient symptoms to warrant a diagnosis of clinical major depression and a full clinical interview.

The use of a mnemonic may likewise be helpful for remembering the symptoms of major depression and dysthymia. SIGECAPS or SIG + Energy + CAPSules is easily remembered and can be used in

Algorithm Annotations

the clinical interview. It was developed by Dr. Carey Gross of Massachusetts General Hospital and stands for:

- Sleep disorder (increased or decreased)
- Interest deficit (anhedonia)
- Guilt (worthlessness, hopelessness, regret)
- Energy deficit
- Concentration deficit
- Appetite disorder (increased or decreased)
- Psychomotor retardation or agitation
- Suicidality

Some clinicians find that either self administered or professionally administered instruments are useful adjuncts to the clinical interview. Some examples which are recognized and validated are PHQ-9, BECK, HAM-D, QIDS-C, and QID-SR. Regardless, it is crucial to document that the patient meets at least 5 symptoms for at least 2 weeks as defined by the DSM-IV TR criteria for major depression. One of the symptoms must be depressed mood or loss of interest or pleasure. See Appendices B, C, and D for example questionnaires.

Clinicians should choose the method that best fits their personal preference, the patient population served and the practice setting.

The primary objective is to use a standardized instrument that will quantify and document future progress, including response and remission rates.

(Carlat, 1998; Kurlowicz, 1999; Preboth, 2000; Rush, 2003; Sheikh, 1991; Spitzer, 1999)

Supporting evidence is of classes: C, D, R

B. Determine history of present illness including:

- Onset may be gradual over months or years or may be abrupt.
- Severity of symptoms and degree of functional impairment:

People diagnosed with major depression have a heterogeneous course from self-limiting to life-threatening. Predictors of poor outcome include higher severity at initial assessment, lack of reduction of social difficulties at follow-up and low educational level. Categorize severity of symptoms and degree of functional impairment as follows:

- Mild: few, if any, symptoms in excess of those required to make the diagnosis and only minor impairment in occupational and/or social functioning
- Moderate: symptoms or functional impairment between mild and severe
- Severe: several symptoms in excess of those necessary to make the diagnosis and marked interference with occupational and/or social functioning

- Number and severity of previous episodes, treatment responses and suicide attempts.
- Ask about concurrent psychiatric conditions. Obtaining a past psychiatric history is important in terms of understanding prognosis and risk factors. For example, knowledge of past episodes of major depression, past co-occurring mental/behavioral health conditions, and past self-harm attempts is important for establishing risk and need to involve other mental health professionals.
- Psychosocial stressors (significant loss, conflict, financial difficulties, life change, abuse).

Algorithm Annotations

- C. A past medical history and brief review of systems is generally sufficient to rule out medical disorders causing major depression. Pertinent medical history that may complicate pharmacological treatments include, for example, prostatism, cardiac conduction abnormalities, impaired hepatic function.

Perform a focused physical examination and laboratory testing as indicated by the review of systems. The benefit of screening laboratory tests, including thyroid tests, to evaluate major depression has not been established.

Reliance on laboratory tests should be greater if:

- The medical review of systems detects symptoms that are rarely encountered in mood or anxiety disorders.
- The patient is older.
- The first major depressive episode occurs after the age of 40.
- The depression does not respond fully to routine treatment.

- D. Determine past history of substance abuse.

- Medications such as steroids, alpha-methyl dopa, and hormonal therapy may be associated with major depression.
- Withdrawal from reserpine and propranolol may be associated with major depression.
- Use of alcohol and hypnotics might be mimicking depression.
- Withdrawal from cocaine, anxiolytics and amphetamines may be mimicking depression.
- Idiosyncratic reactions to other medications can occur and if possible, a medication should be stopped or changed if depression develops after beginning its use. If symptoms persist after stopping or changing medication, re-evaluate for a primary mood or anxiety disorder.

3. \geq 5 DSM-IV TR Criteria Present?

- A. Five or more of the following symptoms have been present and documented during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

Note: Do not include symptoms that are clearly due to a general medical condition, or mood congruent delusions or hallucinations.

- 1) depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful)
- 2) markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)
- 3) significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day
- 4) insomnia or hypersomnia nearly every day
- 5) psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
- 6) fatigue or loss of energy nearly every day

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- 7) feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
 - 8) diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)
 - 9) recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide
- B.** The symptoms do not meet criteria for a mixed episode.
- C.** The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- D.** The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).
- E.** The symptoms are not better accounted for by bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

The assessment of major depressive disorders should include the DSM-IV TR numerical rating of the disorder with all 5 digits, thus including a severity rating. For example, 296.22 [Major depressive disorder, single episode, moderate severity].

(American Psychiatric Association, 2000)

4. Consider Other Mood and Anxiety Disorders or Somatoform Disorders

Patients with some depressive symptoms who do not meet full DSM-IV TR criteria for major depression often respond positively to antidepressant medication and/or psychotherapy. Emerging evidence also supports the use of bright light therapy in some of the cases of milder depression.

Presentations particularly suggestive of an anxiety disorder include:

- medically unexplained symptoms of autonomic excitation such as:
 - cardiac (chest pain, atypical chest pain, palpitations, shortness of breath, hyperventilation)
 - gastrointestinal (epigastric distress, irritable bowel syndrome)
 - neurologic (headache, dizziness, paresthesias)
 - panic attacks
- emergency room visit for medically unexplained somatic symptoms, particularly chest pain

These symptoms can cause significant impairment, suffering, and disability. Antidepressants should be considered, though the evidence for their efficacy is less well established with these disorders than with major depression. Other depression categories include Dysthymic Disorder and Depressive Disorder NOS (not otherwise specified.) See Appendix A.

(Barrett, 2001; Raine, 2002; Williams, 2000)

Supporting evidence is of classes: A, M

5. Is Patient Unsafe to Self or Others?

Key Points:

- Although there are no good predictors of suicide in specific cases, a number of factors point to heightened risk.
- Ongoing case management enhances positive outcomes for depression.

The lifetime rate of suicide attempts is 7% in uncomplicated (no other psychiatric diagnosis) panic disorder and 7.9% in major depression. 19.8% of patients with comorbid panic disorder and major depression have attempted suicide.

Assessing suicidal tendencies is a critical but often difficult process with a depressed patient. Consider asking and documenting the following progression of questions:

1. Do you feel that life is worth living?
2. Do you wish you were dead?
3. Have you thought about ending your life?
4. If yes, have you gone so far as to think about how you would do so?
5. Do you have access to a way to carry out your plan?
6. What keeps you from harming yourself?

Many patients will not answer #4 directly or will add "but I'd never do it." Give them positive feedback (e.g., "I'm glad to hear that.") but do not drop the subject until she/he has told you the specific methods considered (e.g., gun, medication overdose, motor vehicle accident, etc.).

Although there are no good predictors of suicide in specific cases, a number of factors point to heightened risk:

- There are four male suicide completions for every female completion
- Elderly Caucasian and Asian men over the age of 65 years and Asian women over 80 years are at disproportionate risk.
- Two thirds of elderly suicide completers are in relatively good health. White men over the age of 85 years have six times the risk of suicide completion as the general population. The majority of elderly suicides appear associated with late onset, single episodes of depression, and not current poor health. Twenty percent of elderly suicide completers were seen by their physicians within 24 hours of death, 35% within the week, and 75% within the month.
- Substance abuse is a contributing factor in approximately half of suicide completions, although the involvement of intoxication as a risk factor decreases in the elderly.
- The presence of firearms in the home is believed to greatly increase the danger if other risk factors are present. Males in general tend to choose highly lethal means, such as firearms, which greatly increases the risk of death.
- Across all age groups, one in seven suicide completers had contact with their doctor within a week of death.

Algorithm Annotations

- When a patient has high levels of all of the following, risk is very high and hospitalization may be needed immediately:
 - internal emotional pain (e.g., feelings of shame, guilt, humiliation)
 - external stress (e.g., loss of spouse, job, legal troubles)
 - hopelessness

If any one factor can be substantially alleviated, risk is thought to drop sharply.

Suicide remains a rare occurrence relative to the frequency of depression in the general population; between one and five suicides occur per one thousand patient years of follow-up.

Emerging literature suggests that a past history of self harm attempts, in combination with a history of well developed suicide plans, place the patient at a greater eventual risk of completing a suicide attempt. Circumstances such as clear past examples of a sense of competence to execute an attempt, a sense of courage to make the attempt, behaviors that ensure the availability of means and opportunity to complete, concrete preparations to enact the suicide plan, and a current episode of severe depression combine to pose a greater danger of eventual completed suicide. The clinician should consider previous history of suicide attempts; chemical dependency; personality disorder and/or physical illness; family history of suicide; single status; recent loss by death, divorce or separation; insomnia; panic attacks and/or severe psychic anxiety; diminished concentration; anhedonia; hopelessness; or suicidal ideation.

(Bostwick, 2000; Hall, 1999; Jobes; Murphy, 2000; Weissman, 1989)

Ongoing case management enhances positive outcomes for depression (Bruce, 2004).

Supporting evidence is of class: A, C, M, R

7. Substance Abuse or Psychiatric Comorbidity, Especially Bipolar Disorder?

Key Points:

- The medical literature does not support definitive statements about the best way(s) to treat patients who are diagnosed with both major depression and substance abuse/dependence.
- Some patients presenting with a major depressive episode have a bipolar disorder, for which effective treatment may differ significantly from other depressed patients.

Major depression may be associated with other psychiatric problems including personality disorders, anxiety disorders, obsessive-compulsive disorders, eating disorders and substance abuse.

- **Psychosocial Stressors:**

(Karasu, 1993)

- **Medical Illness:**

Major depression may also be associated with medical disorders or the patient's perception of his or her clinical condition. Although thyroid function abnormalities may cause depressive symptoms, screening for thyroid disease in all patients with major depression is not necessary because the prevalence of

Algorithm Annotations

unidentified thyroid disease in patients with major depression is the same as in the general population (Briggs, 1993; Garrard, 2001).

Patients with pheochromocytomas generally do not report anxiety symptoms meeting DSM criteria for panic disorder or generalized anxiety disorder (Starkman, 1985).

- **History of Substance Abuse:**

The CAGE questions are sensitive and specific for diagnosing alcoholism. One positive response has a sensitivity of 85% and a specificity of 89%, and two positive responses has a specificity of 96% (Bush, 1987).

The CAGE(AID) questionnaire broadens the CAGE to include other drug use. Preliminary pilot studies suggest the CAGE(AID) questionnaire may be similar to the CAGE questionnaire in utility (Brown, 1992).

Alcoholism and major depressive disorder are distinct clinical entities and are not different expressions of the same underlying condition. While alcoholism is rarely a consequence of depression, many alcoholics develop depressive symptoms. Although 10-30% of patients with alcoholism suffer from depression at the time of evaluation, the prevalence of alcoholism in patients with primary depression is probably no higher than in the general population (U.S. Department of Health and Human Services Public Health Service, 1993a).

The medical literature does not support definitive statements about the best way(s) to treat patients who are diagnosed with both major depression and substance abuse/dependence. The majority of studies reviewed indicate that success in treating dependency on alcohol, cocaine, and other abused substances is more likely if accompanying depression is addressed. Fewer investigators have looked at whether treating substance abuse is helpful in reducing depression. There is some evidence that patients with major depression which is secondary to their substance abuse may have remission of their depressed mood once the substance abuse is treated. However, it is difficult to separate secondary depression from primary depression that predates or is separate from the substance use.

Studies to assess the efficacy of concurrent treatment of major depression and substance abuse are limited in number and of variable quality. Although results are not fully consistent, the preponderance of available evidence suggests that pharmacotherapy can be of benefit in treating both substance abuse and depression in patients who have both disorders. Agents studied include amantadine (a dopamine agonist), desipramine (a tricyclic antidepressant), and fluoxetine (an SSRI).

(Charney, 2001; Mueller, 1994; Ziedonis, 1991)

The algorithm reflects the uncertainty in this area. At diamond #75 it splits into two possible paths. If yes – a depressed patient is felt to be chemically dependent, treatment of the substance abuse should be considered, either before or while treating the depression. However, if no – a depressed patient refuses treatment for substance abuse, has a medical comorbidity, or is of a special population, it is appropriate to focus primarily on the depression keeping the special circumstances in mind. It is reasonable to attempt to treat the depression while continuing to assist the patient to work toward efforts to understand their special needs.

Evaluation and treatment for chemical dependency is beyond the scope of this guideline. A referral may be appropriate.

Supporting evidence is of classes: A, B, C, D, R

Algorithm Annotations

The CAGE(AID) Screen

Current alcohol or other drug problems can be screened by asking a few questions that can be easily integrated into a clinical interview. A common screen is the CAGE screen.

The CAGE or CAGE(AID) should be preceded by two questions:

1. Do you drink alcohol?
2. Have you experimented with drugs?

If the patient has experimented with drugs, ask the CAGE(AID) questions. CAGE(AID) questions are modified with *italicized* text.

CAGE(AID) Screen

Have you ever:

- C felt you ought to **cut** down on your drinking (*or drug use*)?
- A had people **annoy** you by criticizing your drinking (*or drug use*)?
- G felt bad or **guilty** about your drinking (*or drug use*)?
- E had a drink (*or drug use*) as an **eye opener** first thing in the morning to steady your nerves or get rid of a hangover or to get the day started?

If substance abuse is present or suspected, consider referral for substance abuse assessment.

Each affirmative response earns one point. One point indicates a possible problem. Two points indicate a probable problem.

The CAGE screen is short in length and easy to administer, however other screening tools may also be useful. It is important to screen for substance abuse using a validated tool, and which tool to use depends on the provider/system's preferences and needs.

Examples of Substance Abuse Screening Tools

| Tool | Description | *Sensitivity/Specificity % |
|-------|--|----------------------------|
| AUDIT | 10 item questionnaire – self administered or clinical interview to assess for harmful use; cross cultural validity | Score of 12: 97/28 |
| CAGE | 4 item questionnaire – clinical interview to detect alcoholism | All items positive: 100/37 |
| DAST | 28 item questionnaire – self administered or clinical interview to detect drug problems; adapted from MAST | Score of 6 or more: 96/79 |
| MAST | 25 item questionnaire – self administered or clinical interview to detect alcoholism | Score of 5 or more: 95/98 |
| TWEAK | 5 item questionnaire – clinical interview to detect high risk use; adapted from CAGE | Score of 2: 73/64 |

*Note: Sensitivity/specificity can differ with regard to efficacy for specific subpopulations. Adaptation permission granted from projectcork.org

Algorithm Annotations

Bipolar Disorder

Some patients presenting with a major depressive episode have a bipolar disorder, for which effective treatment may differ significantly from other depressed patients. When assessing a patient, consider asking about manic or hypomanic episodes.

- Has there been a distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least one week?
- During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:
 1. Inflated self-esteem or grandiosity
 2. Decreased need for sleep
 3. More talkative than usual or pressure to keep talking
 4. Flight of ideas or subjective experience that thoughts are racing
 5. Distractibility
 6. Increase in goal-directed activity or psychomotor agitation
 7. Excessive involvement in pleasurable activities that have a high potential for painful consequences

If these criteria are met, the patient may have bipolar disorder. Treatment for this falls out of the scope of this guideline.

Ask patients with major depression about a history of manic symptoms (abnormally elevated, expansive or irritable mood). Patients with a history of manic (bipolar) symptoms now presenting with major depression may be destabilized if treated only with antidepressant drugs. Behavioral health involvement is advised with these patients absent a prior history of successful primary care management.

Be aware of ongoing mental illness diagnosis or other mental health illnesses and comorbidities.

8. Involve Behavioral/Chemical Health

Consider involving same day Behavioral Health for:

- Suicidal thoughts and/or plans which make the clinician uncertain of the patient's safety.
- Assaultive or homicidal thoughts and/or plans which make the clinician uncertain about the safety of the patient or others.
- Recent loss of touch with reality (psychosis).
- Inability to care for self/family.

Involvement could include:

- Appointment with psychiatrist and/or psychotherapist
- Phone consultation with psychiatrist and/or psychotherapist
- Referral to the Emergency Department

(Cahill, 2003; Dieserud, 2001; Ellis, 2002; Hall, 1999; Lambert, 2001; Manber, 2003; Merrill, 2003; Teasdale, 2001; Ward, 2000; Whooley, 2000; Williams, 2000)

Supporting evidence is of classes: A, C, D, M, R

9. Medical Comorbidity and/or Special Population?

Medical Comorbidities

Be aware of the increased incidence of depression in chronic co-morbid conditions such as chronic pain, diabetes, cancer, Parkinson's disease, and cardiovascular disease. Depression may increase in frequency with acute conditions such as fractured leg, back pain with disability, acute MI, stroke, etc. Difficulties coping with a medical condition may also play a role.

The following conditions are particularly important for screening, given the findings.

Cardiovascular Disease

Major depression is associated with an increased risk of developing coronary artery disease (*Rugulies, 2002*), and has also been shown to increase the risk of mortality in patients after myocardial infarction by as much as four-fold (*Frasure-Smith, 1995*). Moderate to severe depression before CABG surgery, and or persistent depression after surgery increases the risk of death after CABG more than two-fold higher than non-depressed patients (*Blumenthal, 2003*).

Several possible mechanisms are proposed to explain why depression increases the risk of developing cardiovascular disease including behavioral issues such as increased smoking, obesity, sedentary lifestyle, and lack of adherence to medication. Biologic explanations associated with depression such as increased inflammatory processes (elevated C-reactive protein or cytokine levels, increased platelet dysfunction (heightened platelet aggregation or adhesiveness), and abnormalities in endothelial function may also explain possible mechanisms for an increased risk (*Katon, 2004b*).

As yet there are no data to support the hypothesis that antidepressant treatment improves cardiac morbidity and mortality (*Jiang, 2005*). **Nevertheless consensus opinion is to treat depressed cardiac patients with a safe drug rather than watchful waiting since they would benefit from symptomatic relief of their depressive symptoms and there is a potential improvement in their cardiovascular risk profile** (*Ballenger, 2001*).

Although tricyclic antidepressants are effective against depression they are associated with cardiovascular side effects including orthostatic hypotension, slowed cardiac conduction, antiarrhythmic activity, and increased heart rate. SSRIs by contrast are well tolerated and have a more benign cardiovascular profile and would be preferred initial agents for treatment of depression in individuals with cardiovascular disease (*Jiang, 2005*).

Supporting evidence is of classes: D, M, R

Diabetes

Major depression is associated with an increased number of known cardiac risk factors in patients with diabetes and a higher incidence of coronary heart disease, therefore screening and treatment of depression in this patient group should be emphasized (*Katon, 2004b*).

Individuals with diabetes have a two-fold higher odds of depression than those without diabetes. High levels of symptoms associated with diabetes that do not correlate with physical or laboratory assessments should prompt the physician to assess for depression (*Ludman, 2004*).

Depression earlier in life increases the risk of developing diabetes by two-fold (*Katon, 2004a*).

Depressive symptom severity is associated with poorer diet, medication compliance, and self care plus functional impairment and higher health care costs (*Ciechanowski, 2000*).

Supporting evidence is of class: D

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Chronic Pain

Depression and pain symptoms commonly coexist, exacerbate or attenuate one another, and appear to share biological pathways and neurotransmitters.

The mean prevalence of pain symptoms in patients with depression is 65% across psychiatric and primary care settings. In contrast, mean prevalence rates vary across settings for concurrent major depression in pain cohorts, e.g., 52% in pain clinics or inpatient pain programs; 38% in psychiatric clinics; 56% in orthopedic clinics; and 27% in primary care clinics. The prevalence of pain in depressed patients and the prevalence of depression in pain patients are higher than the prevalence rates for each condition considered individually.

A recent cross-cultural study has shown that 22% of all patients in primary care suffer from persistent debilitating pain and that these patients are four times more likely to develop depression.

Important Diagnostic and Treatment Findings:

- In primary care, more than 50% of patients with depression report only somatic or physical symptoms of which 60% of these symptoms are pain related; this somatic symptom only presentation interferes with the recognition (diagnosis) and treatment of depression.
- Increasing pain severity, diffuse (multiple site) pain, pain that interferes with functional performance, and pain refractory to treatment are all associated with increased risk of depression, more depressive symptoms, and greater depression severity.
- The reciprocal nature of the depression-pain relationship is well established, i.e., the presence of depression in pain patients or the presence of pain in depressed patients is associated with poorer functional status and resulting disability, decreased quality of life, impaired social functioning, and decreased patient satisfaction.
- Antidepressant treatment of pain conditions generally produces simultaneous improvement of pain and depression symptoms. Evidence for the converse is lacking at this time (*Bair, 2003; Dionne, 1997; Fishbain, 1999; Gureje, 2001*).
- Light therapy cannot be endorsed as an evidence-based treatment for antepartum and postpartum depressed women (*Oren, 2002*).

Key clinical practice recommendations include:

- In those patients presenting with either pain or depressive symptoms, assess both domains. If comorbidity is found, treat both conditions for optimal outcomes.
- Given that depression and pain symptoms appear to follow the same descending pathways of the central nervous system involving a functional deficiency of the neurotransmitters serotonin, norepinephrine, and dopamine, antidepressant medication is warranted, especially the dual-action tricyclic antidepressants such as amitriptyline or dual-action atypical antidepressant re-uptake inhibitors such as venlafaxine or duloxetine.
- Combining pharmacologic treatment and cognitive-behavioral therapy appears to produce the most favorable treatment outcomes.

Supporting evidence is of classes: B, D, M, R

Special Populations

Geriatrics

Depression in the elderly is widespread, often undiagnosed and usually untreated. It is not a part of normal aging. Losses that older patients experience can contribute to depression.

Depression in adults older than 65 years of age ranges from 7 to 36 percent in medical outpatient clinics and increases to 40 percent in the hospitalized elderly. Unlike younger people with depression, the elderly will have a medical comorbidity. The highest rates of depression are found in those with strokes (30 to 60 percent), coronary artery disease (up to 44 percent), cancer (up to 40 percent), Parkinson's disease (40 percent), and Alzheimer's disease (20 to 40 percent). The recurrence rate is also extremely high at 40 percent (Birrer, 2004).

Similar to other groups, the elderly present with nonspecific complaints, such as insomnia, anorexia, and fatigue. Screening the elderly can be accomplished with the 15 question Geriatric Depression Scale. Five or more on this scale suggests depression and 10 or more confirms. Clinicians may find it easier to use than other tools because the questions ask for yes/no answers.

Treatment and prognosis for recovery is the same as for younger patients, however, special considerations must be made in the elderly. It usually takes them longer to achieve a remission, and they should be treated for longer periods than younger patients. When using pharmacotherapy, the physician must carefully consider how the metabolism of the drug may be affected by physiologic changes in the elderly, their comorbid illnesses and the medications used for them. Psychotherapy is also appropriate, being limited only by cognitive impairments.

Recurrent depression is common in the elderly. Maintenance therapy with an SSRI (paroxetine in this study) for two years was shown to be effective in preventing recurrent depression after a first time major depression in the elderly over seventy years of age, Interpersonal psychotherapy alone was ineffective (Reynolds, 2006).

| | |
|---|---------------------|
| Paroxetine plus interpersonal psychotherapy | 35% recurrence rate |
| Paroxetine plus clinical management | 37% recurrence rate |
| Placebo plus interpersonal psychotherapy | 68% recurrence rate |
| Placebo plus clinical management | 58% recurrence rate |

(Hollon 2005; Mitchell, 2005; Sharp, 2002)

Supporting evidence is of classes: A, M, R

Pregnancy

Depression poses risk for pregnancy. Maternal depression and other stress states have been associated with lower birth weight and gestational age of infant offspring, delivery by cesarean section, and admittance to neonatal care units. Other potential consequences of depression during pregnancy include: poor maternal weight gain or frank weight loss and malnutrition (puts infants at risk for low birth weight), long-term hospitalization, marital discord and divorce, poor prenatal care compliance, difficulty caring for other children, loss of employment, increased harmful behaviors such as nicotine, alcohol or drug use and suicide. The challenge is to minimize unnecessary medication exposure to the developing fetus while maintaining the health of the mother. Studies are sparse, specifically regarding the efficacy of psychotherapy and psychotropic treatments. Medication should be used when the risk to the mother and fetus from depression outweighs risks of pharmacotherapy. Maternal illness severity is an important factor in the risk benefit decision-making process. Mild to moderate depressive symptoms may respond to interpersonal psychotherapy which has

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been modified for pregnancy. More severe depression requires psychopharmacological interventions. It is very possible that antidepressant treatment for depression during pregnancy could reduce or avert some of the potential adverse effects of depression on the mother and her developing fetus. Safety of antidepressants during pregnancy has not been clearly established.

For further information on medications during pregnancy, see the "medications" section in Annotation #11, "Treatment Plan."

Consideration should be used for bright light therapy as an option for depressed pregnant women. See Annotation #14, "Consider Other Strategies," for further information.

Cultural Considerations

The concept of depression varies across cultures. In many cultures, for depression to become a problem for which a person seeks medical treatment, symptoms may include psychosis, conversion disorders, or significant physical ailments (*Karasz, 2005*).

- Be aware that psychosocial stressors may be more prevalent with special populations and the health care team may want to take these issues into consideration as a treatment plan is made. Examples of possible stressors include:
 - Housing
 - Daycare
 - Employment
 - Financial stability
 - Food
 - Transportation
 - Immigration status
- Assess for other resources the client may have used such as elders, native or spiritual advisors/healers, or whomever is within their frame of reference. Acknowledge their role and collaborate if possible/appropriate.
- Many assessment tools may not be useful for certain populations. Screening instruments are validated in certain groups. Use caution when using because a tool may not be applicable to all groups.
- Cost implications for patients often affect adherence, including insurance coverage or generic versus brand name medications. Adherence factors are important for providers to discuss with the patient.
- Symptoms of depression may be perceived differently by various cultures. This may lead to under-recognition or misidentification of psychological distress. In some cultures mood, affect and anxiety symptoms are considered social, moral, or spiritual problems.
- The most common somatic symptoms of depression and anxiety are musculoskeletal pain and fatigue. A provider might consider starting the conversation with the patient on physical symptoms since this is a common presentation of depression in some cultures.
- Ten to 75 percent of patients are noncompliant with medication use and rates are higher in inter-cultural settings because of cultural expectations and communication problems (*Kirmayer, 2001*).
- Most empirically supported therapies have been evaluated with white, middle class, English-speaking populations.
- Recent research on depression in low-income minority women in the United States documents significant improvement of symptoms and social functioning regardless of whether treatment was medication or psychotherapy when treatment was sufficiently accessible (availability of child care and transportation).

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- Health care providers can create a more comfortable environment for a patient of another culture by acknowledging the impact of culture and cultural differences on physical and mental health (*Munoz, 2005; Miranda, 2004*).
- A discrepancy between aspiration and achievement may be a better predictor of psychiatric illness than socioeconomic status. The larger the discrepancy between aspiration and achievement, the greater risk of emotional disturbance (*Ialongo, 2004*).

Supporting evidence is of classes: C, D, R

10. Address Secondary Causes and/or Adapt a Plan for the Special Population

People with secondary causes for major depression may also have an underlying primary mood or anxiety disorder. Understanding and addressing nuances of special populations may enhance treatment outcomes.

11. Treatment Plan

Key Points:

- Patient information should include diagnosis, prognosis, and treatment options including costs, duration, side effects, and expected benefits.
- Successful programs for the treatment of depression include: organized treatment protocols, structured follow-up protocols, systematic monitoring of treatment adherence and effectiveness.
- The prevention of relapse is of primary importance in the treatment of major depression.

Educate and Engage Patient

Patient adherence is critical. In addition to medication monitoring, clinical management of patients placed on antidepressants should include the physician's support and reassurance. Often, the depressed patient's pessimism, low motivation, low energy, and sense of social isolation and guilt may lead to noncompliance with treatment (*U.S. Department of Health and Human Services Public Health Service, 1993b*).

Patient information should include diagnosis, prognosis, and treatment options including costs, duration, side effects, and expected benefits. Emphasize the following six points:

- Depression is a medical illness, not a character defect.
- Recovery is the rule, not the exception.
- Treatment is effective for nearly all patients.
- The aim of treatment is complete remission, not just getting better but staying well.
- The risk of recurrence is significant: 50% after one episode, 70% after two episodes, 90% after three episodes.
- Patient and family should be alert to early signs and symptoms of recurrence and seek treatment early if depression returns.

(*U.S. Department of Health and Human Services Public Health Service, 1993b*)

Patient Education

Successful care of major depression as an illness requires active engagement of each patient and their family and on-going patient education, beginning at the time of diagnosis. It is important for the patient to consider and adopt some self-care responsibilities, which may range from simply demonstrating reliable behavior in taking medications and calling the provider with side effects to agreeing to participate in sessions, journaling and completing homework, which is necessary for some cognitive behavioral therapies. Written materials are helpful to reinforce information shared during the discussion. Patients who commit to some self-care responsibilities and receive this education compared with those who do not are more likely to continue, rather than prematurely abandon treatment, and are more likely to attain better outcomes. Education topics should include:

- The cause, symptoms and natural history of major depression
- Treatment options (trial and error approach)
- Information on what to expect during the course of treatment
- How to monitor symptoms and side effects
- Follow-up protocol (office visits and/or telephone contacts)
- Early warning signs of relapse or recurrence
- Length of treatment

When antidepressant therapy is prescribed, the following key messages should be highlighted to support medication adherence and completion:

- Side effects from medication often precede therapeutic benefit and typically recede over time. It is important to expect some discomfort prior to benefit.
- Successful treatment often involves dosage adjustments and/or trial of a different medication at some point, to maximize response and minimize side effects.
- Most people need to be on medication at least 6-12 months after adequate response to symptoms.
- It usually takes from 2-6 weeks before improvement is seen.
- Take the medication as prescribed, even after one feels better.
- Do not stop taking the medication without calling your provider. Side effects can be managed by changes in the dosage or dosage schedule.

Supporting evidence is of class: R

Exercise

Evidence suggests that physical activity at a dose consistent with public health recommendations is a useful tool for easing major depression symptoms. Among individuals with major depression, exercise therapy is feasible and is associated with significant therapeutic benefit, especially if exercise is continued over time (*Artal, 1998; Babyak, 2000; Blumenthal, 1999; Dunn, 2005; Annesi, 2005*). When prescribing exercise either alone or as an adjunct to medication and psychotherapy, the complexity and the individual circumstances of each patient must be considered. When prescribing an exercise prescription, several caveats apply:

- Anticipate barriers – hopelessness and fatigue can make physical exertion difficult
- Keep expectations realistic – some patients are vulnerable to guilt and self-blame if they fail to carry out the regime

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- Introduce a feasible plan – walking, alone or in a group, is often a good option
- Accentuate pleasurable aspects – the specific choice of exercise should be guided by the patient's preferences, and must be pleasurable
- A goal of 30 minutes of moderate-intensity aerobic exercise, 3-5 days a week is recommended for otherwise healthy adults (17.5 kcal/kg/week of total energy expenditure)
- Encourage adherence – greater antidepressant effects are seen when training continues beyond 16 weeks

Supporting evidence is of classes: A, C, R

Institute Treatment Plan

Successful programs for the treatment of depression include:

- Organized treatment protocols
- Structured follow-up protocols
- Systematic monitoring of treatment adherence and effectiveness

Psychotherapy

- Offer a referral for psychotherapy whenever psychological or psychosocial issues are prominent, or if the patient requests it. Individuals perceiving more self-control of their health experience greater depressive symptom reduction (*Brown, 2000*).
- Support and education in the primary care setting are critical and contribute to the likelihood of good follow through on treatment. It may help patients understand their options and resources if the primary care clinic explains that this is not the same as a course of psychotherapy.
- Maintenance psychotherapy is useful in managing chronic forms of Major Depressive Disorder (*Klein, 2004*).

Supporting evidence is of classes: A, C

Medications

For antidepressant medications, adherence to a therapeutic dose and meeting clinical goals are more important than the specific drug selected. The educational messages in Appendix A, (Treatment and Education box) may increase adherence.

Successful treatment often involves dosage adjustments and/or trial of a different medication at some point, to maximize response and minimize side effects (*American Psychiatric Association, 2000*).

Health care providers should carefully evaluate their patient in whom depression persistently worsens, or emergent suicidality is severe, abrupt in onset, or was not part of the presenting symptoms to determine what intervention, including discontinuing or modifying the current drug therapy is indicated (*FDA, 2004*).

The provider should instruct their patient, and their patient's caregiver to be alert for the emergence of agitation, irritability, and the other symptoms. The emergence of suicidality and worsening depression should be closely monitored and reported immediately to the health care provider.

Selection of an Antidepressant Medication

Antidepressant drug selection should be based on:

- the patient's history of response to previous antidepressant medications (if any)

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- the patient's comorbid psychiatric or medical conditions
- clinician familiarity with specific antidepressants

Another resource for medication selection is the Texas Medication Algorithms which can be found at: <http://www.dshs.state.tx.us/mhprograms/disclaimer.shtm>.

There is no evidence regarding choice of brand versus generic based on adverse clinical outcomes.

Pharmaceutical Equivalents

Drug products are considered pharmaceutical equivalents if they contain the same active ingredient(s), are of the same dosage form, have the same route of administration, and are identical in strength or concentration. Pharmaceutically equivalent drug products may differ in shape, scoring configuration, release mechanisms, packaging, excipients (including color, flavors, preservatives), and expiration time (*U.S. Department of Health and Human Services, 2006*).

Therapeutic Equivalents

Products can only be considered therapeutic equivalents if they are already determined to be pharmaceutical equivalents and meet a set list of criteria, including bioequivalence.

Bioavailability is the rate and extent an active ingredient or therapeutic ingredient is absorbed from a drug product and is available at the site of drug action. Bioequivalent drug products are therapeutically equivalent, and therefore, interchangeable.

Two studies reviewing differences between brand name products and their generic equivalents found an average difference of +/- 3.5 percent.

(*U.S. Department of Health and Human Services, 2006*)

Supporting evidence is of class: R

Consider discussing with the patient the specific side effect profiles, costs, and benefits of different antidepressants, including generics. Cost implications for patients needs to be discussed between provider and patient.

1. Selective Serotonin Reuptake Inhibitor (SSRI); venlafaxine, duloxetine, mirtazepine, and bupropion

SSRIs, venlafaxine, duloxetine, mirtazepine and bupropion are frequently chosen as first-line therapy because of simplicity, side effect profiles and community standards.

They generally lack the common adverse reactions (anticholinergic, sedative effects) of the tricyclics and cause fewer problems when taken in overdose. However, they may cause headache, nervousness, insomnia, and sexual side effects and may be more expensive as some may not yet be available as generics. Care must be taken to remain with either the brand name product or the same general product.

2. Secondary Amine Tricyclics

The literature clearly supports the effectiveness of tricyclics. Because of associated side effects, they are used less frequently as first-line agents.

Secondary amine tricyclics cause less orthostatic hypotension and sedation than tertiary amine tricyclics.

These medications should be monitored cautiously in patients with heart problems, or in patients with potential for drug interactions. Monitoring blood levels and EKG may be advised.

3. Monoamine Oxidase Inhibitor (MAOI)

MAOIs, in general, should be restricted for patients who do not respond to other treatments because of their potential for serious side effects and the necessity of dietary restrictions. Patients with major depressive disorders with atypical features are one group for whom several studies suggest MAOIs may be particularly effective. However, in clinical practice, many psychiatrists start with SSRIs in such patients because of the more favorable adverse effect profile.

Medication interactions with antidepressant agents: Many antidepressant agents have clinically significant drug interactions, particularly those agents which undergo cytochrome P450 enzymatic metabolism in the liver. A complete discussion of this topic is beyond the scope of this guideline. Practitioners are advised to consult references such as the Physician's Desk Reference, American Hospital Formulary Service, Epocrates, or Micromedex for more information about drug interactions with specific agents, and to assess the significance of the interaction prior to prescribing antidepressants.

Elderly patients: Because of the potential for decreased renal and hepatic function, concomitant diseases and medications, the elderly are at higher risk of significant side effects or drug interactions with antidepressant medications. For elderly patients with moderate to severe depression, TCAs such as nortriptyline continue to be regarded as the most effective treatment (*Alpert, 2003; Gasto, 2003*). Consider starting at the lowest possible dose and increasing slowly to effective dose or until side effects appear. Tertiary amine tricyclics should generally be avoided in elderly patients because of the high incidence of orthostatic hypotension, sedation, cognitive problems, and cardiac effects with these agents.

Supporting evidence is of classes: A, C

Pregnancy: Approximately 5 to 10% of women experience significant mood or anxiety symptoms during pregnancy. Physicians must help patients weigh the risk of prenatal exposure to psychotropic medications against the risks of untreated psychiatric illness. The first line of treatment for mild to moderate depression includes increased social supports and psychotherapy. When these non-medication options have failed or if patients have severe major depression or other Axis I (clinical disorders, other conditions that may be a focus of clinical attention) diagnoses, then the risks of untreated illness may outweigh the potential detrimental effects of certain psychotropic medications.

We continue to have limited information about the long-term neurobehavioral effects on children exposed in utero to antidepressants. Theoretically, in utero exposure to antidepressants could lead to subtle cognitive, psychological, or developmental effects on children. Two studies have found that preschool children who had been exposed in utero to SSRIs or TCAs during the first trimester or throughout pregnancy had no difference in language, behavioral, or intellectual development compared to non-exposed children.

There is no evidence that the tricyclic antidepressants and the SSRIs (especially fluoxetine) increase the risk of intrauterine death, fetal malformations, pregnancy complications or behavioral toxicity. Therefore, decisions regarding the treatment of depression during pregnancy must balance the risk to the mother and fetus secondary to untreated depression with the relative (although not absolute) safety of antidepressant treatment for this condition.

Patients commonly underestimate the risks of untreated maternal psychiatric illness while overemphasizing the risks of their psychotropic medications. Misperception about risk can lead both physicians and patients to terminate otherwise wanted pregnancies or avoid needed pharmacotherapy. By informing patients about the nature and magnitude of medication risks as well the risks of untreated illness, psychiatrists can help patients reach their own decisions.

U.S. FDA Pregnancy Risk Categories: (A) Controlled studies show no risk. Adequate, well-controlled studies in pregnant women have failed to demonstrate risk to the fetus. No currently available antidepressant medication is rated A. (B) No evidence of risk in humans. Either animal findings show risk, but human

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findings do not; or if no adequate human studies have been done, animal findings are negative. Bupropion and maprotiline are rated B. (C) Risk cannot be ruled out. Human studies are lacking, and animal studies are either positive for fetal risk or lacking. However, potential benefits may justify the potential risks. Amitriptyline, amoxapine, protriptyline, sertraline, trazodone, trimipramine, venlafaxine are rated C. (D) Positive evidence of risk. Investigational or post-marketing data show risk to the fetus. Nevertheless, potential benefits may outweigh the potential risks. If needed in a life-threatening situation or a serious disease, the drug may be acceptable if safer drugs cannot be used or are ineffective. Imipramine and nortriptyline are rated D. (X) Contraindicated in pregnancy. Studies in animals or human, or investigational or post-marketing reports have shown fetal risk which clearly outweighs any possible benefit to the patient. None of the currently available antidepressant medications are rated X.

Among antidepressants, the most reproductive safety information is available for the tricyclic antidepressants (TCAs), fluoxetine, and citalopram. Among the available pregnancy data, there is no evidence that these medications are associated with an increased risk of major congenital malformations. This is also true for sertraline, paroxetine, fluvoxamine, venlafaxine, and bupropion, however, there are fewer documented pregnancies with these medications.

There have been many case reports of perinatal syndromes with TCAs (e.g. jitteriness, irritability, bowel obstruction, urinary retention) as well as different SSRIs, e.g. fluoxetine, paroxetine, and sertraline. Other studies have found an association between prenatal SSRI exposure and preterm delivery. In general, however, these reports have been limited to case reports and small series. To avoid perinatal withdrawal syndromes, some support slowly tapering antidepressants in the weeks prior to delivery. This is a debated treatment strategy since it also theoretically withdraws antidepressants just as women are entering the postpartum period, a time of increased risk for mood or anxiety symptoms.

(Chambers, 1996; Larsen, 2003; Nulman, 1997; Simon, 2002a; Wadhwa, 1993; Wisner, 1999; Wisner, 2000)

Supporting evidence is of classes: B, C, R

Lactation: Antidepressants may appear in breast milk in low concentrations. Because of the long half-life of these drugs and their metabolites, nursing infants may have measurable amounts in their plasma and tissues, such as the brain. This is particularly important during the first few months of life, with immature hepatic and renal function. Because these drugs affect neurotransmitter function in the developing central nervous system, it may not be possible to predict long-term neurodevelopmental effects. Use only when clearly needed and potential benefits outweigh the risks to the nursing infant. (Adapted from AAP Policy Statement, Transfer of Drugs and Other Chemicals Into Human Milk, Pediatrics 2001;108:776-789) Breast-feeding offers several advantages: a) Breast-fed infants have lower rates of gastrointestinal disease, anemia, respiratory ailments, and otitis media compared to formula-fed infants; b) Nursing provides a unique opportunity for maternal-infant bonding. At the same time, the postpartum period (first 3 months following childbirth) is a particularly vulnerable period for psychiatric illness in women. Issues to be addressed when assessing the risks and benefits of psychotropic drug use during breast-feeding include the documented benefits of nursing, the potential adverse impact of untreated maternal mental illness on infant attachment and cognitive and behavioral development, and the effects of untreated mental illness on the mother.

Depression in the postpartum period can be disabling. Trials of cognitive behavioral therapy or interpersonal therapy, while safe, may not be effective – resulting in the need for antidepressant trials and/or electroconvulsive therapy (ECT). The use of antidepressants by nursing mothers is often acceptable as long as the mother-infant pair is monitored for the emergence of adverse effects or complications. Tricyclic antidepressants appear to be safe. However, there was one case report of respiratory distress in an infant of a mother treated with doxepin suggesting that this antidepressant should be avoided during lactation. Data on the SSRIs suggest that sertraline and paroxetine are safe to use in nursing mothers suffering from depression.

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There have been isolated case reports of infant toxicity in nursing mothers taking either doxepin or fluoxetine; however, studies have not revealed a consistent association between infant toxicity and any specific TCAs or SSRIs. The lack of adverse effects in 180 infants exposed to fluoxetine justifies its use especially if prescribed during the pregnancy or if there is a preferential history of response to this medication. Data on citalopram, fluvoxamine, bupropion and venlafaxine are more limited and their use cannot be recommended during breast-feeding at this time. Based on multiple case series, some researchers have recommended that the SSRI sertraline be considered the first-line treatment for nursing mothers with depression, however, sertraline may also carry risk in some mothers as demonstrated in one case report of an excessively high infant sertraline level in one mother-infant pair. Among the TCAs, nortriptyline has been the most studied treatment for nursing mothers, and no evidence of infant toxicity has been reported. Few studies have been done to evaluate the long-term consequences in children following antidepressant exposure through breast milk. One study followed children whose mothers nursed while taking TCAs. At preschool age these children were developmentally similar to non-exposed children. There have been no similar studies following children whose mother nursed while taking SSRIs.

(Burt, 2001; Nulman, 2002; Wisner, 2002)

Supporting evidence is of classes: C, R

Table 1: Classification, Doses, Safety and Side Effects of Antidepressants

| Mechanism of Action and Functional Classification | Starting Dose | Standard Dose | Lethality in Overdose | Side Effects | | | | | | |
|---|---------------|---------------|-----------------------|------------------------|--------------|--------------|-------------------------|------------------------------------|--------------------|--------------|
| | | | | Insomnia and Agitation | Sedation | Hypotension | Anticholinergic Effects | Nausea or Gastrointestinal Effects | Sexual Dysfunction | Weight Gain |
| Reuptake inhibitors | | | | | | | | | | |
| Selective serotonin-reuptake inhibitors (SSRIs) | | | | | | | | | | |
| Fluoxetine (Prozac) | 20 | 20-40 | Low | Moderate | None or mild | None or mild | None or mild | Moderate | Moderate | Mild |
| Paroxetine (Paxil) | 20 | 20-40 | Low | Moderate | None or mild | None or mild | Mild | Moderate | Moderate | Mild |
| Sertraline (Zoloft) | 50 | 50-150 | Low | Moderate | None or mild | None or mild | None or mild | Moderate | Moderate | Mild |
| Fluvoxamine (Luvox) | 50 | 100-250 | Low | Moderate | Mild | None or mild | None or mild | Moderate | Moderate | Mild |
| Citalopram (Celexa) | 20 | 20-40 | Low | Moderate | None or mild | None or mild | None or mild | Moderate | Moderate | Mild |
| Escitalopram (Lexapro) | 10 | 10-20 | Low | Moderate | None or mild | None or mild | None or mild | Moderate | Moderate | Mild |
| Selective norepinephrine-reuptake inhibitors (NRIs) | | | | | | | | | | |
| Reboxetine (Edronax) | 4-8 | 8-12 | Low | Mild | None or mild | None or mild | None or mild | Mild | Mild | None or mild |
| Nonselective norepinephrine-reuptake inhibitors | | | | | | | | | | |
| Desipramine (Norpramine) | 25-50 | 100-300 | High | Mild | None or mild | Moderate | Mild | None or mild | Mild | Mild |
| Nortriptyline (Pamelor) | 25-50 | 75-200 | High | Mild | Mild | Mild | Mild | None or mild | Mild | Mild |
| Maprotiline (Ludiomil) | 75 | 75-200 | High | Mild | None or mild | Mild | Mild | None or mild | Mild | Moderate |
| Mixed or dual-action reuptake inhibitors | | | | | | | | | | |
| Older agents (TCAs) | | | | | | | | | | |
| Amitriptyline (Elavil) | 25-50 | 100-300 | High | None or mild | Moderate | Moderate | Severe | None or mild | Mild | Moderate |
| Dothiepin (Dothep) | 25-50 | 100-300 | High | None or mild | Moderate | Moderate | Moderate | None or mild | Mild | Moderate |
| Clomipramine (Anafranil) | 25-50 | 100-250 | High | Mild | Moderate | Moderate | Moderate | Mild | Mild | Moderate |
| Imipramine (Tofranil) | 25-50 | 100-300 | High | Moderate | Mild | Moderate | Moderate | None or mild | Mild | Moderate |
| Newer Agents (non-TCAs) | | | | | | | | | | |
| Venlafaxine (Effexnor) (NRI plus SRI) | 37-75 | 75-225 | Moderate | Moderate | None or mild | None or mild | None or mild | Moderate | Moderate | None or mild |
| Milnacipran (Ixel) (NRI plus SRI) | 50-100 | 100-200 | Low | Moderate | None or mild | None or mild | None or mild | Moderate | Moderate | None or mild |
| Bupropion (Wellbutrin) (NRI plus DRI) | 150 | 150-300 | Low | Moderate | None or mild | None or mild | Mild | Mild | None or mild | None or mild |
| Duloxetine (Cymbalta) (NRI plus SRI) | 30 | 30-90 | Low | None or mild | Mild | None or mild | Mild | Mild | None or mild | None or mild |

mg/day

Table 1: Classification, Doses, Safety and Side Effects of Antidepressants (continued)

| Mechanism of Action and Functional Classification | Starting Dose | Standard Dose | Lethality in Overdose | Side Effects | | | | | | |
|---|---------------|---------------|-----------------------|------------------------|--------------|--------------|-------------------------|------------------------------------|--------------------|--------------|
| | | | | Insomnia and Agitation | Sedation | Hypotension | Anticholinergic Effects | Nausea or Gastrointestinal Effects | Sexual Dysfunction | Weight Gain |
| MOIs | | | | | | | | | | |
| Irreversible agents | | | | | | | | | | |
| Phenelzine (Nardil) | 15 | 30-90 | High | Moderate | Mild | Moderate | Mild | Mild | Moderate | Mild |
| Tranylpromine (Pamate) | 10 | 20-60 | High | Moderate | Mild | Moderate | Mild | Mild | Moderate | Mild |
| Isocarboxazid (Marplan) | 20 | 20-60 | High | Moderate | None or mild | Moderate | Mild | Mild | Moderate | Moderate |
| Selegiline (Eldepryl) | 10 | 20-40 | Moderate | Mild | None or mild | Mild | Mild | Mild | Mild | Mild |
| Reversible agents | | | | | | | | | | |
| Moclobemide (Manerix) | 150 | 300-600 | Low | Mild | None or mild | None or mild | Mild | Mild | None or mild | None or mild |
| Mixed-action newer agents | | | | | | | | | | |
| Mirtazapine (Remeron) (5-HT ₂ plus 5HT ₃ plus α ₂ -adrenergic receptors) | 30 | 30-60 | Low | None or mild | Severe | Mild | None or mild | None or mild | None or mild | Severe |
| Mianserin (Bolvidon) (5-HT ₂ Plus α ₁ -and α ₂ -adrenergic receptors) | 30 | 60-120 | Low | None or mild | Moderate | Mild | Mild | None or mild | None or mild | Mild |
| Nefazodone (Serzone) (5-HT ₂ receptors) | 100 | 300-600 | Low | None or mild | Moderate | Mild | Mild | Mild | None or mild | Moderate |
| Trazodone (Desyrel) (5-HT ₂ plus α ₁ -adrenergic receptors) | 50-100 | 200-600 | Low | None or mild | Severe | Mild | None or mild | Mild | Moderate | Mild |

These doses are standard in psychiatric practice but may not always conform to doses recommended in the Physician's Desk Reference or drug package insert. More detailed reviews of side effects for all classes of antidepressants may be found in the Guidelines of the American Psychiatric Association 2000 and the Agency for Health Care Policy and Research 1999. NRI denotes norepinephrine-reuptake inhibitor, TCA tricyclic antidepressant, SRI serotonin-reuptake inhibitor, MAOI monoamine oxidase inhibitor, and DRI dopamine-reuptake inhibitor. Symptoms include dry mouth, constipation, sweating, blurred vision, and urinary retention.

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For up-to-date prescribing information, the following drug references may be used:

- The Physician's Desk Reference: <http://www.pdr.net>
- The American Hospital Formulary Service (AHFS): <http://ashp.org/ahfs>
- Micromedex: <http://www.micromedex.com>
- Epocrates: <http://epocrates.com>

Herbals and Dietary Supplements

Caution: many drugs interact with St. John's wort, including other antidepressants, warfarin, oral contraceptives, antiretroviral, anti-cancer and anti-rejection drugs. Care should be taken to ask all patients what medications they are taking, including over-the-counter and supplements, to avoid these interactions.

Hypericum perforatum (St. John's wort) is popularly thought to be an herbal remedy for depression. The Hypericum Depression Trial Study Group concluded that the data does not support the use of Hypericum perforatum instead of antidepressants or psychotherapy. It has no proven efficacy in standard clinical care of patients with major depression.

St. John's wort has been found to interfere with the cytochrome 450 enzyme that the body uses to break down many widely prescribed medications including digoxin and beta blockers, seizure medications and drugs used to prevent organ rejection after transplants.

(Hypericum Depression Trial Study Group, 2002; Gaster, 2000; Health Technology Advisory Committee (HTAC), 2000; Linde, 1996)

SAM-e (S-adenosyl methionine) S-Adenosyl - L-methionine (SAM-e) is a natural compound that has been studied as a treatment option for depression. As of 2002, there were 11 controlled against placebo studies, 14 controlled against tricyclic antidepressant studies, and 2 meta-analysis. Essentially these studies show that SAM-e is superior to placebo and comparable tricyclics in the treatment of outpatients with major depression. Effective oral doses seem to be in the 400-1,600 mg a day range as compared to doses of 400 mg a day of tricyclics. Side effects are less common than with tricyclics (7% with oral and intramuscular SAM-e versus 28% with oral tricyclic) and include mild insomnia, lack of appetite, constipation, nausea, dry mouth, diaphoresis, dizziness and nervousness. Increased anxiety and hypomania have been reported in patients with bipolar depression. Interactions with other medications have not been studied and are unknown. Comparisons to newer antidepressants have not been done yet.

Other herbal remedies and dietary supplements, such as kava-kava, Omega-3 fatty acid, (docosahexaenoic acid) and valerian root, have not been proven effective for the treatment of depression and may or may not be safe.

(Mulrow, 2000; Whooley, 2000)

Herbal products and nutritional supplements are not evaluated or regulated by the U.S. Food and Drug Administration for safety, efficacy or bioavailability.

Supporting evidence is of classes: A, M, R

Establish Follow-Up Plan

Establish and maintain initial follow-up contact intervals (office, phone, other).

Katon et al. found that improving attitudes towards antidepressant medications along with the patient's ability to handle medication side effects are key factors in promoting greater adherence to maintenance treatment and thus greater likelihood of preventing relapse. It is important to recognize that Katon and colleagues worked

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within a relatively small, closed system (Group Health Seattle) where tracking and registry information were readily available. They also had financing available to cover the training of depression prevention specialists as well as the expense of visits, phone calls and follow-up letters. However, from a clinical standpoint, Katon's work demonstrates significant benefit for the patient (*Katon, 2001; Lin, 2003b*).

The prevention of relapse is of primary importance in the treatment of major depression. From 50 to 85% of people who suffer an episode of major depression will have a recurrence, usually within two or three years. Patients who have had three or more episodes of major depression are at 90% risk of having another episode. Focused psychotherapy helps protect against/prevent relapse.

(*American Psychiatric Association, 2000; Crawford, 2002; Hunkeler, 2000; Katon, 1996; Oxman, 2002; Rollman, 2002; Rost, 2001a; Rost, 2001b; Schoenbaum, 2002; Schulberg, 1998; Simon, 2002b; Simon, 2000b; U.S. Preventive Services Task Force (USPSTF), The, 2002; Wells, 2000*)

Interventions toward this end may include patient visits with a depression prevention specialist (PhD, MSN, MSW who has received special training) and follow-up phone calls. Interventions are critical to educating the patient regarding the importance of preventing relapse, safety and efficacy of medications and management of potential side effects.

If symptoms are severe: Weekly contacts may be needed until significant response is achieved. Response is defined as a significant level of improvement; or clinically relevant reduction of more than 50% on a severity scale such as PHQ-9 or the Hamilton Depression rating scale.

If mild or moderate symptoms are present: Contact should be every 2-4 weeks.

This protocol should be in place until remission or best possible response is achieved, then treatment should be spaced out as clinically warranted.

For maintenance medication: Office visits can occur every 3-12 months if everything else is stable.

When considering how long to continue medication after the remission of acute symptoms, two issues need to be considered: maintenance and prophylactic treatment.

After four months, the dose may be gradually tapered and discontinued by the sixth month. If symptoms re-emerge, medications should be restarted at the previous dose and continued for an additional six months followed by another attempt to taper off the medication. Attempting to taper medications off may not be appropriate in certain patients, specifically those with a high risk of recurrence (*Janicak, 1993; Mintz, 1992*).

Some evidence suggests treatment be continued through a two episode cycle for a period of years (*Hirschfied, 1994*). See also Annotation #13: Evaluate Dose, Duration, Type and Adherence with Medication and/or Psychotherapy/Reconsider Accuracy of Diagnosis or Impact of Comorbidities and Annotation #15: Continuation and Maintenance Treatment for 6-12 Months.

There are significant data to support the efficacy of antidepressants in preventing the recurrence of a major depressive episode. Although more research needs to be conducted, current findings indicate that patients who are at highest risk of future episodes have had multiple prior episodes or were older at the time of the initial episode (*Keller, 1998*). These patients are candidates for long-term or lifetime prophylactic treatment.

Lifetime treatment may be indicated for patients:

- Aged > 60 at first episode
- Aged > 40 with > 2 episodes
- With > 3 episodes

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The adjunctive use of targeted psychotherapy may be considered in some patients, both during acute phase treatment as well as during long-term maintenance (*Janicak, 1993; Schulberg, 1998*). Please refer to section discussing role of psychotherapy.

The decision to consider prophylactic treatment is also influenced by multiple factors:

- the severity of the depressive episode
- the frequency of past depressions
- the risk of suicide
- the risk of potential adverse medication effects

(*Janicak, 1993*)

If discontinuation of treatment is thought to be appropriate or necessary despite the known risks, a plan of action should be in place for prompt intervention if relapse occurs (*Greden, 1993*).

Supporting evidence is of classes: A, M, R

Referral

Consider involvement of a behavioral health care provider for the following:

- Patient request for psychotherapy.
- Presence of severe symptoms and impairment in patient.
- Diagnostic question.
- Presence of other psychiatric condition (e.g., personality disorder, history of mania).
- Substance abuse questions.
- Clinician discomfort with the case.
- Initial treatment does not result in a successful outcome.
- Patient request for more specialized treatment.

12. Is Patient Responding Adequately?

The goal of treatment should be to achieve remission. Remission is defined as the absence of depressive symptoms, or the presence of minimal depressive symptoms. Response is defined as a 50% or greater reduction in symptoms (as measured on a standardized rating scale) and partial response is defined as a 25-50% reduction in symptoms. There are different definitions of these issues in the literature, and the time at which one measures is also debated. Studies measure for effectiveness at 4, 8, and 12 weeks. Frequently, the level of response at 4 weeks, is predictive of response at 8 or 12 weeks (*Nierenberg, 1995*). Remission rates from research-based, 8-week randomized placebo-controlled efficacy trials using medications with depressed, symptomatic volunteers range from 25% to 40%.

A patient's response to antidepressant treatment should be evaluated between 4 and 6 weeks. A reasonable criteria for extending the initial treatment is if the patient is experiencing a 25% or greater reduction in baseline symptom severity at 4 weeks of therapeutic dose. If the patient's symptoms are reduced by 25% or more, but they are not yet at remission, and if medication has been well tolerated, then continue to prescribe and raising the dose is recommended. Improvement with psychotherapy is often a bit slower than with pharmacotherapy. A decision regarding progress with psychotherapy and the need to change or augment this type of treatment may require 8 to 10 weeks before evaluation.

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(Quitkin, 1996; Rollman, 2002)

Supporting evidence is of classes: A, D, M

13. Evaluate Dose, Duration, Type and Adherence With Medication and/or Psychotherapy/Reconsider Accuracy of Diagnosis or Impact of Comorbidities

Key Points:

- The key objectives for treatment are:
 - Acute phase goal for treatment of major depression is remission of symptoms. Remission may be expected in up to 40% of patients with single treatment. Remaining patients will need to be reevaluated for reasons for lack of remission and decisions made about next steps. Evidence shows that for these patients, at best, 40% will not be able to achieve remission. For those patients, the goal is to reduce symptoms to manageable levels.
 - Reduction of relapse and recurrence of major depression.
 - Return to previous level of occupational and psychosocial function.

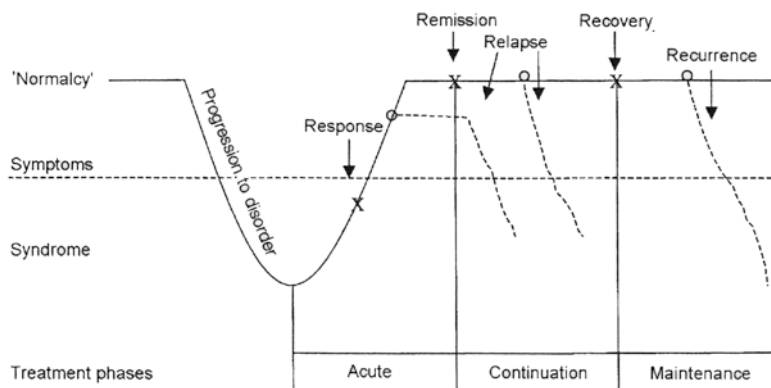


Fig. 1 Response, remission, recovery, relapse and recurrence of depression. From Kupfer (1991).

Treatment of major depression is divided into acute, continuation and maintenance phases as seen in Figure 1. Acute phase strives to achieve marked reduction of acute symptoms. Remission is the goal and usually takes 2-3 months. In the continuation phase, the improvement achieved during the acute phase is preserved until the time the depressive episode could have ended – usually an additional 6 to 12 months. The maintenance phase is designed to prevent the patient from experiencing a new depressive episode.

The terms used in the clinical course of major depression are response, remission, relapse, recovery and recurrence.

- Response is defined as a significant level of improvement; or clinically relevant reduction of more than 50% on a severity scale such as PHQ-9 or the Hamilton Depression rating scale.
- Remission is defined as a condition where only minimal signs of illness remain, or Hamilton Depression rating scale, (HDRS), less than 7 or PHQ-9 score of 4 or less.

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- Recovery is a sustained period of remission representing resolution of the index episode.
- Relapse is a condition where symptoms return during the current episode of depression.
- Recurrence is a new episode of depressive illness following recovery (one must be symptom free for at least 6 months from previous episode of depression.)
- Treatment-resistant depression has several definitions in the literature. It is important to distinguish treatment resistance from a lack of completion of a full course of treatment. The literature further tends to focus on pharmacological treatments in the definition of treatment resistance without consistently incorporating psychotherapeutic modalities. True treatment resistance, is seen as occurring on a continuum from failure to reach remission after an adequate trial of a single antidepressant, to failure to achieve remission despite several trials of antidepressants, augmentation strategies, ECT, and psychotherapy. For our purposes of making recommendations for primary care providers, we define true treatment resistance as: an adequate trial of therapy and two different classes of antidepressants at adequate duration and dosage (*Fava, 2003; Keller, 2005*).

(*Altamura, 1993; Hirschfeld, 2001; Storosum, 2001*)

Supporting evidence is of classes: A, R

Treatment Considerations

When considering treatment options, the primary goal is to achieve remission or to get the patient to be virtually symptom-free (i.e., a PHQ-9 score of ≤ 4 or a HAM-D score of < 7).

A. Pharmacotherapy vs. Psychotherapy

If the presenting symptoms of depression are severe, the initial recommendation is to treat with antidepressants and psychotherapy. If the initial presentation is mild to moderate then either an antidepressant or psychotherapy (or both) is indicated. Psychotherapy, especially focused psychotherapy can significantly reduce symptoms, restore psychosocial and occupational functioning, and prevent relapse in patients with major depression (*Leichsenring, 2004*).

It is useful to take into consideration cultural beliefs and sufficiency of (or lack of) resources such as transportation, finances, and child care when making a decision whether to treat with medication and/or psychotherapy.

- Pharmacologic and/or non-pharmacologic (psychotherapy) interventions are effective in treating depression. Factors to consider in making treatment recommendations are symptom severity, presence of psychosocial stressors, presence of comorbid conditions, and patient preferences.
- Depression treatment should take health beliefs into account. Patients who perceive more self-control of their health experience greater reduction in depressive symptoms, whether treated with psychotherapy or an antidepressant. Therefore, it is important to adequately assess a patient's expectations and beliefs in the controllability of depressive symptoms and functioning in order to treat major depression effectively and to minimize the risk of relapse and recurrence. (See (Annotation #9: Medical Comorbidity and/or Special Population and Annotation #11: Treatment Plan for details.)

(*Blackburn, 1997; Brown, 2000; Keller, 2000; Robinson, 1990; Sampson, 2001*)

- A switch from an antidepressant to psychotherapy or vice versa appears useful for nonresponders to initial treatment (*Schatzberg, 2005*).

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- Psychotherapy may provide better outcomes on adjustment/functional measures such as mood, suicidal ideation, work, and interests; medication treatment may be superior on vegetative symptoms such as sleep and appetite (*Antonuccio, 1995*).

Supporting evidence is of classes: A, C, M, R

B. Pharmacologic Therapy

- If there is less than 25% reduction of symptoms after six weeks at therapeutic dose (i.e., partial positive response to medication), add or substitute another treatment modality.
- When considering how long to continue medication after remission of acute symptoms, two issues need to be considered: continuation and maintenance treatment.

Without long-term antidepressant treatment major depressive relapses and recurrences occur in 50-80% of patients. Double-blind discontinuation studies reveal that antidepressants decrease the risk of relapse and recurrence and have repeatedly shown antidepressants to be more efficacious than placebo substitution.

It has been estimated that patients recovering from primary major depression have a relapse rate of 40-50%. Data also shows that patients who have three or more episodes of depression actually have a 90% risk of relapse.

The best candidates for maintenance therapy are patients who have two previous episodes of major depression, or who have two episodes of major depression but have also had rapid recurrence of episodes, or are older in age at the onset of major depression (more than 60 years of age), have had severe episodes of major depression or a family history of a mood disorder. Maintenance therapy should also be considered for at risk patients with double depression, patients with comorbid anxiety disorder, or substance abuse. Patients whose major depression has a seasonal pattern are also at risk for recurrence.

(*Rush, 1999*)

It has been well established that raising the dose of tricyclics or MAO inhibitors may improve response. Similarly, a controlled study showed that raising the dose of fluoxetine (from 20 mg to 40 or 60 mg) in partially responsive patients was more effective than adding desipramine (25-50 mg per day) or lithium (300-600 mg q.d.) In non-responders, raising the fluoxetine dose was as effective as adding lithium, and both were more effective than adding desipramine.

(*Fava, 1994; Perry, 1994*)

Recent analysis suggests that recurrence rates are reduced by 70% when patients are maintained on antidepressants for 3 years following their previous episode (average recurrence on placebo 41% versus 18% on active treatment) (*Greden, 1993; Hirschfeld, 2001*).

It is suggested that the dose of antidepressant medication that leads to satisfactory acute therapeutic response should be maintained during long-term treatment to prevent relapse and recurrence of depression (*Flint, 2000; Sonawalla, 2001*).

Patients experiencing the first episode of major depression should be withdrawn gradually, (six to 12 months, including acute and continuation therapy). Patients undergoing treatment for the second episode of major depression should continue treatment through a two episode cycle, perhaps four to five years. Patients who have three or more episodes of major depression or who have two episodes with complicating factors (such as rapid recurrence of episodes, more than 60 years at age of onset of major depression, severe episodes or family history), should continue treatment indefinitely (*Hirschfeld, 1994*).

Premature treatment discontinuation can be triggered by a number of factors including lack of adequate education about the disease, failure on the part of either physician or the patient to establish goals for

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follow-up, psychosocial factors and adverse side effects. Early drug discontinuation contributes to probability of relapse and recurrence (*Tollefson, 1993*).

One study with a tricyclic antidepressant showed decreased risk of relapse after 18 months of treatment (*Mavissakalian, 1992*).

Surveys of patient populations have indicated that patients receiving prescriptions for one of the benzodiazepines or other minor tranquilizers or hypnotics tend to use less than prescribed and to reduce their use over time. Benzodiazepine abuse is usually seen as part of a pattern of abuse of multiple drugs often involving alcohol and sometimes opioids (*Woods, 1988*).

Supporting evidence is of classes: A, C, D, R

See also "Establish Follow-Up Plan" in Annotation #11: Treatment Plan and Annotation #15: Continuation and Maintenance Treatment for 6-12 Months.

14. Consider Other Strategies

Key Points:

- When identifying that a patient is treatment resistant, the first steps are to reassess the diagnosis, look for comorbid medical and psychiatric problems that might be interfering with recovery, and to review the adequacy and adherence to previous treatment. For our purposes of making recommendations for primary care providers, we define true treatment resistance as: an adequate trial of therapy and two different classes of antidepressants at adequate duration and dosage.
- Augmentation strategies may be used for partial responders and combinations of antidepressants (when each has a different mechanism) have been shown to be options in those who fail to achieve remission.
- Randomized, controlled studies support the efficacy of psychotherapy in the treatment of depression.
- Partial or full hospitalization may be indicated in patients who have failed outpatient management, particularly if safety issues are a concern.
- Use of bright light therapy for treatment of major depression with a seasonal specifier is well established.
- Electroconvulsive treatment is very effective and can sometimes be administered safely in an outpatient setting.
- Vagus nerve stimulation treatment cannot be considered evidence based.
- Transcranial magnetic stimulation is currently showing some promise as a potential treatment for depression in early studies, but at this time is not approved by the FDA.

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- Although acupuncture is known to be an alternative therapy for the treatment of depression, it has shown mixed results.

If patient is newly involved in psychotherapy

- Return visit in 8-10 weeks to evaluate progress
- Contact with patient in 4-6 weeks
- Communicate with therapist in 4-6 weeks
- Therapy can take 8-10 weeks to show improvement

If the patient has been treated with medication and there is less than a 25% reduction in symptoms when evaluated at 4-6 weeks, switch to a different medication. If there is a partial response and side effects are not prohibitive, increase the dose. As part of the evaluation, using a standardized assessment tool will serve as a documentation of progress.

If the above measures have not achieved remission when re-evaluated 4-6 weeks later, consider:

- Re-evaluating the diagnosis
- Switching to a different antidepressant medication; augmentation strategies (such as lithium or low-dose thyroid); other biological treatments (such as a second antidepressant); adding a new medication. Failure of a drug in one family does not rule out possible benefit from other drugs in that family. This is particularly true for SSRIs (*Brown, 1995; Bull, 2002; Thase, 1997*).
- Referral to psychiatry for possible MAOI, ECT treatment. Many patients unresponsive to tricyclics are responsive to monoamine oxidase inhibitors. Rarely, the combination of tricyclics and MAO inhibitors is used. This combination should be undertaken with extreme caution. Studies measuring response to MAO inhibitors in SSRI non-responders have not been done (*McGrath, 1993; McGrath, 1994*).
- Looking for comorbidities, such as substance abuse issues and involve addiction specialists as needed.
- Consider the possibility of a bipolar diathesis. Bipolar patients require a different treatment approach and may not consistently come forward with their hypomanic, mixed, or manic histories (*Sharma, 2005*).
- Referral to behavioral health provider if there are personality disorders present.
- If only on medication, add psychotherapy
- Whether adequate engagement of patient/family is present and that recommendations are being followed (adherence)
- Obtaining a consultation or referral to behavioral health specialists

Supporting evidence is of classes: A, B, D

Augmentation Therapy is used for those situations where the patient's depression is either treatment-resistant or partially responsive to treatment. This is a good time to consult and/or refer to a behavioral health specialist.

Augmentation methods include:

- Lithium augmentation with TCA's. Lithium augmentation with SSRI (caution – case reports of serotonin syndrome).

Algorithm Annotations

- Seven placebo control studies have found positive evidence of efficacy of lithium augmentation. Combination of lithium and SSRI's have been relatively well-studied. In early studies, the usual dose of lithium was 300 mg three times a day. At this dose, serum lithium levels were usually above 0.4 mEq/L (*Baumann, 1996; Delgado, 1998; Joffe, 1993; Katona, 1995*).

Supporting evidence is of classes: A, D

- T₃ augmentation of TCA.
 - Placebo-controlled studies found mixed results. Usual dose of T₃ varied between 25-50 microgram/day (*Nelson, 2000*).

Supporting evidence is of class: R

- Stimulant drugs augmentation of TCA/SSRI ("jump-start response").
 - Five open studies reported positive results with stimulant augmentation of TCA/MAOI. An open trial of methylphenidate augmentation of SSRI was proved to be efficacious.
- TCA-SSRI combination (caution – elevated TCA level – to be monitored).
 - A 1991 study by Nelson study reported combination to be more rapidly effective and remission was more likely. The dose of TCA should be adjusted to achieve effective TCA levels as SSRI's increase TCA levels. Fluoxetine and Paroxetine raise TCA (desipramine) levels 3-4 fold and Citalopram and Sertraline have modest effects (*Nelson, 1991; Preskorn, 1990*).

Supporting evidence is of classes: C, D

- Bupropion – SSRI combination.
 - Three open series of cases and two other case reports have described beneficial results. The basis of this combination is the addition of a noradrenergic agent to a serotonergic agent to enhance effects; bupropion may also have dopaminergic actions (*Bodkin, 1997; Marshall, 1996; Spier, 1998*).

Supporting evidence is of class: D

- Mirtazapine – SSRI combination.
 - The addition of the alpha-2 antagonist Mirtazapine I is used to augment SSRI. Three controlled studies have found evidence of more rapid effects (*Cappiello, 1995; Dam, 1998; Maes, 1999*).

Supporting evidence is of classes: A, D

- Buspirone – SSRI combination.
 - Five open studies supported potential utility of this treatment and a response rate of approximately 60% was observed (*Bouwer, 1997; Dimitriou, 1998*).

Supporting evidence is of classes: C, D

- Carbamazepine/valproic acid – TCA combination (caution – may decrease TCA level). Carbamazepine/valproic acid – SSRI combination.
 - Case reports indicate marked improvement after addition of carbamazepine to clomipramine and valproic acid to fluoxetine or fluvoxamine. Use of carbamazepine or valproic acid in combination with a TCA should be used with caution and TCA levels should be monitored (*Corrigan, 1992; De la Fuente, 1992*).

Supporting evidence is of class: D

Algorithm Annotations

- Atypical antipsychotic – antidepressant combination
 - Several studies have been published supporting the use of atypical antipsychotics as augmentation agents with antidepressants for treatment resistant depression. These studies have largely been retrospective, or small in size. One study demonstrated robust and early response with addition of risperidone (*Ostroff, 1999*).

Supporting evidence is of class: D

Other Therapies

Based on work group consensus, the following therapies are in order of the likely clinical judgment and decision process of a primary care provider.

Psychotherapy

Randomized, controlled studies support the efficacy of psychotherapy in the treatment of depression. Patient preference, the nature and severity of depressive symptoms, access to resources, affordability of services, and the presence of environmental stressors should be considered as treatment planning is completed. There are numerous types of psychotherapy, just as there are numerous types of medication. If a patient has received psychotherapy and not responded, evaluate the treatment they have received and consider another type. Cognitive-Behavioral Therapy (CBT), Interpersonal Therapy (IPT), Short-Term Psychodynamic Psychotherapy (STPP) and Problem-Solving Therapy (PST) have documented efficacy. In mild to moderate levels of depression, psychotherapy can be equally as effective as medication. With severe depression, antidepressant medication may be more helpful in the acute phases. There is documentation to support lower relapse rates among patients receiving psychotherapy.

Hospitalization

Partial or full hospitalization may be indicated in patients who have failed outpatient management, particularly if safety issues are a concern.

Light Therapy

Use of bright light therapy for treatment of major depression with a seasonal specifier is well established. Additionally, there is preliminary evidence of the efficacy of bright light therapy for some other types of depressive symptom patterns, including non-seasonal depression and milder variations of seasonal depressive patterns. Bright light therapy may also quicken and enhance the effects of antidepressant medication. Preliminary evidence suggests efficacy in special populations such as moderately mentally retarded people and pregnant women. This is of significance as mentally retarded patients may be less likely to benefit from psychotherapy, and there are no antidepressants approved for use by pregnant women. A recent open study of light therapy for treatment of major depression during pregnancy yielded promising results, although further research is needed to clearly establish safety and efficacy during pregnancy. Although the light exposure dosage (typically 5,000-10,000 lux) and exposure length (typically 30-60 minutes) have been fairly standard for seasonal affective disorder treatment, research on bright light therapy for other types of depression has not necessarily utilized standard dosages and exposure times. It is important that any light therapy treatment utilize equipment that eliminates ultraviolet frequencies and produces bright light of known spectrum and intensity. For these reasons, use of client-constructed light therapy units are contraindicated.

(Benedetti, 2003; Golden, 2005; Jorm, 2002; Leppamaki, 2002; Manber, 2002; Oren, 2002; Prasko, 2002)

Supporting evidence is of classes: A, D, M, R

Electroconvulsive Treatment (ECT)

Electroconvulsive treatment is very effective and can sometimes be administered safely in an outpatient setting. ECT does not cure depression, and a successful ECT treatment should be followed by a plan to prevent relapse of the depression. A patient considering ECT would need to be able to tolerate anesthesia, and should consult with a psychiatrist about the risks and benefits (*National Institute for Clinical Excellence, 2003; Sackheim, 2001a; UK ECT Review Group, The, 2003*).

Factors that may suggest a given patient may be an ECT candidate include:

- Geriatric depression
- Antidepressant medications have not been tolerated or pose a significant medical risk
- Antidepressant medication trials have not been successful
- ECT has been successful in previous episodes
- Catatonia is present
- A rapid response is needed because of severe suicide risk or because the patient's health has been significantly compromised by the depression (i.e., severe cachexia, inability to attend to the activities of everyday living)
- Depression with psychotic features
- Melancholic symptoms are predominant
- Depression and Parkinsonism

Supporting evidence is of classes: A, M, R

For more information about ECT, see the Other Resources Available table in the Support for Implementation section.

Vagus Nerve Stimulation (VNS)

VNS involves the use of an implantable device, which provides intermittent stimulation to the left vagus nerve (80% afferent to the central nervous system). It is used as an adjunctive treatment along with other modalities such as use of psychotropic medications. It has only been studied in refractory or treatment resistant depression.

Side effects include: voice alterations (generally just while one is receiving the 30 seconds of stimulation each 5 min), increased rate of neck pain, cough, dyspnea, and dysphagia. At this point in time, VNS is approved by the FDA for treatment resistant depression. However, given the lack of double blind controlled studies and the somewhat disappointing result in the one available; this does not meet the threshold for category A evidenced based at this point in time but a promising new therapy that remains to be fully proven.

(George, 2005; Kraft, 2005; Nahas, 2005; Rush, 2000; Sackeim, 2001b; Sackeim, 2001c)

Supporting evidence is of class: D

Transcranial Magnetic Stimulation

Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive technique that stimulates the brain in vivo using high intensity, pulsed electron-magnetic fields. Recent research has examined the use of rTMS in the treatment of major depressive disorder. In the procedure, a hand-held stimulating coil is applied directly to the patient's head and delivers a magnetic pulse to the cortex. Results of research studies to date have been inconsistent and inconclusive (*Loo, 2003; Martin, 2003; O'Connor, 2003*).

In the past 2-3 years, several randomized control trials have been released supporting statistically significant responses to TMS as compared to sham treatment both as single and adjunct (to an antidepressant) treatment for major depressive disorder. There are also reports showing no significant response and criticism that the positive studies lack sufficient power to support this treatment modality. The FDA has not yet approved rTMS for general clinic use, and it must be considered, at this time, investigational (*Rossini, 2005; Fitzgerald, 2006*).

Another brain stimulation treatment, Magnetic Seizure Therapy, at this time is clearly not evidence based. Research is attempting to use magnetic stimuli to induce focal seizures in the right frontal area, which hopefully will not spread to the hippocampus and get the same confusions and memory side effects that make standard ECT problematic (*Sackeim, 1994*).

Supporting evidence is of classes: A, C, M, R

Acupuncture

Although acupuncture is known to be an alternative therapy for the treatment of depression, it has shown mixed results. Acupuncture may be an alternative for those who reject traditional treatments, for those who do not show adequate response to traditional treatments or for those in whom antidepressants may be contraindicated (frail, elderly or pregnant women). Electro-acupuncture may be a treatment of choice for those who are unable to comply with classic tricyclic antidepressants because of their anticholinergic side effects. It is felt that additional larger controlled and longitudinal studies need to be done for endorsement as a recommended treatment for depression.

In a few small controlled studies, the proportion of patients with some symptom relief with acupuncture, or a combination of acupuncture and amitriptyline are comparable to those of psychotherapy or pharmacotherapy. A negative study compared patients taking the tetracyclic antidepressant mianserin with patients treated with both mianserin and acupuncture or mianserin with sham acupuncture (needling at non-acupoints) and demonstrated no significant differences between the groups (*Ernst, 1998; Gallagher, 2001; Luo, 1998*).

Supporting evidence is of classes: A, R

15. Continuation and Maintenance Treatment for 6-12 Months

Acute treatment (usually the first 3 months of treatment) refers to treating with antidepressant medication in order to achieve remission of major depressive symptoms. Remission is defined as having minimal residual symptoms (Hamilton Depression Scale score less than 7 or PHQ-9 score of 4 or less). **Continuation therapy** is the phase where one continues to treat with antidepressants in order to keep the patient free of symptoms for the duration of the current episode. By definition this is considered to be at least 6 months long, but lately the evidence supports a 6-12 month duration. However, consider in elderly populations it may take longer to respond to acute treatment. Therefore, the maintenance period of treatment may need to be extended. **Maintenance therapy** is designed to prevent recurrence of new or future episodes of major depression.

Evidence-based literature which suggests treating more types of depressed patients with adequate dosages of antidepressants for longer periods is more effective in preventing relapses and recurrence. An adequate dose is generally considered to be the same as the dose required in the acute phase of treatment in order to achieve remission.

(American Psychiatric Association, 2000; Ellis, 2002; Ferrier, 1999; Finley, 2002; Geddes, 2003; Greden, 1993; Katon, 1996; Katon, 1997; Katon, 1999; Oxman, 2002; Paykel, 1995; Rost, 2002; Schoenbaum, 2002; Simon, 2000a; Simon, 2002b; Simon, 2000b; Wells, 2000)

Algorithm Annotations

Complicating factors are those situations where evidence either shows or suggests higher rates of recurrence after stopping antidepressants and include:

- Pre-existing dysthymia
- Inability to achieve remission
- Recurrence of symptoms in response to previously attempted lowering dose or discontinuation

With the wide array of half-lives and therapeutic dose ranges for the various existing antidepressants, it is beyond the scope of this guideline to discuss detailed discontinuation strategies.

When feasible (e.g., the starting dose is not the same as therapeutic doses), it is recommended that the dose be tapered over a period of weeks to several months when discontinuing an antidepressant.

See also "Establish Follow-Up Plan" in Annotation #11: Treatment Plan and Annotation #13: Evaluate Dose, Duration, Type and Adherence with Medication and/or Psychotherapy/Reconsider Accuracy of Diagnosis and Impact of Comorbidities.

Supporting evidence is of classes: A, B, C, M, R

Appendix A – Other Mood Disorders

Generalized Anxiety Disorder DSM-IV TR Criteria:

- A. Excessive anxiety and worry about a number of events (which cause clinically significant distress or impairment in functioning) occurring more days than not for at least six months.
- B. The person finds it difficult to control the worry.
- C. Associated with at least three of the following:
 - 1. Restlessness, feeling "on edge."
 - 2. Fatigue.
 - 3. Difficulty concentrating.
 - 4. Irritability.
 - 5. Muscle tension.
 - 6. Sleep disturbance.

Panic Attack DSM-IV TR Criteria:

Discrete period of intense fear or discomfort in which at least four of the following symptoms develop abruptly and reach a peak within 10 minutes:

- 1. Palpitations, pounding or accelerated heart rate.
- 2. Sweating.
- 3. Trembling or shaking.
- 4. Sensations of shortness of breath or smothering.
- 5. Feeling of choking.
- 6. Chest pain or discomfort.
- 7. Nausea or abdominal distress.
- 8. Feeling dizzy, unsteady, lightheaded or faint.
- 9. Feelings of unreality or being detached from oneself.
- 10. Fear of losing control or going crazy.
- 11. Fear of dying.
- 12. Paresthesias (numbness or tingling).
- 13. Chills or hot flashes.

Useful interview questions for anxiety:

- Are you often worried or anxious?
- Do you have repetitive behaviors or thoughts that are difficult for you to control?
- Do you ever experience sudden attack or fear of losing control, dying, fainting, going crazy, or severe embarrassment?
- Are you particularly anxious when meeting new people, or in groups?
- Are there places, things, or situations that you go out of your way to avoid due to an unusual fear level?

Diagnosis suggestive of any anxiety disorder:

- Atypical chest pain
- Hyperventilation
- Irritable bowel syndrome

Treatment and Education:

Both pharmacologic and non-pharmacologic interventions may be effective depending on the severity of symptoms. For antidepressant medications, adherence with a therapeutic dose is more important than the specific drug selected. The following educational messages may increase adherence:

- 1. Take the medication daily.
- 2. Antidepressants must be taken for two to four weeks for a noticeable effect.
- 3. Continue to take medication for at least 6-12 months even if feeling better.
- 4. Do not stop taking antidepressant without checking with your provider.
- 5. Contact your provider if you have questions about your medication.

Appendix A – Other Mood Disorders

| Examples of Other Mood Disorders: | | |
|---|---|--|
| In many of these circumstances, a referral to mental health is appropriate. | | |
| Disorder | Description | Useful Questions |
| Dysthymia 300.4 | Chronic (> 2 years) and frequent low mood, often experienced as emptiness or sadness, often accompanied with lethargy and self-criticism, and requiring at least 2 other symptoms of MDD. | Do you often feel sad, empty, or unmotivated? |
| Depressive disorder NOS 311 | Depressive symptoms not meeting criteria for another mood disorder. | Do you experience periods where you feel down or depressed? |
| Bipolar disorder 296.80 | History of at least one episode of mania (e.g., high energy, irritability, grandiosity, minimal sleep, pleasure seeking) and commonly severe depression. | Have either you or your family members noticed you've experienced periods of at least a week where you have: <ul style="list-style-type: none"> • talked or thought more and/or faster than usual? • needed significantly less sleep? • felt happier, and/or more irritable than usual? • initiated and engaged more than usual in activities such as spending money, sexual activities, travel? |
| Examples of Anxiety Disorders: | | |
| Social phobia 300.23 | Marked and persistent fear of potentially embarrassing social or performance situations. | Do you worry that you might embarrass yourself in a social or performance situation? |
| Specific phobia 300.29 | Marked and persistent fear of a specific object or situation. | Do you have excessive or unreasonable fears about specific objects or situations? |
| Obsessive compulsive disorder 300.3 | Persistent and intrusive thoughts, ideas, impulses or images associated with repetitive behaviors to reduce distress. | Are you bothered by recurrent thoughts and/or repetitive behaviors? |
| Post traumatic stress disorder 309.81 | Exposure to a traumatic event which is persistently re-experienced with anxiety symptoms lasting more than one month. | Do you have distressing anxiety caused by re-experiencing some past traumatic event? |
| Acute stress disorder 308.3 | Exposure to a traumatic event which is persistently re-experienced with anxiety symptoms lasting two days to four weeks, and occurring within four weeks of the event. | Do you have distressing anxiety caused by re-experiencing some past traumatic event? |
| Anxiety disorder NOS (not otherwise specified) 300.00 | Prominent anxiety of phobic avoidance not meeting criteria for another specific anxiety disorder which, for example, may be episodic, a reaction to a medical condition, or a combination of symptoms from several anxiety disorders. | Do you have episodes of nervousness or excessive worry? |
| Social phobia 300.23 | Marked and persistent fear of potentially embarrassing social or performance situations. | Do you worry that you might embarrass yourself in a social or performance situation? |

Appendix B – Patient Health Questionnaire (PHQ-9)

Patient Questionnaire - PHQ-9 Nine Symptom Checklist

Patient Name: _____ Date: _____

1. Over the *last 2 weeks*, how often have you been bothered by any of the following problems?

| | Not at all | Several days | More than half the days | Nearly every day |
|--|--------------------------|--------------------------|-------------------------------|--------------------------|
| | 0 | 1 | 2 | 3 |
| a. Little interest or pleasure in doing things. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| b. Feeling down, depressed, or hopeless. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| c. Trouble falling/staying asleep, sleeping too much. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| d. Feeling tired or having little energy. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| e. Poor appetite or overeating. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| f. Feeling bad about yourself - or that you are a failure or have let yourself or your family down. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| g. Trouble concentrating on things, such as reading the newspaper or watching television. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| h. Moving or speaking so slowly that other people could have noticed. Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| i. Thoughts that you would be better off dead or of hurting yourself in some way. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

2. If you checked off any problem on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

| | | | |
|--------------------------|--------------------------|--------------------------|--------------------------|
| Not difficult at all | Somewhat difficult | Very difficult | Extremely difficult |
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

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Instructions - How to Score PHQ-9

Major Depressive Syndrome is suggested if:

- Of the 9 items, 5 or more are checked as at least "More than half the days"
- Either #1.a or #1.b is positive, that is, at least "More than half the days"

Other Depressive Syndrome is suggested if:

- Of the 9 items, 2, 3, or 4 are checked as at least "More than half the days"
- Either item #1.a or #1.b is positive, that is, at least "More than half the days"

Also, PHQ-9 scores can be used to plan and monitor treatment. To score the instrument, tally each response by the number value under the answer headings, (not at all = 0; several days = 1, more than half the days = 2, and nearly every day = 3). Add the numbers together to total the score on the bottom of the questionnaire. Interpret the score by using the guide listed below:

PHQ-9 Scoring for Severity Determination

Scoring – add up all checked boxes on PHQ-9

For every check: Not at all = 0; Several days = 1; More than half the days = 2; Nearly every day = 3

| Total Score | Depression Severity |
|--------------------|------------------------------|
| 0-4 | No depression |
| 5-9 | Mild depression |
| 10-14 | Moderate depression |
| 15-19 | Moderately severe depression |
| 20-27 | Severe depression |

Patient responses to the PHQ-9 questions can be one of four: (Not difficult at all, Somewhat difficult, Very difficult, Extremely difficult.) The last two responses suggest that the patient's functionality is impaired. After treatment begins, functional status is again measured to see if the patient is improving.

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Patient Health Questionnaire PHQ-9
Nine Symptom Checklist (Spanish)

Nombre _____ Médico _____ Fecha De Hoy _____

Durante las últimas 2 semanas, ¿cuan qué frecuencia le han molestado los siguientes problemas?

| | Nunca | Varios días | Más de la mitad de los días | Casi todos los días |
|--|--------------------------|--------------------------|-----------------------------------|---------------------------|
| | 0 | 1 | 2 | 3 |
| a. Tener poco interés o placer en hacer las cosas | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| b. Sentirse desanimado/a, deprimido/a, o sin esperanza | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| c. Con problemas en dormirse o en mantenerse dormido/a, o en dormir demasiado | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| d. Sentirse cansado/a o tener poca energía | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| e. Temer poco apetito o comer en exceso | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| f. Sentir falta de amor propio – o que sea un fracaso o que decepcionara a si mismo/a su familia | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| g. Tener dificultad para concentrarse en cosas tales como leer el periódico o mirar la televisión | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| h. Se mueve o habla tan lentamente que otra gente se podria dar cuenta – o de lo contrario, esta tan agitado/a o inquieto/a que se mueve mucho más de lo acostumbrado | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| i. Se le han ocurrido pensamientos de que sería mejor estar muerto/a o de que haría daño de alguna manera* | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

1. Si usted se identificó con cualquier problema en este cuestionario, ¿cuan difícil se le ha hecho cumplir con su trabajo, atender su casa, o relacionarse con otras personas debido a estos problemas?

- Nada en absoluto Algo difícil Muy difícil Extremadamente difícil

11. Si estos problemas le han causado dificultad, ¿le han causado dificultad por dos años o más?

- Sí, he tenido dificultad con estos problemas por dos años o más.
 No, no he tenido dificultad con estos problemas por dos años o más.

**Si tiene pensamientos de que es mejor estar muerto/a o hacerse daño en alguna manera, favor de hablar con su médico, ir a una sala de emergencia o llamar al 911.*

Number of symptoms: _____ Total score: _____

Appendix C – The Hamilton Rating Scale for Depression

(to be administered by a health care professional)

Patient's Name: _____

Date of Assessment: _____

To rate the severity of depression in patients who are already diagnosed as depressed, administer this questionnaire. The higher the score, the more severe the depression.

For each item, write the correct number on the line next to the item. (Only one response per item)

1. DEPRESSED MOOD (Sadness, hopeless, helpless, worthless)

- _____ 0 = Absent
1 = These feeling states indicated only on questioning
2 = These feeling states spontaneously reported verbally
3 = Communicates feeling states non-verbally – i.e., through facial expression, posture, voice, and tendency to weep
4 = Patient reports VIRTUALLY ONLY these feeling states in his spontaneous verbal and non-verbal communication

2. FEELINGS OF GUILT

- _____ 0 = Absent
1 = Self reproach, feels he has let people down
2 = Ideas of guilt or rumination over past errors or sinful deeds
3 = Present illness is a punishment. Delusions of guilt
4 = Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations

3. SUICIDE

- _____ 0 = Absent
1 = Feels life is not worth living
2 = Wishes he were dead or any thoughts of possible death to self
3 = Suicidal ideas or gesture
4 = Attempts at suicide (any serious attempt rates 4)

4. INSOMNIA EARLY

- _____ 0 = No difficulty falling asleep
1 = Complains of occasional difficulty falling asleep – i.e., more than 1/2 hour
2 = Complains of nightly difficulty falling asleep

5. INSOMNIA MIDDLE

- _____ 0 = No difficulty
1 = Patient complains of being restless and disturbed during the night
2 = Waking during the night – any getting out of bed rates 2 (except for purposes of voiding)

6. INSOMNIA LATE

- 0 = No difficulty
1 = Waking in early hours of the morning but goes back to sleep
2 = Unable to fall asleep again if he gets out of bed

7. WORK AND ACTIVITIES

- 0 = No difficulty
1 = Thoughts and feelings of incapacity, fatigue or weakness related to activities, work or hobbies
2 = Loss of interest in activity, hobbies or work – either directly reported by patient, or indirect in listlessness, indecision and vacillation (feels he has to push self to work or activities)
3 = Decrease in actual time spent in activities or decrease in productivity
4 = Stopped working because of present illness

8. RETARDATION: PSYCHOMOTOR (Slowness of thought and speech; impaired ability to concentrate; decreased motor activity)

- 0 = Normal speech and thought
1 = Slight retardation at interview
2 = Obvious retardation at interview
3 = Interview difficult
4 = Complete stupor

9. AGITATION

- 0 = None
1 = Fidgetiness
2 = Playing with hands, hair, etc.
3 = Moving about, can't sit still
4 = Hand wringing, nail biting, hair-pulling, biting of lips

10. ANXIETY (PSYCHOLOGICAL)

- 0 = No difficulty
1 = Subjective tension and irritability
2 = Worrying about minor matters
3 = Apprehensive attitude apparent in face or speech
4 = Fears expressed without questioning

11. ANXIETY SOMATIC: Physiological concomitants of anxiety (i.e., effects of autonomic overactivity, “butterflies,” indigestion, stomach cramps, belching, diarrhea, palpitations, hyperventilation, paresthesia, sweating, flushing, tremor, headache, urinary frequency.) Avoid asking about possible medication side effects (i.e., dry mouth, constipation)

- 0 = Absent
1 = Mild
2 = Moderate
3 = Severe
4 = Incapacitating

12. SOMATIC SYMPTOMS (GASTROINTESTINAL)

- _____ 0 = None
1 = Loss of appetite but eating without encouragement from others. Food intake about normal
2 = Difficulty eating without urging from others. Marked reduction of appetite and food intake

13. SOMATIC SYMPTOMS GENERAL

- _____ 0 = None
1 = Heaviness in limbs, back or head. Backaches, headaches, muscle aches. Loss of energy and fatigability
2 = Any clear-cut symptom rates 2

14. GENITAL SYMPTOMS (Symptoms such as: loss of libido, impaired sexual performance, menstrual disturbances)

- _____ 0 = Absent
1 = Mild
2 = Severe

15. HYPOCHONDRIASIS

- _____ 0 = Not present
1 = Self-absorption (bodily)
2 = Preoccupation with health
3 = Frequent complaints, requests for help, etc.
4 = Hypochondriacal delusions

16. LOSS OF WEIGHT

- _____ **A.** When rating by history:
0 = No weight loss
1 = Probably weight loss associated with present illness
2 = Definite (according to patient) weight loss
3 = Not assessed

17. INSIGHT

- _____ 0 = Acknowledges being depressed and ill
1 = Acknowledges illness but attributes cause to bad food, climate, overwork, virus, need for rest, etc.
2 = Denies being ill at all

18. DIURNAL VARIATION

- _____ **A.** Note whether symptoms are worse in morning or evening. If NO diurnal variation, mark none
0 = No variation
1 = Worse in A.M.
2 = Worse in P.M.
- _____ **B.** When present, mark the severity of the variation. Mark "None" if NO variation
0 = None
1 = Mild
2 = Severe

19. DEPERSONALIZATION AND DEREALIZATION (Such as: Feelings of unreality; Nihilistic ideas)

- _____ **0** = Absent
1 = Mild
2 = Moderate
3 = Severe
4 = Incapacitating

20. PARANOID SYMPTOMS

- _____ **0** = None
1 = Suspicious
2 = Ideas of reference
3 = Delusions of reference and persecution

21. OBSESSIVE AND COMPULSIVE SYMPTOMS

- _____ **0** = Absent
1 = Mild
2 = Severe

Total Score _____

Source: Hamilton M. Development of a rating scale for primary depressive illness. *Br J Soc Clin Psychol* 1967;6:278-96.

Appendix D – Geriatric Depression Scale

Self-administered **Long form:** 30 questions; **Short form:** 15 questions

Time recall: **Long form:** "now or within the past week;" **Short form:** "over the past week"

List of existing translations:

English, Chinese, Danish, Dutch, French, German, Greek, Hebrew, Hindi, Hungarian, Icelandic, Italian, Japanese, Korean, Lithuanian, Malay, Portuguese for Brazil, Romanian, Russian, Spanish, Swedish, Thai, Turkish, Vietnamese, Yiddish.

Geriatric Depression Scale - Short Form

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

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

Answers in **bold** indicate depression. Although differing sensitivities and specificities have been obtained across studies, for clinical purposes a score > 5 points is suggestive of depression and should warrant a follow-up interview. Scores > 10 are almost always depression.

Source: The Hartford Institute for Geriatric Nursing Division of Nursing, New York University.



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SYSTEMS IMPROVEMENT

Supporting Evidence:

Major Depression in Adults in Primary Care

Document Drafted
May – Jul 1995

First Edition
Jan 1996

Second Edition
Feb 1997

Third Edition
Apr 1998

Fourth Edition
Apr 1999

Fifth Edition
June 2001

Sixth Edition
June 2002

Seventh Edition
Oct 2003

Eighth Edition
June 2004

Ninth Edition
Begins Jun 2006

Availability of references

References cited are available to ICSI participating member groups on request from the ICSI office. Please fill out the reference request sheet included with your guideline and send it to ICSI.

Released in May 2006 for Ninth Edition.

The next scheduled revision will occur within 24 months.

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- Class B: Cohort study
- Class C: Non-randomized trial with concurrent or historical controls
Case-control study
Study of sensitivity and specificity of a diagnostic test
Population-based descriptive study
- Class D: Cross-sectional study
Case series
Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

- Class M: Meta-analysis
Systematic review
Decision analysis
Cost-effectiveness analysis
- Class R: Consensus statement
Consensus report
Narrative review
- Class X: Medical opinion

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This section provides resources, strategies and measurement specifications for use in closing the gap between current clinical practice and the recommendations set forth in the guideline.

The subdivisions of this section are:

- Priority Aims and Suggested Measures
 - Measurement Specifications
- Key Implementation Recommendations
- Knowledge Products and Resources
- Other Resources Available

Priority Aims and Suggested Measures

1. Increase the accuracy of diagnosis of major depression.

Possible measure of accomplishing this aim:

- a. Percentage of patients with a new diagnosis of major depression with documentation of DSM-IV TR criteria at the time of the initial diagnosis.

2. Improve the frequency of assessment of response to treatment in patients with major depression.

Possible measures of accomplishing this aim:

- a. Percentage of patients who have a depression follow-up contact within three months of initiating treatment.
- b. Percentage of patients whose symptoms are reassessed by the use of a quantitative symptom assessment tool (PHQ-9) within three months of initiating treatment.

3. Improve the outcomes of treatment for major depression.

Possible measures of accomplishing this aim:

- a. Percentage of patients whose results on two quantitative symptom assessment tools (such as PHQ-9) decrease by 50 percent within six months (+/- 30 days) after diagnosis (response rate).
- b. Percentage of patients whose results on two quantitative symptom assessment tools (such as PHQ-9) scores of < 5 or Hamilton Depression Scale of 7 or less) within six months (+/- 30 days) after diagnosis (remission rate).

4. Increase the percent of patients with major depression who continue on antidepressants for an adequate length of time.

Possible measures of accomplishing this aim:

- a. Percentage of patients with an initial episode of major depression who stay on antidepressants for 6 months.
- b. Percentage of patients with depression who have a prior episode of major depression who stay on antidepressants for 3 years.
- c. Percentage of patients with depression who have two prior episodes of major depression who continue with antidepressants indefinitely.

5. Increase the assessment for major depression of primary care patients presenting with any additional chronic condition such as diabetes, cardiovascular disease, or chronic pain.

Possible measures of accomplishing this aim:

- a. Percentage of patients with diabetes with documentation of screening for major depression.
- b. Percentage of patients with cardiovascular disease with documentation of screening for major depression.
- c. Percentage of patients with chronic pain with documentation of screening for major depression.

Priority Aims and Suggested Measures

6. Improve communication between the primary care physician and the mental health care provider (if patient is co-managed).

Possible measure of accomplishing this aim:

- a. Percentage of patients whose primary care records show documentation of any communication between the primary care physician and the mental health care provider in either direction.
7. Improve the frequency of assessment of patients with major depression for the presence of substance abuse.

Possible measure of accomplishing this aim:

- a. Percentage of depressed patients who are assessed for the presence of substance abuse at the time of diagnosis or within six months of diagnosis.

Measurement Specifications

Possible Success Measurement #1a

Percentage of patients with a new diagnosis of major depression, with documentation of DSM-IV TR criteria within the three months prior to initial diagnosis.

Population Definition

Adults greater than 18 years with a new primary care diagnosis* of major depression.

Data of Interest

medical records containing documentation of DSM-IV TR criteria within the three months prior to initial diagnosis

medical records reviewed for patients newly diagnosed with major depression

Numerator/Denominator Definitions

Numerator: Number of records containing documentation of DSM-IV TR criteria within the three months prior to initial diagnosis.

Denominator: Number of primary care patients reviewed greater than 18 years with new diagnosis* of major depression that has not been treated for depression in the previous six months.

Suggested ICD-9 codes include: 296.2X, 296.3X

*New diagnosis = no diagnosis in the six-month period prior to the target quarter.

Documentation of DSM-IV TR Criteria

Must have a **total of five** symptoms for at least two weeks. **One** of the symptoms **must** be depressed mood or loss of interest.

1. Depressed mood
2. Markedly diminished interest or pleasure in all or almost all activities
3. Significant (>5% body weight) weight loss or gain, or decrease or increase in appetite
4. Insomnia or hypersomnia
5. Psychomotor agitation or retardation
6. Fatigue or loss of energy
7. Feeling of worthlessness or inappropriate guilt
8. Diminished concentration or indecisiveness
9. Recurrent thoughts of death or suicide

Method/Source of Data Collection:

Claims, encounter data, scheduling information, or list of diagnosis codes from other automated sources may be used to identify those patients who meet the inclusion criteria for this measure. A random sample of 20 patients is suggested. The medical record will be reviewed to determine if DSM-IV TR criteria are documented as used. The presence of narrative comments reflecting application of DSM-IV TR criteria in making the diagnosis is acceptable evidence for this measure.

Time Frame Pertaining to Data Collection

The suggested time period is a calendar month.

Priority Aims and Suggested Measures

Possible Success Measurement #2a

Percentage of patients who have a depression follow-up contact* within three months of initiating treatment.

Population Definition

Adults greater than 18 years with a new primary care diagnosis** of major depression.

Data of Interest

A. Frequency of Follow-up

of patients who have a depression follow-up contact* within three months of initiating treatment

medical records reviewed for patients newly diagnosed with major depression

Numerator/Denominator Definitions

Numerator: Number of patients who have a depression follow-up contact within three months of initiating treatment.

Denominator: Number of primary care patients reviewed greater than 18 years with new diagnosis** of major depression in previous six months.

Suggested ICD-9 codes include: same as measurement #1

* Contact = an office visit with physician or other care provider, phone, other

**New diagnosis = no diagnosis in the six-month period prior to the target quarter.

Method/Source of Data Collection:

Same as measurement #1

Time Frame Pertaining to Data Collection

The suggested time period is a calendar month.

Priority Aims and Suggested Measures

Possible Success Measurement #2b

Percentage of patients whose symptoms are reassessed by the use of a quantitative symptom assessment tool (such as PHQ-9) within three months of initiating treatment.

Population Definition

Adults greater than 18 years with a new primary care diagnosis* of major depression.

Data of Interest

of patients whose symptoms are reassessed by the use of a quantitative symptom assessment tool (such as PHQ-9) within three months of initiating treatment

medical records for patients newly diagnosed with major depression with a quantitative symptom assessment tool (such as PHQ-9) documented

Numerator/Denominator Definitions

Numerator: Number of patients whose symptoms are reassessed by the use of a quantitative symptom severity scale instrument (such as PHQ-9) within three months of initiating treatment

Denominator: Number of primary care patients reviewed greater than 18 years with a new diagnosis* of major depression with initial quantitative symptom assessment tool (such as PHQ-9) documented

Suggested ICD-9 codes include: same as measurement #1

*New diagnosis = no diagnosis in the six-month period prior to the target quarter.

Method/Source of Data Collection:

Same as measurement #1

Time Frame Pertaining to Data Collection

The suggested time period is a calendar month.

Priority Aims and Suggested Measures

Possible Success Measurement #3a

Percentage of patients whose results on 2 quantitative symptom assessment tools (such as PHQ-9) decrease by 50 percent within six months (+/- 30 days) after diagnosis.

Population Definition

Adults greater than 18 years with a new primary care diagnosis* of major depression.

Data of Interest

Response Rate

of patients whose results on 2 quantitative symptom assessment tools (such as PHQ-9) decrease by 50% within 6 months of (+/- 30 days) after diagnosis

medical records of patients diagnosed with new major depression with documented 2 quantitative symptom assessment tool (such as PHQ-9) results

Numerator/Denominator Definitions

Numerator: Number of patients whose results on 2 quantitative symptom assessment tools (PHQ-9) decrease by 50% from the previous result documented within 6 months (+/- 30 days)

Denominator: Number of primary care patients greater than 18 years with new diagnosis* of major depression, with documented 2 quantitative symptom assessment results in their medical chart.

Suggested ICD-9 codes include: same as measurement #1 & #2

*New diagnosis = no diagnosis in the six-month period prior to the target quarter.

Method/Source of Data Collection

Identify base population through claims, encounter data, scheduling information, or list of diagnosis codes to determine those with previous PHQ-9 or other instrument score documented.

Time Frame Pertaining to Data Collection

The suggested time period is a calendar month.

Priority Aims and Suggested Measures

Possible Success Measurement #3b

Percentage of patients whose results on 2 PHQ-9s score < 5 or similar testing (Hamilton Depression Scale 7 or less) within 6 months (+/- 30 days) after diagnosis.

Population Definition

Adults greater than 18 years with a new primary care diagnosis* of major depression.

Data of Interest

Remission Rate

of patients whose results on 2 quantitative symptom assessment tools (such as PHQ-9) scores < 5 or Hamilton Depression Scale of 7 or less) within 6 months (+/- 30 days) after diagnosis

medical records of patients diagnosed with new major depression with 2 PHQ-9 results, or similar testing

Numerator/Denominator Definitions

Numerator: Number of patients whose results on 2 PHQ-9s or similar testing show remission within 6 months (+/- 30 days) after diagnosis

Denominator: Number of primary care patients greater than 18 years with new diagnosis* of major depression, with documented 2 PHQ-9 results in their medical chart within the last 6 months.

Suggested ICD-9 codes include: same as measurement #1 & #2

*New diagnosis = no diagnosis in the six-month period prior to the target quarter.

Method/Source of Data Collection:

Identify base population through claims, encounter data, scheduling information, or list of diagnosis codes to determine those with previous PHQ-9 or other instrument score documented.

Time Frame Pertaining to Data Collection

The suggested time period is a calendar month.

Priority Aims and Suggested Measures**Possible Successes Measurement #6a**

Percentage of patients with diabetes with documentation of screening for depression.

Population Definition

Adults greater than 18 years with a diagnosis of diabetes.

Data of Interest

patients with documentation in the medical record of screening for depression

total # of patients seen with diabetes

Numerator/Denominator Definitions

Numerator: Number of patient records containing documented evidence of screening for depression at the time the diagnosis was made using the key interview questions recommended in the guideline.

Denominator: Number of patients greater than 18 years with a diagnosis of diabetes during the target quarter.

Method/Source of Data Collection

The medical group will develop a method to identify patients who meet the inclusion criteria for this measure. This screening should only be done in systems where appropriate treatment systems are in place, as screening alone has not been shown to be helpful. Claims, encounter data, scheduling information, or list of diagnosis codes from other automated sources may be used to produce the list. From this list, a random sample of a maximum of 20 patients with diabetes seen in the target quarter will be selected for review. A medical record review will be used to determine if the screening occurred at the time of the visit.

Was there an interview for key symptoms of major depression?

The two-question screen:

Over the past month, have you been bothered by:

- Little interest or pleasure in doing things?
- Feeling down, depressed or hopeless?

Time Frame Pertaining to Data Collection

It is suggested that data is collected quarterly.

Key Implementation Recommendations

1. Detection and diagnosis
 - Systems in place to reliably determine if a patient is depressed
 - Use of DSM-IV TR criteria and structured questionnaires (such as PHQ-9)
2. Patient-centered care, education and self-management programs
 - Structured attention to patient preferences
 - Patient and family education materials/protocols
 - Patient self-management skills such as journal writing or self-monitoring
 - Involving families as well in care management programs
3. Mental health/behavioral medicine specialist involvement
 - Shared care – collaborative care between behavioral health specialists and primary care providers in the primary care setting
 - Appointment availability – access to behavioral health in timely manner
 - Structured patient co-management – two-way communication between behavioral health and primary care
4. Outcomes measurement
 - Build in plans for outcome measures as well as ongoing process measures
 - Response rate to various treatments
 - Remission rates – improvement in response is stable over time
5. Systems to coordinate care, ensure continuity and keep providers informed of status
 - Build automated processes for the first 4 core elements wherever possible
 - Reduce dependence on human behavior to ensure delivery of patient care processes
 - Use of components of the chronic care model for depression care, i.e., use of registries, community outreach etc.
 - Structured frequent monitoring and follow-up with patient
 - Nurse phone care and use of other modalities for patient follow-up

Knowledge Products and Resources

Criteria for Selecting Resources

The following resources were selected by the *Major Depression in Adults in Primary Care* guideline work group as additional resources for providers and/or patients. The following criteria were considered in selecting these sites.

- The site contains information specific to the topic of the guideline.
- The content is supported by evidence-based research.
- The content includes the source/author, and contact information.
- The content clearly states revision dates or the date the information was published.
- The content is clear about potential biases, noting conflict of interest and/or disclaimers as appropriate.

Resources Available to ICSI Members Only

The following materials are available to ICSI members only. Also available is a wide variety of other knowledge products including tool kits on CQI processes and Rapid Cycling that can be helpful. To obtain copies of these or other Knowledge Products, go to <http://www.icsi.org/knowledge>.

To access these materials on the website you must be logged in as an ICSI member.

Recorded Presentations

Video

- Management of Depression in Primary Care, Michael Trangle, M.D., 2004

Educational Resources

Summary Reports

- 2004 Depression Action Group Summary Report
- Report on Depression Coding

Tool kits

- Depression Pocket Card
- Depression, ICSI Guideline Quick Reference
- SMDC Depression/Suicide Protocol

Other Resources Available

| Title/Description | Audience | Author/Organization | Websites/Order Information |
|---|---|--|--|
| Provides mental health news, on-line CME programs and legislation. Links to MEDEM for patient information. | Patients and Families/Health Care Professionals | American Psychiatric Association | http://www.psych.org |
| Training manuals and tools to download | Health Care Professionals | Health Disparities Collaboratives | http://www.healthdisparities.net |
| Advocacy, links to Minnesota chapter support groups | Patients and Families/Health Care Professionals | National Alliance for the Mentally Ill | http://www.nami.org |
| This government-sponsored site provides comprehensive information on the following topics: clinical trials, research and funding opportunities, and patient education materials for adults and children. Links to PubMed, MedlinePlus and other relevant sites are available. | Patients and Families/Health Care Professionals | National Institute of Mental Health | http://www.nimh.nih.gov |
| This government-sponsored comprehensive site provides information on medications, diagnosis, treatments, clinical trials and links to other relevant sites. Spanish versions of some patient education materials are also provided. | Patients and Families/Health Care Professionals | National Library of Medicine MedlinePlus | http://www.nlm.nih.gov/medlineplus |
| Provides patient information, depression screening tool, community resources and discussion board. | Patients and Families/Health Care Professionals | National Mental Health Association | http://www.nmha.org |
| Provides parents of children and adolescents information about pediatric depression, treatment alternatives and the latest science and research findings. | Patients and Families/Health Care Professionals | American Psychiatric Association/American Academy of Child and Adolescent Psychiatry | http://www.parentsmedguide.org |
| Hope and Help for Your Nerves; 204-page book | Patients and Families | Weekes | Bookstores; \$4.99 |
| Depression; 23-page booklet | Patients and Families | Department of Health and Human Services | Dept. of HHS (301)443-4140 or (800)421-4211 NIH Pub #00-3561; Limited quantities available at no cost. Information in the public domain and can be reprinted without permission |

Other Resources Available

| Title/Description | Audience | Author/Organization | Websites/Order Information |
|---|---|--|--|
| Depression: What Every Woman Should Know; 24-page booklet | Patients and Families | National Institutes of Health | Dept. of HHS (301)443-4140 or (800)421-4211 NIH Pub; Limited quantities available at no cost |
| Understanding Depression; 3-fold brochure | Patients and Families | Park Nicollet Institute | PDF available at http://icsi.org/knowledge/detail.asp?catID=240&itemID=2030 |
| Let's Talk About Depression; 8-page booklet written above the average reading level | Patients and Families | American Psychiatric Association | American Psychiatric Press, Inc. (800)368-5777 #2351; \$22.00/50 |
| Feeling Good Handbook; book | Patients and Families | Dr. David Burns | Bookstores |
| Hope and Help for Depression Self-Care Handbook; 31-page booklet | Patients and Families | Channing Bete | Channing Bete 1-800-628-7733 |
| Mind over Mood; 215-page workbook | Patients and Families | Dennis Greenburger and Christine Padesky | Bookstores |
| Depression: Electroconvulsive Therapy Handout | Patients and Families/Health Care Professionals | American Academy of Family Physicians | http://familydoctor.org/058.xml |
| Electroconvulsive Therapy Handout | Patients and Families | American Psychiatric Association | http://ps.psychiatryonline.org Psychiatry Serv 52:1145-1146, September 2001 |