ICSI

Institute for Clinical Systems Improvement

Health Care Guideline

The information contained in this *ICSI Health Care Guideline* is intended primarily for health professionals and the following expert audiences:

- physicians, nurses, and other health care professional and provider organizations;
- health plans, health systems, health care organizations, hospitals and integrated health care delivery systems;
- medical specialty and professional societies;
- researchers;
- federal, state and local government health care policy makers and specialists; and
- employee benefit managers.

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This *ICSI Health Care Guideline* is designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and is not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. An *ICSI Health Care Guideline* rarely will establish the only approach to a problem.

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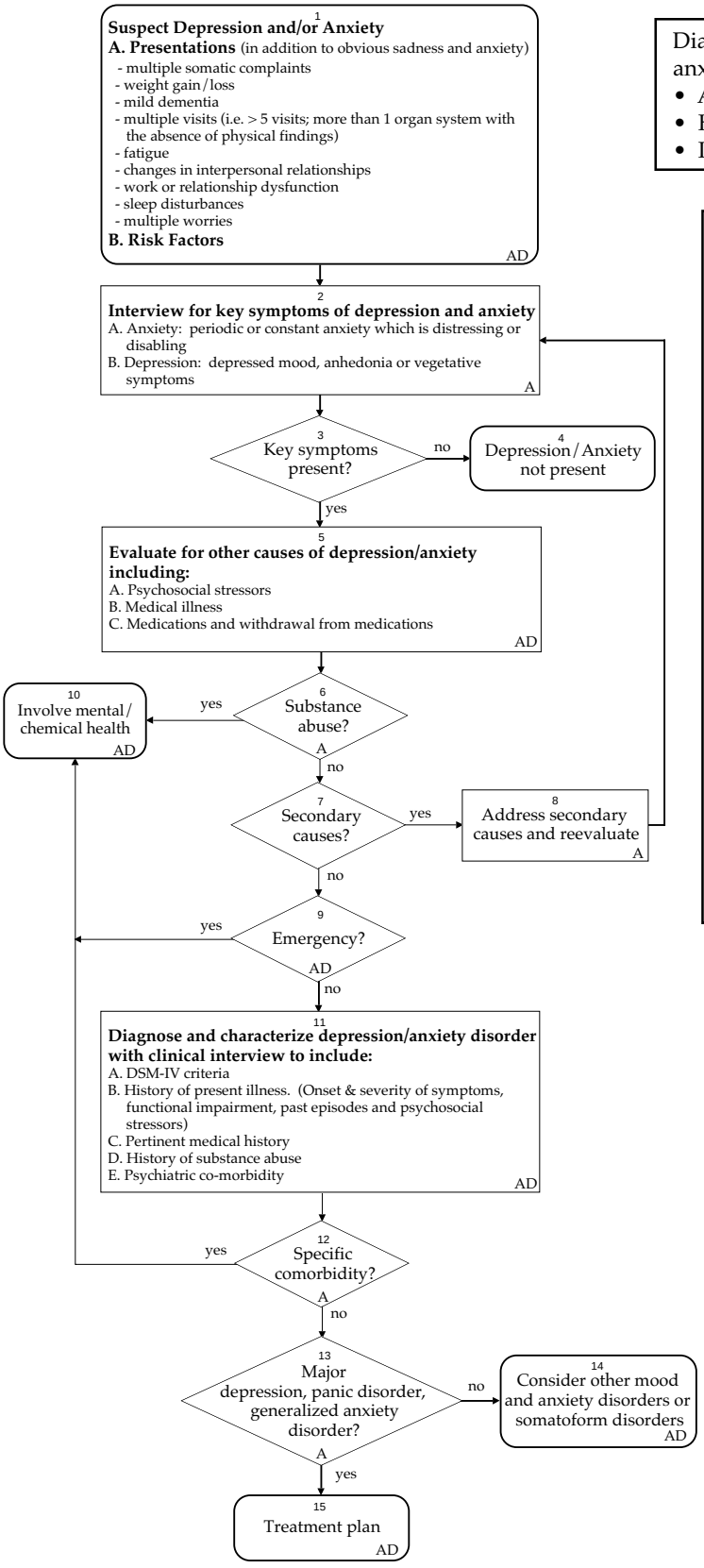
INSTITUTE FOR CLINICAL SYSTEMS IMPROVEMENT

Health Care Guideline:

Major Depression, Panic Disorder and Generalized Anxiety Disorder in Adults in Primary Care



Diagnosis Suggestive of an anxiety disorder:

- Atypical chest pain
- Hyperventilation
- Irritable bowel syndrome

Useful interview questions:

For Depression:

- Are you often sad, down, blue or teary?
- Do you have your usual interest in, and look forward to, enjoyable activities?
- Are you able to have fun or experience joy?

For Anxiety:

- Are you often worried? (are you a high-strung or nervous person?)
- Do you ever experience an "out of the blue" attack of fear of losing control, dying, fainting, "going crazy" or severe embarrassment?
- Are there places (e.g., shopping malls) or situations (e.g., parties) that you avoid or endure?

A = Annotation
D = Discussion

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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.

Table of Contents

SCOPE AND TARGET POPULATION

All adults greater than 18 years of age.

RELATED ICSI SCIENTIFIC DOCUMENTS

Other ICSI guidelines whose scope and/or recommendations are closely related to the content of this guideline are:

1. Major Depresion in Adults for Mental Health Care Providers
2. Preventive Counseling and Education

CLINICAL HIGHLIGHTS FOR INDIVIDUAL CLINICIANS

1. Presentations for depression and/or anxiety include:
   - Multiple (>5/year) medical visits
   - Multiple unexplained symptoms
   - Work or relationship dysfunction/changes in interpersonal relationships
   - Fatigue
   - Weight gain/loss
   - Sleep disturbances
   - Multiple worries or distress
   - Panic attacks
   - Dementia

   (Annotation #1)
2. Presentations particularly suggestive of an anxiety disorder include:
   - Medically unexplained symptoms of autonomic excitation such as:
     - cardiac (chest pain, palpitations, shortness of breath)
     - gastrointestinal (particularly epigastric distress)
     - neurologic (headache, dizziness, paresthesia)
     - panic attacks
   - Emergency room visits for medically unexplained somatic symptoms, particularly chest pain

   (Annotation #1)

3. Diagnosis particularly suggestive of an anxiety disorder include:

   - Atypical chest pain
   - Hyperventilation
   - Irritable bowel syndrome

   (Annotation #1)

4. If other psychiatric problems are present or suspected, such as psychosis or eating disorders, involve mental health. *(Annotation #12)*

5. Antidepressant medications and/or referral for psychotherapy are recommended as treatment for major depression without other non mental health conditions or substance abuse or other specific psychiatric comorbidities. Physical activity and tailored patient education are also useful tools in easing symptoms of depression. *(Annotation #15)*

6. When antidepressant therapy is prescribed, medication compliance and completion is critical:

   - Most people need to be on medication at least 6 months.
   - It may take from 1-6 weeks before improvement is seen.
   - Take the medication as prescribed.
   - Do not stop taking the medication without calling your provider. Side effects can be managed by changes in the dosage or dosage schedule.

   (Annotation #15)

PRIORITY AIMS AND SUGGESTED MEASURES FOR HEALTH CARE SYSTEMS

1. Increase the use of DSM-IV criteria in the detection and diagnosis of panic disorder, generalized anxiety and depression in primary care.

   Possible measures of accomplishing this aim:

   a. Percentage of patients with a new diagnosis of depression, panic disorder or generalized anxiety disorder with documentation of DSM-IV criteria at the time of the initial diagnosis.

2. Increase the assessment for depression and anxiety disorders of primary care patients presenting with more than 5 visits in the past year with problems in more than one organ system.

   Possible measures of accomplishing this aim:

   a. Percentage of patients with a new diagnosis of fatigue with documentation of screening for depression and anxiety disorder.

   b. Percentage of patients with a new diagnosis of irritable bowel syndrome with documentation of screening for depression and anxiety disorder.

   c. Percentage of patients with a new diagnosis of sleep disturbance with documentation of screening for depression and anxiety disorder.

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 Discussion and References section of the guideline.

ALGORITHM ANNOTATIONS

1. Suspect Depression and/or Anxiety

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

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

Presentations for depression and/or anxiety include:

- multiple (>5/year) medical visits
- multiple unexplained symptoms
- work or relationship dysfunction
- fatigue
- changes in interpersonal relationships
- weight gain or loss
- sleep disturbance
- multiple worries or distress
- panic attacks
- dementia

Presentations particularly suggestive of an anxiety disorder include:

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

Evidence supporting this recommendation is of classes: B, C, D, R

Physical symptoms particularly suggestive of an anxiety disorder include:

- atypical chest pain
- hyperventilation
- irritable bowel syndrome

Evidence supporting this recommendation is of classes: C, D, R

Depression risk factors include family history of depression and/or alcoholism; history of anxiety disorder and/or depression; recent loss; and chronic illness.

Anxiety risk factors include family history of anxiety disorder and/or alcoholism; history of depression and/or anxiety disorder; age < 40 at onset of symptoms; and history of alcohol abuse.

Evidence supporting this recommendation is of classes: C, D, R

2. Interview for Key Symptoms of Depression and Anxiety

A. Depressed mood or anhedonia (diminished interest or pleasure in activities) is necessary to diagnose **DEPRESSION**. If you suspect depression on the basis of risk factors or common presentations, ask about depressed mood and anhedonia. Useful questions include:

Over the past two weeks, have you often been bothered by:

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

If the patient answers "yes" to either one of the above questions, consider using a questionnaire to further assess whether the patient has sufficient symptoms to warrant a diagnosis of clinical depression and a full clinical interview. An example of such a questionnaire is the PHQ-9. Please see our Discussion and References section for this questionnaire.

B. Anxiety and/or avoidance behavior that causes significant distress or impairment of routines are necessary to diagnose an **ANXIETY DISORDER**. Anxiety may occur in brief episodes (panic attacks), may be continuous (generalized anxiety disorder) or may be tied to specific situations (phobias). Most patients with panic disorder present with somatic concerns, not complaints of anxiety or panic. These patients may not label their emotional distress as anxiety or panic and it may be necessary to ask in various ways about their discomfort. **Brief, episodic somatic complaints reaching a peak within 10 minutes and accompanied by any sense of emotional discomfort are suggestive of panic attacks.**

Useful interview questions include:

- Are you a worrier? (Are you a high strung/nervous person?)
- Do you ever "out of the blue" experience an attack of intense fear of losing control, dying, fainting, "going crazy" or severe embarrassment?
- Are there places (e.g. shopping malls) or situations (e.g. parties) that you avoid or endure?
- How does your anxiety or avoidant behavior affect your daily life? Does it cause you significant distress?

5. Evaluate for Other Causes of Depression/Anxiety

A. Psychosocial Stressors

Stressful life events include loss (death of a loved one, divorce), domestic abuse/violence, traumatic events (car accident) and major life changes (job change). Emotional and behavioral reactions to these social stressors can include symptoms of depression and anxiety.

Patients with adjustment reactions may only need time and support. However, if symptoms are persistent or debilitating, medication and/or psychotherapy should be considered.

Since these adjustment reactions can develop into a major depression or anxiety disorder, follow-up and re-evaluation should be offered.

General depressive conditions may follow childbirth. The transient 7-10 day depressive condition referred to as "post-partum blues" typically is too mild to meet the criteria for major depression and does not require medication.

Evidence supporting this recommendation is of class: R

B. Medical Illness

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

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

A past medical history and brief review of systems is generally sufficient to rule out medical disorders causing depression and anxiety.

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 depression and anxiety has not been established. It is not necessary to test for pheochromocytoma when typical panic attack symptoms occur.

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 depressive or anxious episode occurs after the age of 40.
- The depression or anxiety does not respond fully to routine treatment.

Evidence supporting this recommendation is of classes: C, D

C. **Medications and Withdrawal from Medications**

Reserpine, steroids, alpha-methyldopa, propanolol and hormonal therapy may be associated with **DEPRESSION**. Excessive caffeine causes **ANXIETY**. Thyroxine, theophylline, neuroleptics, sympathomimetics, antihistamines, steroids and antidepressants may be associated with **ANXIETY**.

Withdrawal from alcohol, cocaine, sedatives, anxiolytics, hypnotics and amphetamines may be associated with depression and/or anxiety.

Idiosyncratic reactions to other medications can occur and if possible, a medication should be stopped or changed if depression or anxiety develops after beginning its use. If symptoms persist after stopping or changing medication, re-evaluate for a primary mood or anxiety disorder.

6. Substance Abuse?

The CAGEAID Screen broadens the CAGE to include other drug use. See Annotation Appendix A for details.

8. Address Secondary Causes and Reevaluate

People with secondary causes for depression and anxiety may also have an underlying primary mood or anxiety disorder. If symptoms persist after secondary cause is addressed, re-evaluate for primary mood or anxiety disorder.

9. Emergency?

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 men are at disproportionate risk
- Two thirds of elderly suicide completers are in relatively good health
- Substance abuse is often a contributing factor, especially in younger people
- The presence of firearms in the home is believed to greatly increase the danger if other risk factors are present
- 75% of elderly suicide completers were seen by their doctor within one month of death
- Across all age groups, one in seven suicide conpleters had contact with their doctor within a week of death
- 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)
    - agitation (e.g. from sleep loss or drug use)
    - hopelessness

There are no good predictors of suicide. The clinician should consider previous history of suicide attempts; chemical dependency, personality disorder and/or physical illness; family history of sui-

cide; single status; recent loss by death, divorce or separation; insomnia; panic attacks and/or severe psychic anxiety; diminished concentration; anhedonia; hopelessness; or suicidal ideation.

Evidence supporting this recommendation is of class: C

10. Involve Mental/Chemical Health

Consider involving Mental Health same day 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.
- Loss of touch with reality (psychosis).
- Significant or prolonged inability to work and care for self/family.

11. Diagnose and Characterize Depression/Anxiety Disorder with Clinical Interview

Depression and anxiety disorders are diagnosed on the basis of specific (DSM IV) criteria obtained through a clinical interview.

A. **DSM-IV criteria** (see Annotation Appendix A)

Major depression, panic attacks and generalized anxiety disorder (see Annotation Appendix A)

Panic Disorder and Agoraphobia

- Panic disorder is the presence of recurrent (at least two) unexpected panic attacks followed by at least one month of persistent concern about having another panic attack, worry about the possible implications or consequences of the panic attacks, or a significant behavioral change related to the attacks.
- Agoraphobia is anxiety about being in places or situations from which escape might be difficult or embarrassing, or in which help may not be available in the event of having a panic attack or panic like symptoms. The situations are avoided or are endured with distress. Typical situations include being outside the home alone; being in a crowd or standing in line; being on a bridge; and traveling in trains, planes and automobiles.

Panic disorder and agoraphobia may occur together or separately.

Evidence supporting this recommendation is of classes: C, D, R

B. **History of present illness including:**

- Onset
- Severity Of Symptoms and Degree of Functional Impairment:

  People diagnosed with depression and anxiety disorders have a heterogeneous course from self-limiting to life-threatening. Predictors of poor outcome include 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

Ask patients with **ANXIETY** about avoidance of work, social gatherings, malls, stores, churches and transportation.

- Number and severity of previous episodes, treatment responses and suicide attempts.
- Psychosocial stressors (significant loss, conflict, financial difficulties, life change, abuse).

C. **Pertinent medical history** that may complicate treatment (e.g. prostatism, cardiac conduction abnormalities, impaired hepatic function).

D. Past history of **substance abuse**.

12. Specific Comorbidity?

Ask patients with depression about a history of manic symptoms (abnormally elevated, expansive or irritable mood). Patients with a history of manic (bipolar) symptoms now presenting with depression may develop manic symptoms with antidepressant drugs. Consider involving Mental Health with these patients. If other psychiatric problems are present or suspected, involve Mental Health. If other psychiatric problems such as psychosis or eating disorders are suspected or present, involve mental health.

13. Major Depression, Panic Disorder or Generalized Anxiety Disorder?

If criteria for major depression, panic disorder or generalized anxiety disorder are met, record appropriate diagnosis in chart and service record.

14. Consider Other Mood and Anxiety Disorders or Somatoform Disorders

Patients with some depressive symptoms who do not meet full DSM-IV criteria for Major Depression often respond positively to antidepressant medication and/or psychotherapy. These depressive syndromes 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. Non-Major Depression includes Dysthymic Disorder and depressive state NOS (not otherwise specificed).*

Examples of Other Anxiety Disorders:

*In many of these circumstances referral to mental health is appropriate

Disorder	Description	Useful Questions
Social phobia	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	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	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	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	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)	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?

Examples of Other Mood Disorders:

Disorder	Description	Useful Questions
Dysthymia	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	Depressive symptoms not meeting criteria for another mood disorders, which, for example, may be episodic or possibly due to a medical condition.	Do you experience periods where you feel down or depressed?
Bipolar Disorder	Recurrent severe mood swings involving episodes of mania (e.g., high energy, irritability, grandiosity, minimal sleep, pleasure seeking) and commonly severe depression.	Do you experience sharp mood swings?

Distinguishing features of Multiple Somatic Complaints:

Condition	Distinguishing Feature
Somatization disorder pain disorder	Distressing physical symptoms or pain with no diagnosable medical condition.
Panic disorder	Symptoms occur primarily during panic attacks.
GAD	Focus of anxiety and worry not limited to physical complaints.
Depression	Symptoms always in context of depression and remit with treatment of depression.
Hypochodriasis	Somatic preoccupation which can't be accounted for by one of the above conditions.

Consider treatment and/or involvement with Mental Health for these patients based on their distress and disability.

15. Treatment Plan

A. The key objectives of treatment are:

1. Acute phase goal for treatment of depression is total symptom remission. This necessitates some measurement of symptom severity at critical decision points during and at the end of treatment to determine whether remission has been attained.
2. Reduction of recurrence of depression and panic disorder.
3. Return to previous level of occupational and psychosocial function.

B. Treatment Considerations

1. Pharmacologic Therapy vs. Psychotherapy

- Pharmacologic and/or non-pharmacologic interventions (psychotherapy) are effective in treating both depression and anxiety disorders. Patient preferences should be considered. Factors to consider in making treatment recommendations are symptoms severity, presence of psychosocial stressors, presence of co-morbid conditions, and patient preferences.
- Depression treatment should take health beliefs into account. Patients who perceive more self-control of their health experienced greater reduction in depression 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 depression effectively and to minimize the risk of relapse and recurrence.

2. Pharmacologic Therapy

- Treatment of choice for major depression may include pharmacology and psychotherapy. For patients with mild to moderate depression, psychotherapy and/or pharmacology is indicated. For severe depression, a combination therapy is indicated
- If the initial medication response is incomplete after six weeks at therapeutic dose (e.g., 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.

Acute Phase involves stabilization of acute symptoms (usually 3 months.)

Continuation treatment, (usually lasting 6-12 months after the acute treatment), consists of prolonged administration of treatment after disappearance of acute depressive symptoms and aims to maintain a euthymic state or a duration of the episode.

Maintenance treatment consists of long-term efforts to prevent new episodes of recurrences and can extend for years. It should be strongly considered for all patients at the risk of recurrence. Risk factors include:

1. Three previous major depressive episodes.
2. Two prior episodes with associated risk factors of family history of depression or bipolar, or psychotic or severe episodes.
3. Pre-existing dysthymia.

4. Severe episodes.
5. Seasonal patterns.
6. Familial history of affective disorder
7. A poor response to continuation therapy.
8. Comorbid anxiety.
9. Substance abuse problems.
10. Age more than or equal to 50 at first episode.
11. Age more than or equal to 40 with more than or equal to two episodes.
12. Reoccurrence of symptoms in response to previously attempted discontinuation.

Continuation treatment and Maintenance Treatment should consist of full dose antidepressant therapy.

RECOMMENDED GUIDELINES FOR TREATMENT OF DEPRESSION

EPISODE	TREATMENT DURATION
First	Up to 1 year
Second	4-5 years
Second with complicating factors	Indefinitely
Third	Indefinitely

- Providers and patients often have strong opinions regarding the use of certain medications such as benzodiazepines, or whether to rely on psychotherapy or medication. Offer patients a menu of effective treatments. Medications and/or cognitive behavioral treatments may be effective for PD and GAD. Benzodiazepines and Selective Serotonin Re-uptake Inhibitors (SSRIs) have proven efficacy for panic disorder.

3. Psychotherapy

- Outcome studies support the efficacy of various psychotherapeutic approaches (cognitive-behavioral, interpersonal, structured educational group therapy).
- Consider early referral for psychotherapy if psychological and psychosocial issues are prominent and/or patient requests it. Referral for psychotherapy may have maximum benefit as symptom severity diminishes.
- Supportive therapy by the physician in the primary care setting is not the same as a course of psychotherapy with a mental health professional. However, education, support and reassurance by the physician are critical. Support/reassurance includes asking the patient for his/her ideas regarding the cause of the depression, anxiety or the panic, and about their expectations of recovery. Ask patients with panic attacks "What is your greatest fear?" Do not accept "I don't know." The most common fears are physical (fainting or death from stroke, heart attack or suffocation) and psychological (embarrassment, humiliation or going crazy). Reassure patients that anxiety attacks are not dangerous. Inform patients with depression that they have a good chance of improving with an antidepressant.

4. Exercise

Physical activity is a useful tool for easing 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. When prescribing exercise 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 vulnerable to guilt and self-blame if they fail to carry out the regime
- 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 thepatient's preferences, and must be pleasurable
- State specifics - a goal of 30 minutes of moderate-intensity exercise, 3-5 days a week is reasonable for otherwise healthy adults
- Encourage compliance - greater antidepressant effects are seen when training continues beyond 16 weeks

C. Patient Education

1. Successful care of depression requires tailored and on-going patient education, beginning at the time of diagnosis. Written materials are helpful to reinforce information shared during the discussion. Patients who 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 regime (office visits and/or telephone contacts)
- Early warning signs of relapse or recurrences
- Length of treatment

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

- Most people need to be on medication at least 6 months.
- It may take from 1-6 weeks before improvement is seen.

- Take the medication as prescribed.
- Do not stop taking the medication without calling your provider. Side effects can be managed by changes in the dosage or dosage schedule.

D. Medications

SSRI's and TCA's

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

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

Benzodiazepines

Benzodiazepines are effective for GAD and panic disorder. The benzodiazepines are not identical with regard to potency, onset and duration of action or presence of active metabolites; therefore if a patient's response is less than optimal, try a different drug. Benzodiazepines with long half lives or active metabolites are more convenient to administer but may cause toxicity in older patients or patients with liver disease.

Benzodiazepines as a class have a small potential for abuse and physical dependency addiction is rare in patients with no history of drug or alcohol abuse. Screen for past or present chemical dependency and use benzodiazepines with care, if at all, with chemically dependent patients.

Patients on long-term benzodiazepines are usually taking lower rather than higher doses after years of treatment. Some clinicians consider benzodiazepines only for short-term use, or when other drugs have failed to control symptoms, or have significant side-effects. Research data do not support forbidding or continuing the long-term use of benzodiazepines.

When evaluating patients for long-term treatment with benzodiazepines, consider using the following Dupont criteria and document the continued appropriate use of the drug. If you can answer yes to the following questions, it is reasonable to document answers and continue treatment:

1. Does the problem being treated justify continued benzodiazepine treatment? Has the patient significantly benefited from treatment?
2. Is the use of benzodiazepines within reasonable limits? Has use been stable over time? Has the patient avoided use of other prescription or non-prescription substances?
3. Has the patient been free of toxic symptoms, side effects or impairments from benzodiazepine use?
4. Are the above confirmed by a family member who can monitor the patient?

Evidence supporting this recommendation is of classes: A, C, D, M, R

E. Herbals

Hypericum perforatum (St. John's wort), an herbal remedy marketed as a dietary supplement, appears to be more effective than placebo and as effective as low-dose tricyclic anti-depressants for the treatment of mild depression. It appears better tolerated, especially in the elderly or for

patients with cardiac conductive dysfunction. It may be as effective as SSRI anti-depressants for mild to moderate depression in some patients. It may also have a place as an initial treatment for moderate depression, and may be effective for seasonal affective disorder (SAD.) St. John's wort does not appear to be effective for the treatment of major depression. Side effects appear to be infrequent and mild, headache being most common (41% v 25% for placebo.)

Herbal products and nutritional supplements are not evaluated or regulated by the U.S. Food and Drug Administration for safety, efficacy or bioavailability. **Caution: many drugs interact with St. John's wort, including other anti-depressants, 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.**

Other herbal remedies, such as kava-kava or valerian root, have not been proven effective for the treatment of depression.

F. Follow-up

Initial Follow-up Contact Intervals (office, phone, other)

- One to four weeks after initiation of medication, depending on symptom severity.
- If treatment is going well, follow-up every one to two months until patient is stable, then every three to six months.
- If treatment is not going well after four to six week medication trials at a therapeutic dose of one or two medications, re-evaluate the diagnosis, then consider referral to Psychiatry.

Length of initial treatment and follow-up:

DEPRESSION: Unless maintenance treatment is planned, antidepressant medication is discontinued at four to nine months after complete remission, and tapered over several weeks.

Consider life-long maintenance treatment if three or more episodes of major depression.

ANXIETY: Although anxiety disorders are often chronic, there are no research studies evaluating long-term treatment. Three to six months is a reasonable length of initial treatment. Follow the patient for at least another six to 12 months to ascertain that key objectives of treatment are maintained. If key objectives are not maintained, review treatment options with the patient. If anxiety symptoms recur after two careful medication tapers, consider lifetime maintenance.

Office visits for maintenance medication can occur every six to 12 months.

G. Referral

Consider involvement of a mental health provider for the following:

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

ANTIDEPRESSANTS: SSRIS, TCAS AND OTHERS

Drug name	Usual Dosage Range (mg / day)	Reuptake inhibition		Adverse Effects						FDA Approved indications	Cost (AWP) **
		Norepi	Serotonin	Anticholinergic	Sedation	Orthostatic hypotension	cardiac arrhythmias	GI distress	Weight Gain		
FIRST GENERATION ANTIDPRESSANTS											
Tricyclic Antidepressants - Tertiary Amines											
Amitriptyline (Elavil, generics)	50 - 300	Moderate	High	4+	4+	4+	3+	1	4+	Depression	10mg 0.05¢ 25mg 0.18¢ 50mg 0.20¢ 75mg 0.25¢ 100mg 0.30¢ 150mg 0.17¢
Clomipramine (Anafranil, generics)	25 - 250	Moderate	High	4+	4+	2+	3+	1+	4+	OCD	25mg 0.75¢ 50mg $1.10 75mg $1.40
Doxepin (Sinequan, generics, concentrate)	25 - 300	Low	Moderate	3+	4+	2+	2+	0	4+	Psychoneurotic patients with depression or anxiety; depression or anxiety with alocholism or organic disease; or psychotic depressive disorders associated with anxiey including involutional depression or manic-depressive disorders.	10mg 0.12¢ 25mg 0.41¢ 50mg 0.55¢ 75mg 0.91¢ 100mg 0.99¢ 10mg/ml conc'n 0.17¢/ ml
Imipramine HCl (Tofranil, generics)	30 - 300	Moderate	Moderate	3+	3+	4+	3+	1+	4+	Depression, Childhood enuresis	10mg 0.28¢ 25mg 0.47¢ 50mg 0.69¢
Imipramine Pamoate (Tofranil-PM)	100 - 300	Moderate	Moderate	3+	3+	4+	3+	1+	4+	Depression	75mg $2.12 100mg $2.78 125mg $3.47 150mg $3.96
Trimipramine (Surmontil, generics)	50 -300	Low	Low	4+	4+	3+	3+	0	4+	Depression	25mg 0.85¢ 50mg $1.40 100mg $2.03

ANTIDEPRESSANTS: SSRIS, TCAS AND OTHERS (CONTINUED)

Tricyclic Antidepressants – Secondary Amines											
	Usual Dosage Range	Reuptake inhibition		Adverse Effects							
Drug name	**(mg / day)**	**Norepi**	**Serotonin**	Anticholinergic	Sedation	Orthostatic hypotension	Cardiac Arrhythmias	GI distress	Weight Gain	**FDA Approved indications**	**Cost (AWP) ****
Amoxapine (Asendin, generics)	50 - 600	Moderate	Low	2+	2+	2+	2+	0	2+	Depression accompanied by anxiety or agitation	25mg 0.61¢ 50mg 0.99¢ 100mg $1.67 150mg $2.63
Desipramine (Norpramin, generics)	25 - 300	High	Low	1+	2+	2+	2+	0	1+	Depression	10mg 0.22¢ 25mg 0.28¢ 50mg 0.59 75mg 0.72¢ 100mg $1.07 150mg $2.21
Nortriptyline (Pamelor, Aventyl, generics)	30 - 100	Moderate	Low	2+	2+	1+	2+	0	1+	Depression	10mg 0.35¢ 25mg 0.80¢ 50mg $1.54 75mg $2.35 10mg/5ml Solution 0.10¢/ml
Proptriptyline (Vivactil, generics)	15 - 60	Moderate	Low	2+	1+	2+	3+	0	0	Depression	5mg 0.44¢ 10mg 0.64¢
SECOND GENERATION ANTIDEPRESSANTS											
Older Second Generation Antidepressants											
Maprotiline (Ludiomil, generics)	50 - 225	Moderate	Low	2+	3+	2+	2+	0	2+	Depression in patients with depressive neurosis (dysthymic disorder) and manic-depressive illness, depressed type	25mg 0.50¢ 50mg 0.74¢ 75mg 0.93¢
Trazodone (Desyrel, generics)	150 - 600	Very Low	Moderate	0	4+	3+	1+	1+	2+	Depression	50mg 0.56¢ 100mg 0.73¢ 150mg $1.46 300mg $4.27 300mg Desyrel Dividose $5.82
Newer Second Generation Antidepressants											
Bupropion (Wellbutrin, generics)	200 - 450 ***	Very Low****	Very Low****	0	0	0	1+	1+	0	Depression	75mg 0.72¢ 100mg 0.96¢
Bupropion Extended Release (Wellbutrin SR)	100 - 400 '***	Very Low****	Very Low****	0	0	0	1+	1+	0	Depression	100mg $1.49 150mg $1.60

ANTIDEPRESSANTS: SSRIs, TCAs AND OTHERS (CONTINUED)

Third Generation Antidepressants - Selective Serotonin Reuptake Inhibitors											
	Usual Dosage Range	Reuptake Inhibition		Adverse Effects						FDA Approved indications	Cost (AWP) **
Drug name	(mg / day)	Norepi	Serotonin	Anticholinergic	Sedation	Orthostatic Hypotension	Cardiac Arrhythmias	GI Distress	Weight Gain		
Citalopram (Celexa tablets and liquid)	20 - 60	Very Low	Very High	0	0	0	0	3+ *	0	Depression	20mg $2.16 40mg $2.75 10mg/5ml solution 0.45¢/ml
Fluoxetine (Prozac, Serafem, Prozac Weekly, generics - capsules, tablets and solution)	20 - 80	Very low	high	0	0	0	0	3+ *	0	Depression, OCD, Bulemia Nervosa (Prozac, fluoxetine), PMDD (Serafem)	10mg $2.59 20mg $2.67 40mg $5.34 90mg Weekly $18.90 20mg/5ml solution 0.99¢/ml Serafem 10mg $3.03 20mg $3.11
Fluvoxamine (Luvox, generic)	50 - 300	Very Low	Very High	0	0	0	0	3+ *	0	OCD	25mg $2.30 50mg $2.57 100mg $2.64
Paroxetine (Paxil tablets and suspension)	10 - 50	Very low	Very High	1+	1+	0	0	3+ *	1+	Depression, OCD, Panic Disorder, Social Anxiety Disorder, GAD	10mg $2.42 20mg $2.53 30mg $2.61 40mg $3.07 10mg/5ml suspension 0.54¢/ ml
Sertaline (Zoloft tablets and concentrate)	50 - 200	Very Low	Very High	0	0	0	0	3+ *	0	Depression, OCD, Panic Disorder, PTSD	25mg $2.34 50mg $2.42 100mg 2.49 20mg/ml conc'n $1.00/ml
Serotonin / Norepinephrine Reuptake inhibitors											
Venlafaxine (Effexor)	75 - 375	Very high	Very High	1+	1+	0	0	3+ *	0	Depression	25mg $1.28 37.5mg $1.32 50mg $1.54 75mg $1.44 100mg $1.73
Venlafaxine extended release (Effexor XR)	75 - 225	Very high	Very High	1+	1+	0	0	3+ *	0	Depression, GAD	37.5mg $2.14 75mg $2.40 150mg $2.61
Atypical Antidepressants with 5HT2 Receptor Antagonist Properties											
Mirtazapine (Remeron and Remeron Softabs)	15 - 45	Very Low	Very Low	1+	3+	0	0	0	3	Depression	15mg $2.54 30mg $2.61 45mg $2.78 Softabs 15mg $2.77 30mg $2.86 45mg $2.91
Nefazadone (Serzone)	200 - 600	Very Low	high	1+	1+	0	0	1+	0	Depression	50mg $1.29 100mg $1.31 150mg $1.32 200mg $1.33 250mg $1.61

ANTIDEPRESSANTS: SSRIS, TCAS AND OTHERS (CONTINUED)

** Average Wholesale Price from 2001 Drug Topics Red Book. Generic prices quoted where applicable.
*** Not to exceed 150mg per dose to minimize seizure risk
**** Norepinephrine and Serotonin reuptake inhibition minimal, but inhibits dopamine reuptake
Selection of antidepressant medication: Base antidepressant drug selection on the patient's history of response (if any), the drug's side effect profile relative to patient medical conditions and other factors, and clinician familiarity with specidfic antidepressants. Secondary amine tricyclics cause less orthostatic hypotension and sedation. SSRIs generally lack the adverse reactions (anticholinergic, sedative effects) of the tricyclics and cause fewer problems when taken in overdose. However, they may cause headache, nervousness or insomnia. Non-monoamine oxidase inhibitors are used more frequently because they do not carry the risk of hypertensive crises when taken with tyramine containing foods that may occur with MAO-Is. However, when used in therapeutic doses, MAO-Is are probably equally as effective for depression.
Medication interactions with antidepressant agents: Many antidepressant agents have clinically significant drug interactions, particularly those agents which undergo cytochrome P450 enymatic 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. Consider start at the lowest possible dose and increase 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, and cardiac effects with these agents.
Pregnancy: Safety of these agents during pregnancy has not been clearly established. Use only when clearly needed and the potential benefits outweigh the potential hazards to the fetus. US FDA Pregnancy Risk Categories: (B): Bupropion, maprotiline. (C): Amitriptyline, amoxapine, citalopram, clomipramine, desipramine, fluoxetine, fluvoxamine, mirtazapine, nefazadone, paroxetine, protriptyline, sertaline, trazodone, trimipramine, venlafaxine. (D): Imipramine, nortriptyline.
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)

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 used drugs 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 chemical dependency assessment.

5

Major Depressive Episode
DSM-IV 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.

10

Generalized Anxiety Disorder
DSM-IV 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.

10

Treatment and Education:

Both pharmacologic and non-pharmacologic interventions may be effective depending on the severity of symptoms. For antidepressant medications, compliance 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 medicine 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.

Effective medications include, but are not limited to:

	SSRI	TCA	BZDP	Buspirone
Depression	yes	yes	no	no
Panic	yes	yes	yes	no
GAD	yes	yes	yes	yes

13

Panic Attack
DSM-IV 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.

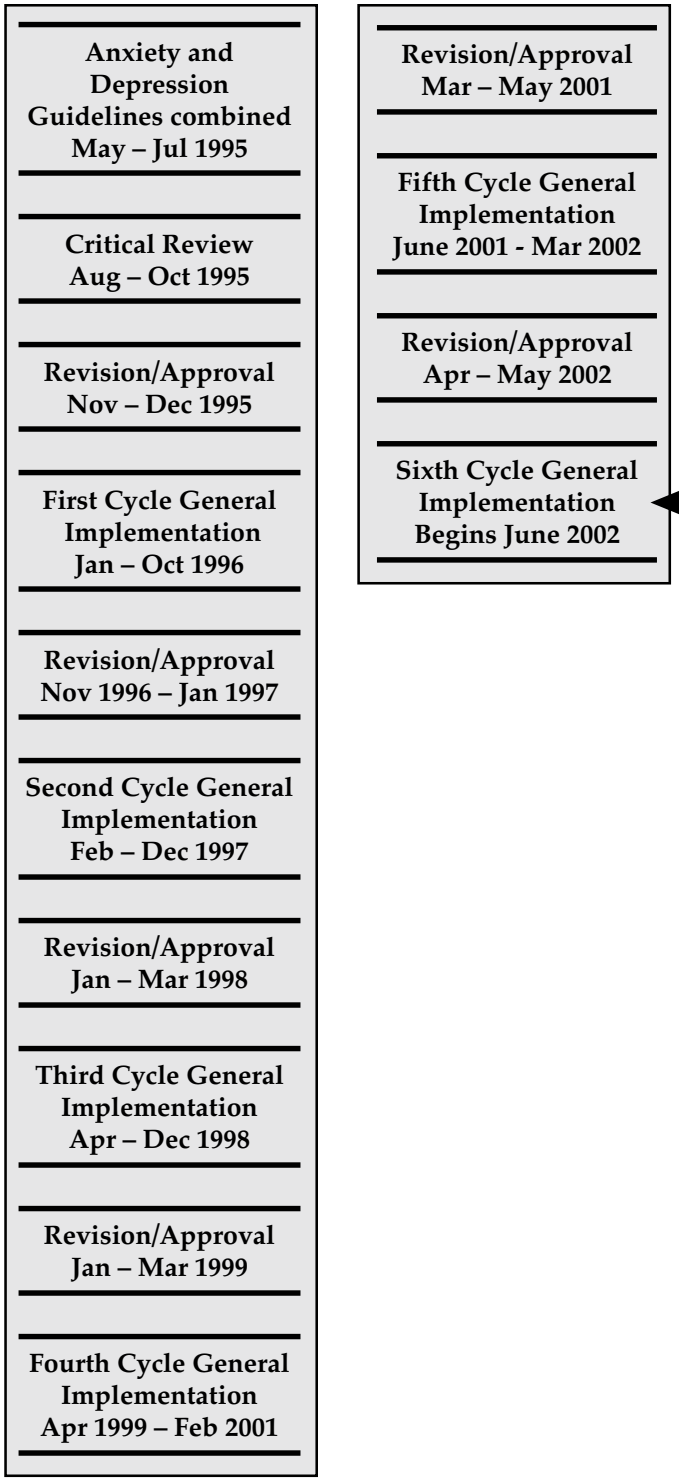
10

GLOSSARY OF TERMS

BZDP	Benzodiazapines
GAD	Generalized Anxiety Disorder
MDD	Major Depression Disorder
PD	Panic Disorder
SSRI	Selective Serotonin Re-uptake Inhibitors
TCA	Tricyclic Anti Depressants

Discussion and References:

Major Depression, Panic Disorder and Generalized Anxiety Disorder in Adults in Primary Care



Released in May 2002 for General Implementation.
The next scheduled revision will occur within 18 months.

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I. CLASSES OF RESEARCH REPORTS

A. Primary Reports of New Data Collection:

Class A: Randomized, controlled trial

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-benefit analysis
Cost-effectiveness study

Class R: Narrative review
Consensus statement
Consensus report

Class X: Medical opinion

1. Suspect Depression and/or Anxiety

The 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.

Some clinicians find self-administered instruments (e.g. Beck Depression Inventory and Inventory to Diagnose Depression [IDD]) useful adjuncts to the clinical interview. They may be used to supplement but not replace the clinical interview. 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.

> "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 questionnaire 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.

Importance of Depression/Anxiety

> The depression syndrome is a treatable cause of pain, suffering, disability and death, yet primary care providers detect depression in only 1/3 to 1/2 of their patients with major depression.
>
> > Schonfeld WH, Verboncoeur CJ, Fifer SK, et al. "The functioning and well-being of patients with unrecognized anxiety disorders and major depressive disorder." *J Affect Disord* 43:105-19, 1997. (Class C)
> >
> > Williams JW Jr, Noel PH, Cordes JA, et al. "Is this patient clinically depressed?" *JAMA* 287:1160-70, 2002. (Class R)
>
> Depressed individuals are high utilizers of medical services, and are as functionally impaired as patients with severe chronic medical disorders.
>
> > Katon W, Von Korff M, Lin E, et al. "Distressed high utilizers of medical care: DSM-III-R diagnoses and treatment needs." *Gen Hosp Psychiatry* 12:355-62, 1990. (Class C)
> >
> > Weissman MM, Myers JK, Thompson WD. "Depression and its treatment in a U.S. urban community – 1975-1976." *Arch Gen Psychiatry* 38:417-21, 1981. (Class C)
> >
> > Wells KB, Stewart A, Hays RD, et al. "The functioning and well-being of depressed patients: results from the medical outcomes study." *JAMA* 262:914-19, 1989. (Class C)
>
> 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. Depression in Primary Care. Volume 1. Detection and Diagnosis. p. 23, 1993. (Class R)

Approximately 15% of patients hospitalized for depression eventually commit suicide.

Guze SB, Robins E. "Suicide and primary affective disorders." *Brit J Psychiat* 177:437-38, 1970. (Class R)

Clinically significant depressive syndromes may be detectable in 12-36% of patients with general medical disorders.

U.S. Department of Health and Human Services Public Health Service. Depression in Primary Care. Volume 1. Detection and Diagnosis. pp. 55-56, 1993. (Class R)

The point prevalence of major depression in the general population is 4.5% to 9.3% for women and 2.3 to 4.5% for men.

Myers JK, Weissman MM, Tischler GL, et al. "Six-month prevalence of psychiatric disorders in three communities." *Arch Gen Psychiatry* 41:959-67, 1984. (Class C)

The depressive syndrome is common in primary care. The estimated prevalence of major depression in primary care outpatients is 4.8% to 8.6%, and the estimated prevalence of dysthymic disorder is 2.1% to 3.7%.

U.S. Department of Health and Human Services Public Health Service. Depression in Primary Care. Volume 1. Detection and Diagnosis. pp. 23-24, 31-33, April 1993. (Class R)

These statistics indicate that depression is the first or second most prevalent condition in primary care. (Hypertension is the most frequent diagnosis, recorded in an internal medicine practice occurring in 9.6% of visits.) Although depression is prevalent in primary care, there is insufficient evidence to recommend for or against the routine screening of all patients for depression.

U.S. Preventive Services Task Force. Report: Guide to Clinical Preventive Services. Screening for Depression. pp. 541-46, Williams and Wilkins, 1996. (Class R)

Anxiety disorders are common in the general population. The prevalence of panic disorder in women is 1.4 - 2.9% and .4 - 1.7% in men. Panic attacks not meeting the full criteria for panic disorder occur in 3.6-10% of the population. The prevalence of generalized anxiety disorder is 2.5-6.4%.

Myers JK, Weissman MM, Tischler GL, et al. "Six-month prevalence of psychiatric disorders in three communities." *Arch Gen Psychiatry* 41:959-67, 1984. (Class C)

Weissman MM, Merikangas KR. "The epidemiology of anxiety and panic disorders: an update." *J Clin Psychiatry* 47(6, Suppl):11-17, 1986. (Class R)

Anxiety disorders occur frequently in a primary care population. Panic disorder alone may occur in 6.5% of primary care patients and an additional 6.5% may have co-morbid panic disorder and depression.

Katon W, Vitaliano PP, Russo J, et al. "Panic disorder: epidemiology in primary care." *J Fam Pract* 23:233-39, 1986. (Class D)

The guideline focuses on adults 18-64 years old but may apply to other ages.

A. **Presentations**

Non-mood presentations of 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 K, Wood DR, Mangelsdorff AD, et al. "Chronic fatigue in primary care: prevalence, patient characteristics, and outcome." *JAMA* 260:929-34, 1988. (Class C)

Pain or other somatic symptoms are experienced by 60-100% of depressed patients and 27% of patients diagnosed with depression in a primary care practice presented with pain.

> Katon W. "Depression: somatic symptoms and medical disorders in primary care." *Compr Psychiatry* 23:274-87, 1982. (Class R)

Patients with undiagnosed depression average more than 6 visits per year with their primary care providers.

> Weissman MM, Klerman GL. "The chronic depressive in the community: unrecognized and poorly treated." *Compr Psychiatry* 18:523-32, 1977. (Class C)

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 P, Matthews DA, Lane TJ. "The mental health of patients with a chief complaint of chronic fatigue: a prospective evaluation and follow-up." *Arch Intern Med* 148:2213-17, 1988. (Class D)

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 WE, Blazer DG, George LK, Tse CK. "Depression, disability days, and days lost from work in a prospective epidemiologic survey." *JAMA* 264:2524-28, 1990. (Class B)

> Fredman L, Weissman MM, Leaf PJ, Bruce ML. "Social functioning in community residents with depression and other psychiatric disorders: results of the New Haven Epidemiologic Catchment Area Study." *J Affect Disord* 15:103-12, 1988. (Class C)

Age at onset of panic attacks peaks between ages 15-19 and the onset of panic attacks is rare after age 40.

> Von Korff MR, Eaton WW, Reyl PM. "The epidemiology of panic attacks and disorder: results of three community surveys." *Am J Epidemiol* 122:970-81, 1985. (Class C)

90% of patients with panic disorder present with somatic symptoms. The three most common presentations are cardiac symptoms (chest pain, tachycardia, irregular heart beat), gastrointestinal symptoms (especially epigastric distress) and neurological symptoms (headache, dizziness/vertigo, syncope or parasethesias.) 80% of patients have pain as one of their presenting symptoms (epigastric, headache, chest pain, back pain and left lower quadrant abdominal pain.)

> Katon W. "Panic disorder and somatization: review of 55 cases." *Am J Med* 77:101-06, 1984. (Class D)

People with panic disorder have the highest risk of having multiple medically unexplained symptoms and of being high utilizers of medical ambulatory services compared to people with and without psychiatric disorders in the community. Among patients with five or more current

unexplained symptoms, panic disorder is 12 times more likely than depression. The lifetime prevalence of panic disorder in distressed high utilizers of primary care is 30%. Patients with emergency room visits for medically unexplained somatic complaints have a high prevalence of panic disorder.

Katon WJ, Von Korff M, Lin E. "Panic disorder: relationship to high medical utilization." *Am J Med* 92(suppl, 1A):7S-11S, 1992. (Class R)

Katon W, Von Korff M, Lin E, et al. "Distressed high utilizers of medical care: DSM-III-R diagnoses and treatment needs." *Gen Hosp Psychiatry* 12:355-62, 1990. (Class C)

Simon GE, VonKorff M. "Somatization and psychiatric disorder in the NIMH Epidemiologic Catchment Area Study." *Am J Psychiatry* 148:1494-1500, 1991. (Class C)

Wulsin LR, Hillard JR, Geier P, et al. "Screening emergency room patients with atypical chest pain for depression and panic disorder." *Int J Psychiatry Med* 18:315-23, 1988. (Class D)

13% -29% of patients with a complaint of chronic fatigue may have panic disorder.

Katon WJ, Buchwald DS, Simon GE, et al. "Psychiatric illness in patients with chronic fatigue and those with rheumatoid arthritis." *J Gen Intern Med* 6:277-85, 1991. (Class C)

Manu P, Matthews DA, Lane TJ. "Panic disorder among patients with chronic fatigue." *South Med J* 84:451-56, 1991. (Class C)

The prevalence of panic disorder in patients with chest pain and normal coronary angiography is approximately 33-43%. One third of patients with irritable bowel syndrome may have panic disorder. Panic disorder may be present in 13% of patients with medically unexplained dizziness.

Bass C. "Chest pain and breathlessness: relationship to psychiatric illness." *Am J Med* 92(1A):12S-17S, 1992. (Class R)

Katon W, Hall ML, Russo J, et al. "Chest pain: relationship of psychiatric illness to coronary arteriographic results." *Am J Med* 84:1-9, 1988. (Class C)

Linzer M, Felder A, Hackel A, et al. "Psychiatric syncope: a new look at an old disease." *Psychosomatics* 31:181-88, 1990. (Class D)

Linzer M, Varia I, Pontinen M, et al. "Medically unexplained syncope: relationship to psychiatric illness." *Am J Med* 92(suppl, 1A):18S-25S, 1992. (Class D)

Walker EA, Roy-Byrne PP, Katon WJ, et al. "Psychiatric illness and irritable bowel syndrome: a comparison with inflammatory bowel disease." *Am J Psychiarty* 147:1656-61, 1990. (Class C)

B. **Risk Factors**

Risk factors for depression include previous depression, chronic illness, female gender, recent loss and family history of depression. One previous episode of 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. "Mood disorders: pharmacologic prevention of recurrences." *Am J Psychiatry* 142:469-76, 1985. (Class R)

U.S. Department of Health and Human Services Public Health Service. Depression in Primary Care. Volume 1. Detection and Diagnosis. p. 73-75, 1993. (Class R)

Most studies indicate that in 40 to 60% of patients a major life event precedes the first episode of depression.

Post RM. "Transduction of psychosocial stress into the neurobiology of recurrent affective disorder." *Am J Psychiatry* 149:999-1010, 1992. (Class R)

The lifetime risk of panic disorder in the relatives of probands with panic disorder is approximately 25%. A family history of alcoholism may occur in as many as 27% of patients with agoraphobia. The risk of alcoholism in patients with panic disorder is greater than four times that of the general population. The lifetime prevalence of panic disorder among patients treated in inpatient alcohol treatment centers may be as high as 21%.

There is an 18.8 fold increased risk of panic disorder in patients with a history of major depression.

Cloninger CR, Martin RL, Clayton P, Guze SB. "A blind follow-up and family study of anxiety neurosis: preliminary analysis of the St. Louis 500." *In* Klein DF, Rabkin J (eds). Anxiety: New Research and Changing Concepts. New York: Raven Press, 1981. (Class D)

Cowley DS. "Alcohol abuse, substance abuse, and panic disorder." *Am J Med* 92(suppl 1A):41S-48S, 1992. (Class R)

Crowe RR, Noyes R, Pauls DL, Slymen D. "A family study of panic disorder." *Arch Gen Psychiatry* 40:1065-69, 1983. (Class C)

Munjack DJ, Moss HB. "Affective disorder and alcoholism in families of agoraphobics." *Arch Gen Psychiatry* 38:869-71, 1981. (Class D)

Panic attacks predict increased risk for panic disorder and/or depression.

Lecrubier Y, Ustun TB. "Panic and depression: a worldwide primary care perspective." *Int Clin Psychopharmacol Ar* 4(13 suppl):S7-S11, 1998. (Class D)

Patient Questionnaire - PHQ-9[6]

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 every days	Nearly day
	0	1	2	3
a. Little interest or pleasure in doing things.	☐	☐	☐	☐
b. Feeling down, depressed, or hopeless.	☐	☐	☐	☐
c. Trouble falling/staying asleep, sleeping too much.	☐	☐	☐	☐
d. Feeling tired or having little energy.	☐	☐	☐	☐
e. Poor appetite or overeating.	☐	☐	☐	☐
f. Feeling bad about yourself - or that you are a failure or have let yourself or your family down.	☐	☐	☐	☐
g. Trouble concentrating on things, such as reading the newspaper or watching television.	☐	☐	☐	☐
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.	☐	☐	☐	☐
i. Thoughts that you would be better off dead or of hurting yourself in some way.	☐	☐	☐	☐

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 othe people?

Not difficult at all	Somewhat difficult	Very Difficult	Extremely Difficult
☐	☐	☐	☐

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 or #2 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 or #2 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:

Guide for Interpreting PHQ-9 Scores

Score	Action
≤ 4	The score suggests the patient may not need depression treatment.
≥ 5 - 14	Physician uses clinical judgement about treatment, based on patient's duration of symptoms and functional impairment.
≥ 15	Warrants treatment for depression, using antidepressant, psychotherapy and/or a combination of treatment.

Patient responses 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.

Spitzer RL, Kroenke K, Williams JBW, Patient Health Questionnaire Primary Care Study Group, The. "Validation and utility of a self-report version of prime-md: the PHQ primary care study." *JAMA* 282:1737-44, 1999. (Class C)

5. Evaluate for Other Causes of Depression/Anxiety

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

- Psychosocial Stressors:

  Karasu TB, Docherty JP, Gelenberg A, et al. "Depression during pregnancy or following childbirth." *In* Practice Guideline for Major Depressive Disorder in Adults. Washington, DC: American Psychiatric Association, 1993. (Class R)

- Medical Illness:

  The depressive syndrome may also be associated with medical disorders or perception of his or her clinical condition. Although thyroid function abnormalities may cause depressive symptoms, screening for thyroid disease in all patients with depression is not necessary because the prevalence of unidentified thyroid disease in patients with depression is the same as in the general population.

  Briggs JH, Bauer MS, McBride L, et al. "Screening for thyroid disease in ambulatory patients with depression." *American Psychiatric Association Abstracts* NR144, 1993. (Class D)

  Garrard JM. "Patient outcomes associated with antidepressant drugs." Agency for Healthcare Research and Quality (AHRQ). AHRQ 2001-64. April 2001. (Class B)

  Patients with pheochromocytomas generally do not report anxiety symptoms meeting DSM criteria for panic disorder or generalized anxiety disorder.

  Starkman MN, Zelnik TC, Nesse RM, Cameron OG. "Anxiety in patients with pheochromocytomas." *Arch Intern Med* 145:248-52, 1985. (Class C)

- 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 B, Shaw S, Cleary P, et al. "Screening for alcohol abuse using the CAGE questionnaire." *Am J Med* 82:231-35, 1987. (Class C)

  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 RL. "Identification and office management of alcohol and drug disorders." *In* Fleming MF and Bary KL, eds. Addictive Disorders. Saint Louis: Mosby Yearbook pp. 25-43, 1992. (Class R)

  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. Depression in Primary Care. Volume 1. Detection and Diagnosis. pp. 43-47, 1993. (Class R)

9. Emergency?

20% of patients with panic disorder and 12% of patients with panic attacks who do not meet the full criteria for panic disorder have attempted suicide. 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 co-morbid panic disorder and major depression have attempted suicide.

Although women and girls are three times more likely to attempt suicide, there are four male completers for every female completion. Males in general tend to choose highly lethal means, such as firearms, which greatly increases the risk of death. 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. 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. Four general classes of risk factors are believed to combine to increase suicide attempt risk. These include:

- internal emotional pain
- external stress
- agitation
- sense of hopelessness

When all factors are high, risk is very high and hospitalization may be necessary. If any one factor can be substantially alleviated, risk is thought to drop sharply.

Hall RCW, Platt DE, Hall RCW. "Suicide risk assessment: a review of risk factors for suicide in 100 patients who made severe suicide attemps: evaluation of suicide risk in a time of managed care." *Psychosomatics* 40:18-27, 1999. (Class R)

Jobes DA, Peterson EM, Nunno KM, Bergman PD. "American association of suicidology. Elderly fact sheet." (Class not assignable)

Johnson J, Weissman MM, Klerman GL. "Panic disorder, comorbidity, and suicide attempts." *Arch Gen Psychiatry* 47:805-08, 1990. (Class C)

Murphy SL. "Deaths: final data for 1998. National vital statistics report, 48 (11) Hyattsville, MD: National center for health statistics, DHHS Publiaton No. (PHS) 2000 - 1120. (Class not assignable)

Weissman MM, Klerman GL, Markowitz JS, Ouellette R. "Suicidal ideation and suicide attempts in panic disorder and attacks." *N Engl J Med* 321:1209-14, 1989. (Class C)

10. Involve Mental/Chemical Health

Dieserud G, Roysamb E, Ekeberg O, Kraft P. "Toward an integrative model of suicide attempt: a cognitive psychological approach." *Suicide Life Threat Behav* 31:153-68, 2001. (Class C)

11. Diagnose and Characterize Depression/Anxiety Disorder with Clinical Interview

Major depression occurs in 44% to 91% of patients with panic disorder. In patients with major depression, 15%-33% may have recurrent panic attacks during a depressive episode. Patients with comorbid panic disorder and major depression may have more severe symptoms, more disability and more suicide attempts than patients with either condition alone. Follow up studies indicate that these

patients are more chronically ill and have a poorer response to treatment than patients with uncomplicated panic disorder or depression.

Clayton P. "The comorbidity factor: establishing the primary diagnosis in patients with mixed symptoms of anxiety and depression." *J Clin Psychiatry* 51(11, suppl):35-39, 1990. (Class R)

Kessler RC, McGonagle KA, Zhao S, et al. "Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey." *Arch Gen Psychiatry* 51:8-19, 1994. (Class C)

Ronalds C, Creed F, Stone K, et al. "Outcome of anxiety and depressive disorders in primary care." *Br J Psychiatry* 171:427-33, 1997. (Class D)

Sartorius N, Ustun TB, Costa e Silva JA, et al. "An international study of psychological problems in primary care. Preliminary report from the World Health Organization collaborative project on psychological problems in general health care." *Arch Gen Psychiatry* 50:819-24, 1993. (Class not assignable)

Stein MB, Uhde TW. "Panic disorder and major depression: a tale of two syndromes." *Psychiatric Clinics of North America* 11:441-61, 1988. (Class R)

14. Consider Other Mood and Anxiety Disorders or Somatoform Disorders

DSM-IV Diagnostic Criteria for Dysthymic Disorder

Depressed mood for at least half of the time for at least two years and at least three of the following:

1. Low self-esteem or self-confidence or feelings of inadequacy.
2. Feelings of pessimism, despair or hopelessness.
3. Generalized loss of interest or pleasure.
4. Social withdrawal.
5. Fatigue.
6. Feelings of guilt, brooding about the past.
7. Irritability or excessive anger.
8. Decreased activity, effectiveness or productivity.
9. Difficulty in thinking (poor concentration, poor memory or indecisiveness).

15. Treatment Plan

B. Treatment Considerations

1. Pharmacologic Therapy vs. Psychotherapy

Psychotherapy, specifically CPT and ITP, can significantly reduce symptoms, restore psychosocial and occupational functioning, and prevent relapse in patients with major depression. In severe depression, psychotherapy may be most effective when combined with antidepressant medication.

Blackburn IM, Moore RG. "Controlled acute and follow-up trial of cognitive therapy and pharmacotherapy in out-patients with recurrent depression." *Br J Psychiatry* 171:328-34, 1997. (Class A)

Brown C, Schulberg HC, Prigerson HG. "Factors associated with symptomatic improvement and recovery from major depression in primary care patients." *Gen Hosp Psychiatry* 22:242-50, 2000. (Class C)

Keller MB, McCullough JP, Klein DN, et al. "A comparison of nefazodone, the cognitive behavioral-analysis system of psychotherapy, and their combination for the treatment of chronic depression." *N Engl J Med* 342:1462-70, 2000. (Class A)

Mintz J, Mintz LI, Arruda MJ, Hwang SS. "Treatments of depression and the functional capacity to work." *Arch Gen Psychiatry* 49:761-68, 1992. (Class M)

Robinson LA, Berman JS, Neimeyer RA. "Psychotherapy for the treatment of depression: a comprehensive review of controlled outcome research." *Psychol Bull* 108:30-49, 1990. (Class M)

Sampson SM. "Treating depression with selective serotonin reuptake inhibitors: a practical approach." *Mayo Clin Proc* 76:739-44, 2001. (Class R)

2. Pharmacologic Therapy

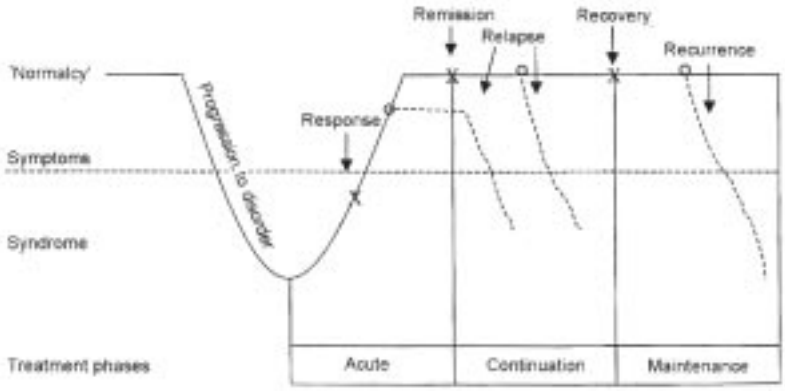

Fig. 1 Response, remission, recovery, relapse and recurrence of depression. From Kupfer (1991).

Treatment of depression is divided into acute continuation and maintenance phases as seen in Figure 1. Acute phase strives to achieve marked reduction of acute symptoms (usually 2-3 months). In the continuation phase the stabilization achieved during the acute phase and is maintained 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 depression are response, remission, relapse, recovery and recurrence.

- Response can be defined as a significant level of improvement; the responder should be qualitatively different from a nonresponder or clinically relevant reduction of more than 50% on a severity scale of Hamilton Depression rating scale.
- Remission is defined as a condition where only a few signs of illness remain, or Hamilton Depression rating scale, (HDRS), less than 7. This scale is available at the end of this Discussion piece.
- Recovery is a sustained period of remission representing resolution of the index episode.

- Relapse is a condition of symptomatic exacerbation occurring after a response but before achieving sustained remission during the same episode.
- Recurrence is a new episode of depressive illness following recovery.

Altamura AC, Percudani M. "The use of antidepressants for long-term treatment of recurrent depression: rationale, current methodologies, and future directions." *J of Clin Psychiatry* 54:29-37, 1993. (Class R)

Hirschfeld RMA. "Clinical importance of long-term antidepressant treatment." *Br J Psychiatry Suppl* 179:S4-S8, 2001. (Class R)

Hirschfeld, RMA. "Guidelines for the Long-Term Treatment of Depression." *J Clin Psychiatry*, 55:61-69, 1994. (Class R)

Kupfer DJ. "Long-term treatment of depression." *J of Clin Psychiatry* 52:28-34, 1991. (Class R)

Storosum JG, van Zwieten BJ, Vermeulen HDB, et al. "Relapse and recurrence prevention in major depression: a critical review of placebo-controlled efficacy studies with special emphasis on methodological issues." *Eur Psychiatry* 16:327-35, 2001. (Class R)

Without long-term antidepressant treatment 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 depression have a relapse rate of 15-22%. Data also shows that patients who have three or more episodes of depression actually have a 40% risk of relapse.

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

Hirschfeld RMA. "Guidelines for the long-term treatment of depression." *J Clin Psychiatry* 55:61-69, 1994. (Class R)

Rush AJ. "Strategies and tactics in the management of maintenance treatment for depressed patients." *J of Clin Psychiatry* 60:21-26, 1999. (Class R)

The following patients are likely to benefit from lifetime treatment:

1. Those who are 50 years or older at the time of first onset.
2. Those who are 40 of years or older at the time of first onset and have experienced two or more episodes of major depression.
3. Those who have three or more episodes regardless of the age of onset or current age.

Greden JF. "Antidepressant maintenance medications: when to discontinue and how to stop." *J of Clin Psychiatry* 54:39-45, 1993. (Class R)

Hirschfeld RMA. "Clinical importance of long-term antidepressant treatment." *Br J Psychiatry Suppl* 179:S4-S8, 2001. (Class R)

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 AJ, Rifat SL. "Maintenance treatment for recurrent depression in late life." *Am J of Geriatr Psychiatry* 8:2, 2000. (Class D)

Sonawalla SB. "Citalopram in the maintenance treatment of major depressive disorder." *J of Clin Psychiatry* 62:12, 2001. (Class R)

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

Hirschfeld, RMA. "Guidelines for the long-term treatment of depression." *J Clin Psychiatry*, 55:61-69, 1994. (Class R)

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

Tollefson GD. "Adverse drug reactions/interactions in maintenance therapy." *J of Clin Psychiatry* 54:8, 1993. (Class R)

Selective Serotonin Re-uptake Inhibitors (SSRIs) are effective for panic disorder and depressive symptoms. Paroxetine is the best studied SSRI for panic disorder.

Black DW, Wesner R, Bowers W, Gabel J. "A comparison of fluvoxamine, cognitive therapy, and placebo in the treatment of panic disorder." *Arch Gen Psychiatry* 50:44-50, 1993. (Class A)

Kroenke K, West SL, Swindle R, et al. "Similar effectiveness of paroxetine, fluoxetine, and sertraline in primary care: a randomized trial." *JAMA* 286:2947-55, 2001. (Class A)

Oehrberg S, Christiansen PE, Behnke K, et al. "Paroxetine in the treatment of panic disorder: a randomised, double-blind, placebo-controlled study." *Br J Psychiatry* 167:374-79, 1995. (Class A)

Rasanen P, Hakko H, Jokelainen J, Tiihonen J. "Outcome of different types of long-term antidepressant treatments: a 3-year follow-up study of 14,182 patients." *J of Affective Disorders* 55:67-71, 1999. (Class B)

Classic medication studies of anxiety disorders have used imipramine but nortriptyline is effective and better tolerated. Less is known about dosing nortriptyline in anxiety disorders than in depression. Clinical practice dictates starting and stopping at a lower dose and titrating more slowly.

Lydiard RB, Ballenger JC. "Antidepressants in panic disorder and agoraphobia." *J Affect Disord* 13:153-68, 1987. (Class R)

Munjack DJ, Usigli R, Zulueta A, et al. "Nortriptyline in the treatment of panic disorder and agoraphobia with panic attacks." *J Clin Psychopharmacol* 8:204-07, 1988. (Class D)

One study with a tricyclic antidepressant showed decreased risk of relapse after 18 months of treatment.

Mavissakalian M, Perel JM. "Protective effects of imipramine maintenance treatment in panic disorder with agoraphobia." *Am J Psychiatry* 149:1053-57, l992. (Class C)

Alprazolam is currently the only benzodiazepine drug FDA approved for panic disorder but other benzodiazepines may be as effective. All benzodiazepines are effective in controlling GAD symptoms. Consequently differential efficacy is not a major selection factor in this class of drugs. The benzodiazepines are not identical with regard to onset and duration of action and presence of active metabolites; therefore if a patient's response is less than optimal, try a different drug. Alprazolam has a rapid onset of action, relatively short half life and no active metabolites. Lorazepam was chosen for use in GAD because it has no active metabolites to accumulate and cause oversedation.

Dubovsky SL. "Generalized anxiety disorder: new concepts and psychopharmacologic therapies." *J Clin Psychiatry* 51(1, suppl):3-10 , 1990. (Class R)

Jonas JM, Cohon MS. "A comparison of the safety and efficacy of alprazolam versus other agents in the treatment of anxiety, panic, and depression: a review of the literature." *J Clin Psychiatry* 54(10, suppl):25-45, 1993. (Class R)

Roy-Byrne P, Wingerson D, Cowley D, Dager S. "Psychopharmacologic treatment of panic, generalized anxiety disorder, and social phobia." *Psychiatric Clinics of North America* 16:719-33, l993. (Class R)

Shader RI, Greenblatt DJ. "Use of benzodiazepines in anxiety disorders." *N Engl J Med* 328:1398-1405, 1993. (Class R)

Surveys of patient populations have indicated that patients receiving prescriptions for one of the benzodiazepines or other minor tranquilizers or hypnotes 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 JH, Katz JL, Winger G. "Use and abuse of benzodiazepines: issues relevant to prescribing." *JAMA* 260:3476-80, 1988. (Class R)

3. Psychotherapy

Studies indicate that cognitive behavioral therapy of panic disorder is consistently more effective than wait-list and placebo groups. In general, cognitive behavioral therapy has been shown more beneficial than supportive therapy.

Borkovec TD, Costello E. "Efficacy of applied relaxation and cognitive–behavioral therapy in the treatment of generalized anxiety disorder." *J Consult Clin Psychol* 61:611-19, l993. (Class A)

Chambless DL, Gillis MM. "Cognitive therapy of anxiety disorders." *J Consult Clin Psychol* 61:248-60, l993. (Class R)

Gelder MG. "Psychological treatment of panic anxiety." *Psychiatric Annals* 20:529-32, l990. (Class R)

Rapee RM. "Psychological factors in panic disorder." *Adv Behav Res Ther* 15:85-102, l993. (Class R)

Robinson S, Birchwood M. "The relationship between catastrophic cognitions and the components of panic disorder." *J Cogn Psychotherapy* 5:175-86, 1991. (Class D)

Salkovskis PM, Clark DM. "Cognitive therapy for panic attacks." *J Cogn Psychotherapy* 5:215-26, 1991. (Class R)

4. Exercise:

Physical activity is a useful tool for easing 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 M, Sherman C. "Exercise Against Depression." *The Physician and Sports Med* Available at: http://www.physsportsmed.com/issues/1998/10Oct/artal.htm. (Class R)

Babyak M, Blumenthal JA, Herman S, et al. "Exercise treatment for major depression: maintenance of therapeutic benefit at 10 months." Psychosom Med 62:633-38, 2000. (Class A)

Blumenthal JA, Babyak MA, Moore KA, et al. "Effects of exercise training on older patients with major depression." *Arch Intern Med* 159:2349-56, 1999. (Class A)

C. Patient Education

Patient compliance 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. Depression in Primary Care. Volume 2. Treatment of Major Depression. pp.43-44, 1993. (Class R)

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.

U.S. Department of Health and Human Services Public Health Service. Quick Reference Guide for Clinicians. Depression in Primary Care: Detection, Diagnosis and Treatment. p. 10, 1993. (Class R)

Patient and family should be alert to early signs and symptoms of recurrence and seek treatment early if depression returns.

Studies show that medications and/or cognitive behavioral treatments are effective in treating anxiety disorders. Medications can attenuate or block anxiety symptoms but equally important is empowering patients to control symptoms and reduce ambient stress in their lives. Like diabetes or hypertension, anxiety disorders are often chronic, with a waxing and waning course. Patient education is critical to treatment success. Patients are often demoralized after experiencing debilitating symptoms for which there has been no sufficient explanation or they are told "it

is all in your head." Clinical trials of patients with mild GAD have shown a 50-60% placebo response rate, indicating that supportive interventions may be as successful as medications.

Rickels K, Schweizer E. "The clinical course and long-term management of generalized anxiety disorder." *J Clin Psychopharmacol* 10:101S-110S, l990. (Class R)

Roy-Byrne P, Wingerson D, Cowley D, Dager S. "Psychopharmacologic treatment of panic, generalized anxiety disorder, and social phobia." *Psychiatr Clin North Am* 16:719-33, l993. (Class R)

E. Herbal Remedies:

Hypericum perforatum (St. John's wort), an herbal remedy marketed as a dietary supplement, appears to be more effective than placebo and as effective as low-dose tricyclic anti-depressants for the treatment of mild depression. Side effects are infrequent. St. John's wort has been found to interfere with the enzyme 450 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. Other herbal remedies, such as kavakava or valerian root, have not proved effective for the treatment of depression.

"Effect of Hypericum perforatum (St John's wort) in major depressive disorder: a randomized controlled trial." *JAMA* 287:1807-14, 2002. (Class A)

Gaster B, Holroyd J. "St. John's wort for depression: a systemic review." *Arch Intern Med* 160:152-52, 2000. (Class M)

Health Technology Advisory Committee (HTAC). "St. John's Wort." December 2000. (Class R)

Linde K, Ramirez G, Mulrow CD, et al. "St John's wort for depression--an overview and meta-analysis of randomised clinical trials." *BMJ* 33:253-58, 1996. (Class M)

Mulrow CD, Williams JW Jr, Chiquette E, et al. "Efficacy of newer medications for treating depression in primary care patients." *Am J Med* 183:54-64, 2000. (Class M)

Whooley MA, Simon GE. "Managing depression in medical outpatients." *N Engl J Med* 343:1942-50, 2000. (Class R)

F. Follow-up:

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. CBT and ITP help protect against/prevent relapse.

American Psychiatric Association. "Practice guideline for major depressive disorder in adults." *Am J Psychiatry* 150(4 suppl):1-26, 1993. (Class R)

Janicak PG, Davis JM, Preskorn SH, Ayd FJ. Principles and Practice of Psychopharmacotherapy. Baltimore: Williams and Wilkins, 1993, pp. 224-25. (Class R)

U.S. Department of Health and Human Services Public Health Service. Depression in Primary Care. Volume 1. Detection and Diagnosis. 1993. (Class R)

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 recurrent episode potential.

Janicak PG, Davis JM, Preskorn SH, Ayd FJ. Principles and Practice of Psychopharmacotherapy. Baltimore: Williams and Wilkins, 1993, p. 225. (Class R)

Mintz J, Mintz LI, Arruda MJ, Hwang SS. "Treatments of depression and the functional capacity to work." *Arch Gen Psychiatry* 49:761-68, 1992. (Class M)

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. These patients are candidates for long-term or lifetime prophylactic treatment. See diagram below:

Lifetime treatment may be indicated for patients:

- Aged $\geq$ 50 at first episode
- Aged $\geq$ 40 with $\geq$ 2 episodes
- With $\geq$ 3 episodes

Greden JF. "Antidepressant maintenance medications: when to discontinue and how to stop." *J Clin Psychiatry* 54(8, Suppl):39-45, 1993. (Class R)

Keller MB, Kocsis JH, Thase ME, et al. "Maintenance phase efficacy of sertraline for chronic depression: a randomized controlled trial." *JAMA* 280:1665-72, 1998. (Class A)

The adjunctive use of targeted psychotherapies may be considered in some patients, both during acute phase treatment as well as during long-term maintenance. Please refer to section discussing role of psychotherapy.

Janicak PG, Davis JM, Preskorn SH, Ayd FJ. Principles and Practice of Psychopharmacotherapy. Baltimore: Williams and Wilkins, 1993, pp. 224-25. (Class R)

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 PG, Davis JM, Preskorn SH, Ayd FJ. Principles and Practice of Psychopharmacotherapy. Baltimore: Williams and Wilkins, 1993, pp. 246-57. (Class R)

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 JF. "Antidepressant maintenance medications: when to discontinue and how to stop." *J Clin Psychiatry* 54(8, Suppl):39-45, 1993. (Class R)

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)

The Hamilton Rating Scale for Depression (cont)

_____ **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, hyper-ventilation, 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

The Hamilton Rating Scale for Depression (cont)

_____ **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, headache, 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

The Hamilton Rating Scale for Depression (cont)

_____ 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. OBSESSIONAL AND COMPULSIVE SYMPTOMS

0 = Absent
1 = Mild
2 = Severe

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

When measuring for improvement it is critical that the measurements used are responsive to the individual health care organizations and support their clinical improvements. The Measurement Specifications are an aid to the organizations' implementation efforts. It is likely that organizations may need to adapt these measures to specific clinical practice or administrative systems.

OVERVIEW

The following aims were identified by the guideline work group as key areas in which medical groups may receive benefits in implementing this guideline.

The measures associated with these aims are presented as suggested measures. Measures of aim help medical groups determine progress in achieving a particular aim. However, additional approaches may be customized by individual medical groups to ferret out improvement information important to the medical group's individual practice.

PRIORITY AIMS AND SUGGESTED MEASURES FOR HEALTH CARE SYSTEMS

1. Increase the use of DSM-IV criteria in the detection and diagnosis of panic disorder, generalized anxiety and depression in primary care.

   Possible measures of accomplishing this aim:

   a. Percentage of patients with a new diagnosis of depression, panic disorder or generalized anxiety disorder with documentation of DSM-IV criteria at the time of the initial diagnosis.

2. Increase the assessment for depression and anxiety disorders of primary care patients presenting with more than 5 visits in the past year with problems in more than one organ system.

   Possible measures of accomplishing this aim:

   a. Percentage of patients with a new diagnosis of fatigue with documentation of screening for depression and anxiety disorder.

   b. Percentage of patients with a new diagnosis of irritable bowel syndrome with documentation of screening for depression and anxiety disorder.

   c. Percentage of patients with a new diagnosis of sleep disturbance with documentation of screening for depression and anxiety disorder.

Possible Success Measurement #1a

Percentage of patients with a new diagnosis of depression, panic disorder and generalized anxiety disorder patients containing documentation of DSM-IV criteria at the time of the initial diagnosis.

Population Definition

Adults greater than 18 years with a new primary care diagnosis of depression, panic disorder and/or generalized anxiety disorder.

Data of Interest

$$\frac{\text{\# medical records containing documentation of DSM-IV criteria at the time of the initial diagnosis}}{\text{total \# medical records for newly diagnosed depression, panic disorder and generalized anxiety disorder patients reviewed}}$$

Numerator/Denominator Definitions

Numerator: Number of records containing documentation of DSM-IV criteria at the time of the initial diagnosis.

Denominator: Number of primary care patients greater than 18 years with new diagnosis* of depression, panic disorder and/or generalized anxiety disorder in previous six months.

Suggested ICD-9 codes include: 296.2, 296.3, 300.01, 300.02, 300.00 and 311.

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

Method/Source of Data Collection

Claims/encounter data/scheduling information may be used to identify those patients who meet the inclusion criteria for this measure. A random sample of a maximum of 20 patients will be drawn. The medical record will be reviewed to determine if DSM-IV criteria are documented as used. Either the documentation of a statement "DSM-IV criteria applied" or the presence of narrative comments reflecting application of DSM-IV criteria in making the diagnosis is acceptable evidence for this measure.

Panic Attack DSM-IV 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 hear rate.
2. Sweating.
3. Trembling or shaking.
4. Sensations or 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.

Generalized Anxiety Disorder DSM-IV Criteria

Excessive anxiety and worry about a number of events (which causes clinically significant distress or impairment in functioning) occurring more days than not for at least six months. The person finds it difficult to control the worry.

Associated with **at least three** of the following:

1. Restlessness, feeling "on edge."
2. Fatigue.
3. Difficulty concentrating or mind going blank.
4. Irritability.
5. Muscle tension.
6. Sleep disturbance.

Major Depressive Episode DSM-IV 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.

Possible Successes Measurement #2a

Percentage of patients with a new diagnosis of fatigue with documentation of screening for depression and anxiety disorder.

Population Definition

Adults greater than 18 years with a new primary care diagnosis of fatigue.

Data of Interest

$$\frac{\text{\# patients with documentation in the medical record of screening for depression and/or anxiety disorder}}{\text{total \# of patients newly seen for fatigue}}$$

Numerator/Denominator Definitions

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

Denominator: Number of primary care patients greater than 18 years in primary care who have been newly diagnosed* with fatigue (suggested ICD-9 780.7) during the target quarter.

*New diagnosis is defined as no fatigue diagnosis in the six-month period prior to 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. Claims/encounter data/scheduling information may be used to produce the list. From this list, a random sample of a maximum of 20 patients newly diagnosed 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 the diagnosis was made.

Was there an interview for key symptoms of depression and anxiety?

Key symptoms:

Depressed mood

Anhedonia (diminished interest or pleasure in activities)

Vegetative symptoms (sleep disturbances, changes in appetite and energy level)

Periodic or constant anxiety which was distressing or disabling

If **any symptom** is documented in the record, it is counted as "Yes."

Time Frame Pertaining to Data Collection

It is suggested that data is collected quarterly.

PROBING MEASURES

1. For measure #2a, b, c, which key symptoms are not being addressed most often? Is there a performance difference between sites or type of provider?
2. For measure #2a, b, c, compare differences in performance based on:
   a) whether screening occurs; and
   b) when the screening activity is performed.

Is the problem that screening is not being performed, or is it that screening is not performed at the time the diagnosis is made?

SYSTEMS APPROACHES TO IMPLEMENTATION FOR THIS GUIDELINE

1. To diagnose and characterize depression/anxiety disorder, develop a clinical interview process that includes:
    - DSM-IV criteria
    - Severity of symptoms and degree of functional impairment
    - Psychosocial stressors
    - Previous history of depression/anxiety
    - Identifies patients with risk factors and frequent presentations.
    - Medical illness.
    - Medications and withdrawal from medications.
    - Current substance abuse.
    - Review medical and psychiatric co-morbidity including:
        - Co-morbid depression and anxiety disorder.
        - Medical history
    - Establish appropriate treatment and follow-up plan which includes education, support, and may include medications, and/or cognitive/behavioral therapy.

*Recommended Website Resources**

Note: Websites are listed in alphabetical order, not in order of work group preference.

Website Sponsor	Key Subject/ Target Audience	Description	Website Address
National Institute of Mental Health	Consumer/Health professionals	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, Medline Plus and other relevant sites are available.	www.nimh.nih.gov
National Mental Health Association	Consumer/Health professionals	Provides patient information, depression screening tool, community resources and discussion board.	www.nmha.org
American Psychiatric Association	Consumer/Health professionals	Provides mental health news, on-line CME programs and legislation. Links to MEDEM for patient information.	www.psych.org
National Library of Medicine MEDLINEplus	Consumer/Health professionals	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.	www.nlm.nih.gov/medlineplus

These websites were reviewed by the ICSI *Major Depression, Panic Disorder, Anxiety Disorder* guideline work group as credible resources. ICSI does not have the authority to monitor the content of these sites. Any health-related information offered from these sites should not be interpreted as giving a diagnosis or treatment.

*** Criteria for Selecting Websites**

The preceding websites were selected by the *Major Depression, Panic Disorder, Anxiety Disorder* guideline work group as additional resources for practitioners and the public. The following criteria were considered in selecting these sites.

- The site contains information specific to the particular disease or condition addressed in the guideline.
- The site contains information that does not conflict with the guideline's recommendations.
- The information is accurate and/or factual. The author of the material or the sponsor of the site can be contacted by means other than e-mail. For example, a nurse line or other support is provided.
- The material includes the source/author, date and whether the information has been edited in any way. The site clearly states revision dates or the date the information was placed on the Internet.
- The site sponsor is an objective group without an obvious or possible bias. For example, the site does not promote a product, service or other provider.
- The coverage of the topic is appropriate for the guideline's target audience. It is clearly written, well-organized and easy to read. The site is easy to navigate.