



INSTITUTE FOR CLINICAL
SYSTEMS IMPROVEMENT

Health Care Guideline

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- 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
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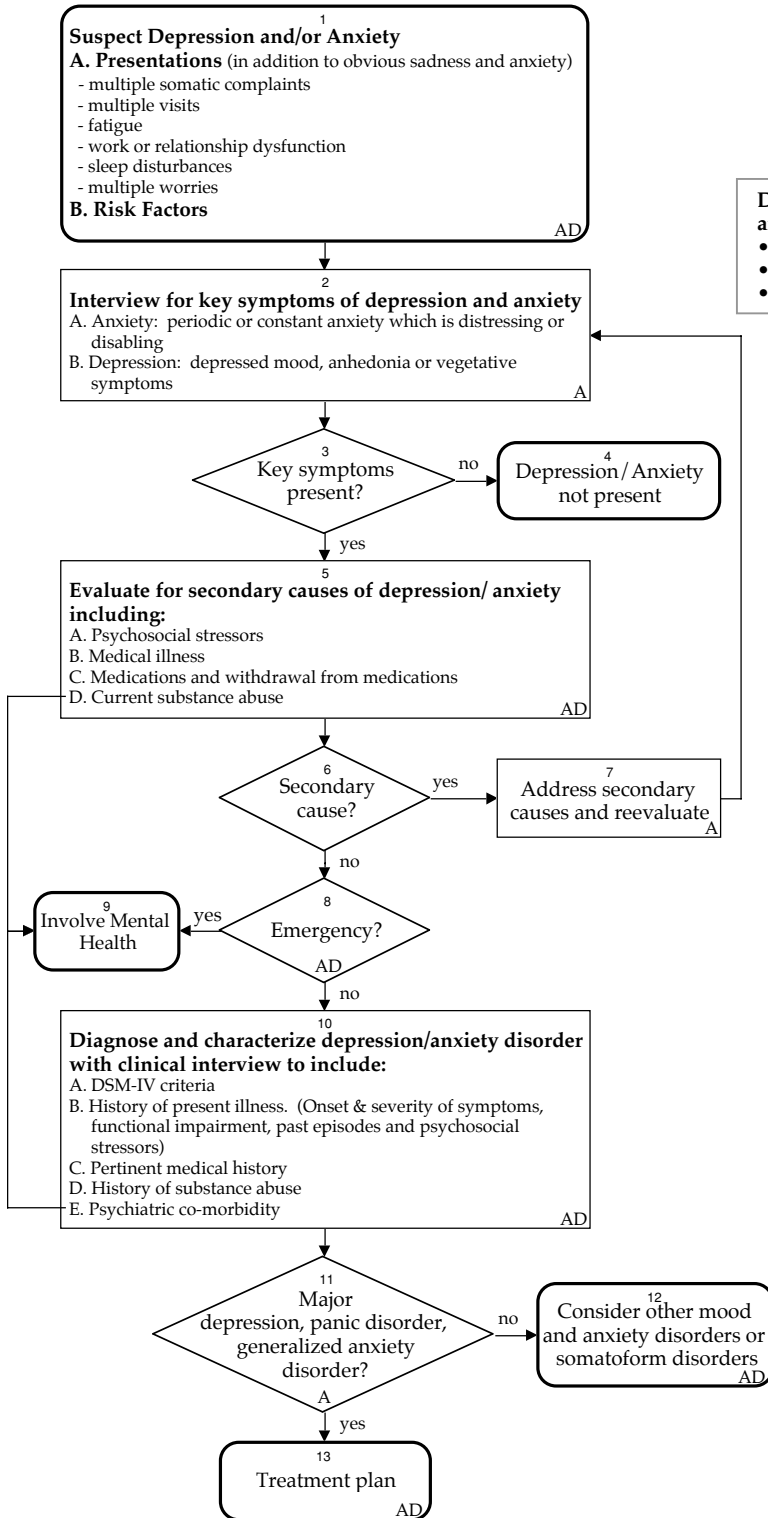
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Health Care Guideline:
Major Depression, Panic Disorder and Generalized Anxiety Disorder in Adults in Primary Care



Diagnoses 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?

General Implementation
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A = Annotation
 D = Discussion

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.

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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.

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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.

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Treatment:

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

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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.

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Targeted Population

Adults 18–64 years old.

Priority Aims for Medical Groups When Using This Guideline

1. Increase the detection and diagnosis of panic disorder, generalized anxiety and depression in primary care through application of specific criteria.

Possible measures of accomplishing this aim:

- a. 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.

2. Increase provider knowledge that patients with depression/anxiety disorders frequently present in primary care with somatic complaints.

Possible measures of accomplishing this aim:

- a. Percentage of patients with a new diagnosis of fatigue containing documentation of screening for depression and anxiety disorder.
- b. Percentage of patients with a new diagnosis of irritable bowel syndrome containing documentation of screening for depression and anxiety disorder.
- c. Percentage of patients with a new diagnosis of sleep disorder containing 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 this guideline.

In future versions of this guideline, selected conclusions will include a statement of the grade assigned to the conclusion.

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 are present.

Presentations for depression and/or anxiety include:

- multiple (>5/year) medical visits
- multiple unexplained symptoms
- work or relationship dysfunction
- fatigue
- sleep disturbance
- multiple worries or distress
- panic attacks

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

Diagnoses particularly suggestive of an anxiety disorder include:

- atypical chest pain
- hyperventilation
- irritable bowel syndrome

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.

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:

- 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 joy?

Occasionally, depressed patients will initially deny depressed mood and anhedonia. If you still suspect depression, ask about vegetative symptoms (sleep disturbances, changes in appetite and energy level). If vegetative symptoms are present, ask again about depressed mood and anhedonia. If either is endorsed, proceed to a full clinical interview.

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 Secondary 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.

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 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.

C. Medications and Withdrawal from Medications

Reserpine, steroids, alpha-methyldopa, propranolol 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.

- D. **Current Substance Abuse** The CAGEAID Screen broadens the CAGE to include other drug use.

See screen on page 2 for details.

7. Address Secondary Cause of Depression/Anxiety and Re-evaluate

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.

8. Emergency "Same Day" Involvement of Mental 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.

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?

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.).

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

10. 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 page 2)

Major depression, panic attacks and generalized anxiety disorder (See page 2).

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.

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**.

E. **Psychiatric co-morbidity**. 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.

11. 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.

12. 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. 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 (Depressed mood for at least two years, more days than not accompanied by additional depressive symptoms that do not meet criteria for major depressive episode).

Other Anxiety Disorders:		
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?

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.
Hypochondriasis	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.

13. Treatment Plan

A. The key objectives of treatment are:

1. Reduction and eventual remission of symptoms of depression and panic disorder. Reduction of symptoms of GAD.
2. Reduction of recurrence of depression and panic disorder.
3. Return to previous level of occupational and psychosocial function.

B. Treatment Considerations

1. Pharmacologic and/or non-pharmacologic interventions (psychotherapy), are effective in treating both depression and anxiety disorders. Factors to consider in making treatment recommendations are symptoms severity, presence of psychosocial stressors, presence of co-morbid conditions, and patient preferences.
2. 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. Educational objectives include:
 - a. Provide basic information on the causes, diagnosis, treatment and management of depression/anxiety.
 - b. Encourage patients to help manage their illness in conjunction with their provider.

3. 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.
4. Antidepressant medications are up to 70% effective for treating major depression and are recommended as the first line of treatment for moderate to severe depression. The treatment of choice for mild to moderate depression is a combination of psychopharmacology and psychotherapy.
5. 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. Tricyclic Antidepressants (TCAs), benzodiazepines and Selective Serotonin Re-uptake Inhibitors (SSRIs) have proven efficacy for panic disorder.
TCA drugs, benzodiazepines and buspirone have proven efficacy for GAD. Some clinicians empirically use SSRI medications for GAD.
6. 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.

C. Medications

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 on page 2 may increase compliance.

Effective medications for specific disorders status are listed on page 2.

Table I
Antidepressants: SSRIs, TCAs and Others
Tables displayed do not replace comprehensive references.

SSRIs

General comments: can use anorgasmia, decreased libido, agitation, nausea, headache, insomnia; non-lethal in overdose; blood levels not useful.

Name	Starting dose (range)	Predominant effects
fluoxetine (Prozac)	10-20 mg (10-80 mg qd)	long half-life, drug-drug interactions
fluvoxamine (Luvox)	50 mg (100-300 mg qd)	*currently FDA-approved for OCD only
paroxetine (Paxil)	10-20 mg (10 -50 mg qd)	somnolence, dry mouth, constipation, decreased libido. Withdrawal syndrome involves flu-like symptoms and paresthesia
sertraline (Zoloft)	25-50 mg (25-200 mg qd)	loose stools, anorexia, decreased libido. Withdrawal syndrome involves flu-like symptoms and paresthesia
citalopram	(20-60 mg qd)	loose stools, anorexia

TRICYCLIC ANTIDEPRESSANTS

General comments: use caution in advanced atrio-ventricular delay, potentially lethal in overdose, blood levels useful for some like desipramine and nortriptyline. Can cause dry mouth, constipation, blurred vision, urinary retention, postural hypotension, tachycardia, somnolence, weight gain.

Name	Starting dose (range)	Predominant effects
desipramine (Norpramin)	25-50 mg (75-300 mg qd)	relatively more activating than other tricyclics
nortriptyline (Pamelor, Aventyl)	10-25 mg (20-150 mg qd)	relatively more sedating than most other tricyclics

TABLE 1 CONTINUED ON NEXT PAGE

OTHERS		
Name	Starting dose (range)	Predominant effects
bupropion (Wellbutrin)	75-100 mg (150-450 mg qd)	dizziness, nausea, dry mouth, constipation, sweating, headache agitation
bupropion SR (Wellbutrin)	150 mg bid (300-400 mg qd)	<i>seizures have been reported in high dose and in bulimics with pre-existing seizure risk, e.g., CNS lesion</i>
trazodone (Desyrel)	25-50 mg qhs-insomina (25-150 mg qhs) 50-75 mg bid-depression (100-600 mg qd)	drowsiness, dizziness, dry mouth, fatigue <i>priapism has been reported</i>
nefazadone (Serzone)	100 mg bid (100-600 mg qd)	headache, dry mouth, somnolence, nausea
venlafaxine (Effexor SR)	37.5 mg bid (75-375 mg qd)	nausea, headache, insomnia, sweating, nervousness, hypertension may occur in doses over 300 mg <i>significant hypertension has been reported. Withdrawal syndrome involves flu-like symptoms and paraesthesia</i>
mirtazapine	(15-45 mg qd)	sedation, weight gain, hypercholesterolemia, hepatitis, and agranulocytosis

- 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?

Table II		
Benzodiazepines/Buspirone		
<i>Tables displayed do not replace comprehensive references.</i>		
BENZODIAZEPINES		
General comments: can cause falls, drowsiness, psychomotor and cognitive impairment, physical dependency and disinhibition.		
A. Intermediate Half-Life (no active metabolites)		
	Name	Starting Dose (range)
	alprazolam (Xanax)	.25-.5 mg tid (.75-4 mg qd)
	lorazepam (Ativan)	.5 bid-qid (1-6 mg qd)
	oxazepam (Serax)	10 mg tid (30-60 mg qd)
B. Long Half-Life (active metabolites)		
	Name	Starting Dose (range)
	chlordiazepoxide (Librium)	5-10 mg tid (5-100 mg qd)
	clonazepam (Klonopin)	.5-1.5 mg qd (.5-4.0 mg qd)
	diazepam (Valium)	2-10 mg qd (2-40 mg qd)
BUSPIRONE		
Name	Starting dose (range)	Predominant effects
buspirone (BuSpar)	5 mg TID (15-60 mg qd)	insomnia, nausea, dizziness, restlessness, agitation Not habit forming.

D. 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.

E. 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.

Discussion and References:

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

Anxiety and Depression Guidelines combined May – Jul 1995
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Revision/Approval Nov – Dec 1995
General Implementation (First Cycle) Jan – Oct 1996
Revision Approval Nov 1996 – Jan 1997
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Revision/Approval Jan – Mar 1998
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Revision/Approval Jan – Mar 1999
General Implementation (Fourth Cycle) Begins Apr 1999

Response Deadline

Released in March 1999 for General Implementation.
The next revision will occur within one year.



Discussion and References – Evidence Grading

Major Depression, Panic Disorder , Anxiety Disorder

I. CLASSES OF RESEARCH REPORTS

A. Primary Reports of New Data Collection:

- Class A: Randomized, controlled trial
- Class B: Prospective cohort study
Case-control study nested within a prospective cohort study
- Class C: Non-randomized trial with concurrent or historical controls
Case-control study (except as above)
Retrospective cohort 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
Decision analysis
Cost-benefit analysis
Cost-effectiveness study
- Class R: Review article
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.

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.

Katon W. "The epidemiology of depression in medical care." *Int J Psychiatry Med* 17:93-112, 1987. (Class R)

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)

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. 23–4, 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. 541–546, 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 paresthesias.) 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.

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

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)

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.

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)

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

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

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. 73-5, 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)

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)

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

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)

5. Evaluate for Secondary 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.

- Medical Illness:

The depressive syndrome may also be associated with medical disorders. 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)

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, 1992. pp. 25-43. (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)

8. Emergency "Same Day" Involvement of Mental Health?

20% of patients with panic disorder and 12% of patients with panic attacks 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.

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)

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

10. Diagnose and Characterize 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)

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)

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)

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)

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)

12. 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).

13. Treatment Plan

Psychotherapy contributes significantly to symptom reduction, restoration of psychosocial and occupational functioning, and relapse prevention in patients with Major Depression. It is most effective when combined with antidepressant medication and in the acute phase of mild to moderate depressions or after a successful medication trial in severe depressions.

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)

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)

U.S. Department of Health and Human Services Public Health Service. Depression in Primary Care. Volume 2. Treatment of Major Depression. pp. 71-74, 1993. (Class R)

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.

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, 1993. (Class R)

Rickels K, Schweizer E. "The clinical course and long-term management of generalized anxiety disorder." *J Clin Psychopharmacol* 10:101S-110S, 1990. (Class R)

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.

Chambless DL, Gillis MM. "Cognitive therapy of anxiety disorders." *J Consult Clin Psychol* 61:248-60, 1993. (Class R)

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, 1993. (Class A)

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

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

Gelder MG. "Psychological treatment of panic anxiety." *Psychiatric Annals* 20:529-32, 1990. (Class R)

Rapee RM. "Psychological factors in panic disorder." *Adv Behav Res Ther* 15:85-102, 1993. (Class R)

Selective Serotonin Re-uptake Inhibitors (SSRIs) are effective for panic disorder. 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)

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)

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, 1992. (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.

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)

Dubovsky SL. "Generalized anxiety disorder: new concepts and psychopharmacologic therapies." *J Clin Psychiatry* 51(1, suppl):3-10, 1990. (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, 1993. (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 hypnotics tend to use less than prescribed and to reduce their use over time. Benzodiazepine abuse is usually seen as part of a pattern of abuse of multiple drugs often involving alcohol and sometimes opioids.

Woods JH, Katz JL, Winger G. "Use and abuse of benzodiazepines: issues relevant to prescribing." *JAMA* 260:3476-80, 1988. (Class R)

Maintenance and 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.

Janicak PG, Davis JM, Preskorn SH, Ayd FJ. Principles and Practice of Psychopharmacotherapy. Baltimore: Williams and Wilkins, 1993, pp. 224-225. (Class R)

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

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)

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

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 ≥ 50 at first episode
- Aged ≥ 40 with ≥ 2 episodes
- With ≥ 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. 224-225. (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. 246-257. (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)

St. Johns Wort:

Although there is growing evidence that St. Johns Wort has antidepressant effects, the work group feels it is too early to recommend St. Johns Wort as a therapeutic alternative. *The British Medical Journal* (volume 313, pages 253-257, August 1996) reviewed 23 randomized trials of St. Johns Wort. Their conclusion was that further studies were necessary. In most of the trials that diagnosis of depression was not well established, the placebo response was lower than in most other studies, the doses of antidepressants were small, the duration of the trials was short and the doses of active hypericin (St. Johns Wort) varied 6 fold. *The Medical Letter* (November 21, 1997) concluded the same. Hypericin probably has properties of a MAO inhibitor and has potentially significant side effects.

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

When measuring for improvement, it is critical that the measurements used are responsive to individual medical groups, and support medical groups' own clinical improvements. The following section of Specifications for Selected Measures is included in the guideline document to serve as an aid to the medical groups' own implementation efforts. It is likely that medical groups may need to adapt these measures to specific clinical practice or administrative systems.

Measurement – Overview

Major Depression, Panic Disorder, Anxiety Disorder

Overview of Ideas for Measurement

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 for Medical Groups When Using This Guideline

1. Increase the detection and diagnosis of panic disorder, generalized anxiety and depression in primary care through application of specific criteria.

Possible measures of accomplishing this aim:

- a. 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.

2. Increase provider knowledge that patients with depression/anxiety disorders frequently present in primary care with somatic complaints.

Possible measures of accomplishing this aim:

- a. Percentage of patients with a new diagnosis of fatigue containing documentation of screening for depression and anxiety disorder.
- b. Percentage of patients with a new diagnosis of irritable bowel syndrome containing documentation of screening for depression and anxiety disorder.
- c. Percentage of patients with a new diagnosis of sleep disorder containing 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 18–64 with a new primary care diagnosis of depression, panic disorder and/or generalized anxiety disorder.

Data of Interest

medical records containing documentation of DSM-IV criteria at the time of the initial diagnosis
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 18–64 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 medical records for patients with a new diagnosis of fatigue containing documentation of screening for depression and anxiety disorder.

Population Definition

Adults 18–64 with a new primary care diagnosis of fatigue.

Data of Interest

$$\frac{\# \text{ medical records containing documentation of screening for depression and/or anxiety disorder}}{\text{total \# of patients newly seen for fatigue}}$$

Numerator/Denominator Definitions

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

Denominator: Number of primary care patients 18–64 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?

Key symptoms:

Depressed mood

Anhedonia

Vegetative symptoms

Period 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?

Measure 1a: Percent of medical records for newly diagnosed depression, panic disorder and generalized anxiety disorder patients containing documentation of DSM-IV criteria at the time of the initial diagnosis.

The following are criteria that will be applied to the medical record review 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 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.

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.

(continues)

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 of 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.

Measure 2a:

Percent of medical records for patients with a new diagnosis of fatigue containing documentation of screening for depression and/or anxiety disorder.

The following are criteria that will be applied to the medical record review for this measure:

Key symptoms:

1. Depressed mood.
2. Anhedonia.
3. Vegetative symptoms
4. Periodic or constant anxiety which was distressing or disabling.