



Observer extra:
Depression

An internist's guide to screening, diagnosing and treating clinical depression.

An initial approach to diagnosing and treating depression

“Depression is not the soul’s annihilation; men and women who have recovered from the disease—and there are countless—bear witness to what is probably its only saving grace: its conquerability.”
—William Styron, *Darkness Invisible*

It’s the challenge posed to internal medicine physicians, who are increasingly on the front lines of patient care for depression: How to better recognize and treat patients suffering from symptoms.

Major depressive disorder is the most common psychiatric disorder, affecting nearly 10% of adults annually. This means that 25% of patients in primary care have a mood disorder; 10% to 15% have major depressive disorder and 8% to 10% have dysthymia. Only about half of patients with a major depressive disorder are diagnosed and treated.

The key to meeting this challenge is for physicians to understand how to assess the illness, including redesigning the office practice for routine screening, and how to recognize socioeconomic and medical risk factors. Physicians also need to be aware of the spectrum of depressive disorders: from mild to severe symptoms, from brief to life-long duration, and from presenting alone to presenting with another mood or psychiatric disorder. There have been recent advances in non-drug and drug therapies that should be considered and used appropriately. Recent recommendations support the creation of office-based systems to promote screening, diagnosis, management and treatment and to provide effective follow-up.

The *ACP Observer’s* “Initial Approach to diagnosing and treating depression” is intended as an introduction to depression assessment and management for the primary care physician.

Screening

According to a U.S. Preventive Services Task Force meta-analysis, screening is associated with a 13% reduction in relative risk and a 9% absolute reduction in the proportion of patients with persistent depression. The Task Force recommends screening adults for depression in clinical practices that have “systems in place to assure accurate diagnosis, effective treatment and follow-up.”

There is little evidence to recom-

mend one screening method over another, so physicians can choose the method that best suits their patient population and practice setting. The Primary Care Evaluation of Mental Disorders (PRIME-MD) is a multi-staged instrument that has been shown to be effective. The initial two-question screen asks patients:

- ◆ “Over the past two weeks have you felt down, depressed, hopeless?”
- ◆ “Over the past two weeks have

you felt little interest or pleasure in doing things?”

If the patient answers “yes” to at least one of these questions, ask this follow-up question: “Is this something with which you would like help?” and continue to part two of the screening (see box, “Diagnostic instruments for depression,” page 7).

Automatic screening protocols have been shown to be more successful than physician-initiated procedures. In a study of 2,263 patients in a primary care clinic, use of a patient self-report screen was only 11% when initiated by physicians compared with 80% when administered systematically by other clinic staff. Similarly, physicians were more likely to complete a follow-up evaluation when prompted by staff.

The Edinburgh Postpartum Depression Scale, which is available in multiple languages (see http://pier.acponline.org/physicians/pdf/pregpat_fit3-1_134.pdf), is useful for screening

Consider recurrent screening in patients with a history of depression

women deemed to be at particularly high risk for depression. High-risk categories include women with prior episodes of major depression, premenstrual dysphoric disorder, psychosocial stress during pregnancy or inadequate social support.

In the elderly, the Geriatric Depression Screen is the preferred tool because it takes into account the patient’s level of cognition and visual deficits that are common at this age. Questions range from “Do you frequently get upset over little things?” to “Do you feel that your life is empty?”

Although the optimal interval for screening is unknown, consider recurrent screening in patients with a history of depression, multiple unexplained or unrelated somatic complaints, comorbid psychological conditions (panic disorder or generalized anxiety), substance abuse, chronic pain, or lack of response

to usually effective treatments for comorbid medical conditions.

Consider screening for hypothyroidism in all patients with depression, especially in women aged 50 and older because hypothyroidism is common in this group. Symptoms of hypothyroidism are similar to symptoms of depression and subclinical hypothyroidism carries increased lifetime risk for depression. Treatment of hypothyroidism may improve depressive symptoms. Depression and hypothyroidism may be comorbid, and antidepressants may be required in addition to thyroid replacement.

Diagnosis

Because diagnosing clinical depression is based on patient history and exclusion of alternate diagnosis, the interview is particularly important. It establishes whether the patient meets established criteria for major depression, dysthymia or a different psychiatric condition.

The diagnosis of depression is confirmed if patients report experiencing at least five out of the following nine symptoms nearly everyday for at least two weeks (according to the Criteria for Major Depressive Episode based on DSM-IV):

- ◆ Depressed mood most of the day
- ◆ Diminished interest or pleasure in activities
- ◆ Significant unexplained weight loss or weight gain; or decrease or

Complicated grief

Major depression may be transiently present in normal grief; however, sadness without the complete syndrome is more common. Duration, intensity of symptoms and associated change in function are variable and commonly affected by cultural and societal factors. Pervasive and generalized guilt and persistent vegetative signs and symptoms that seem outside the boundaries of normal grief should be considered red flags. Bereavement is often a precipitant of true mood disorder, and patients in this state should be carefully assessed and followed. They should be offered supportive counseling as well.

Making a differential diagnosis among normal grieving, pathologic

grief, and depression can be problematic. In a study group of 82 recently widowed elderly individuals, seven symptoms constituted complicated grief:

- ◆ searching
- ◆ yearning
- ◆ preoccupation with thoughts of the deceased
- ◆ crying
- ◆ disbelief regarding the death
- ◆ feeling stunned by the death
- ◆ lack of acceptance of the death

The symptoms of complicated grief were distinct from depressive symptoms and were associated with enduring functional impairments requiring specialized treatment.

increase in appetite

- ◆ Insomnia or hypersomnia
- ◆ Psychomotor agitation or retardation
- ◆ Fatigue or loss of energy
- ◆ Feelings of worthlessness or excessive or inappropriate guilt
- ◆ Diminished ability to think or concentrate
- ◆ Recurrent thoughts of death, recurrent suicidal ideation without a specific plan.

Structured methods that assess the presence or absence of a mood disorder

and the presence of other psychiatric disorders are efficient because assessment of comorbidity is an essential component of evaluating the depressed patient. The PRIME-MD, PHQ, and SDDS-PC (see box, "Diagnostic instruments for depression," page 7) are examples of structured screening modalities that assess a spectrum of psychiatric disorders in addition to the principal mood disorders. The overall accuracy of PRIME-MD is 88%.

Once the diagnosis of major depression has been established, current evidence supports assessing the severity of depressive symptoms in guiding treatment options. The PHQ-9 is the mood module of the PHQ that assesses the presence and severity of the nine symptoms of major depression. It can be used to assess and follow severity of depressive symptoms over time and score ranges can be used as guides for treatment. (see "Diagnostic instruments for depression," page 7)

More than 90% of the 30,000 Americans who complete suicides each year have psychiatric disorders, and more than half of them suffer from clinical depression. Mental and addictive disorders, such as alcohol abuse, are the most powerful risk factors for suicide in

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Assessment tools and patient information

Disease	Characteristics	Treatment
Major depressive disorder	Depressed mood or loss of interest or pleasure in almost all activities characterizes major depression. In addition, symptoms must occur nearly every day for at least two weeks and a total of five DSM-IV symptoms must be present.	Drug therapy and psychosocial interventions effective.
Dysthymia	Dysthymia is a chronic mood disorder characterized by depressed mood or anhedonia at least half the time for at least two years accompanied by two or more vegetative or psychological symptoms and functional impairment.	Drug therapy effective.
Subsyndromal (minor) depression	Subsyndromal depression is an acute depression that is less symptomatic than major depression, causing less impairment in social or occupational functioning than major depression.	Unclear if drug therapy or psychotherapy improves patient outcomes. Consideration should still be given to treatment even if criteria for major depression are not strictly met.
Major depression in partial remission or recurrence	Fewer than five symptoms of major depression are present but past history is consistent with a major depressive episode.	Natural history of depression and risk of full relapse suggest that patient be treated with medication, therapy, or both.
Situational adjustment reaction with depressed mood	Subsyndromal depression with clear precipitant. Usually resolves with resolution of acute stressor without medication.	Careful brief observation may be indicated in patients with mild syndrome of major depression associated with clear stressful precipitant. Supportive counseling should also be initiated.
Bipolar disorder	Characterized by one or more manic or mixed episodes, usually accompanied by major depressive disorder.	Requires mood-stabilizing medication in addition to and usually before antidepressant medication. Usually requires referral to psychiatrist.
Seasonal affective disorder	A subtype of major depression, occurring with seasonal change, typically fall or winter onset and seasonal remission. Rarely onset is in the spring with remission in the fall or winter. Has occurred in the two previous years without non-seasonal depression. More common in northern latitudes.	Responds to bright-light therapy and adjuvant therapy.

all age groups, accounting for more than 90% of all completed suicides.

Most patients who commit suicide see their physicians in the preceding months.

Diagnostically, the “No Harm Contract”—a verbal or written agreement in which the suicidal patient is asked to agree not to harm or kill himself for a particular period of time—can be used to assess the nature and severity of a patient’s suicidality. The patient may agree with the proposal verbally or by signing a written statement, suggest modifications, refuse compliance or choose not to answer. In the assessment of suicidality, it is important to involve the family and obtain early psychiatric evaluation in all cases.

A physical examination of a patient suffering from depression may be normal. However, symptomatic individuals may appear anxious and exhibit poor eye contact, depressed mood, decreased psychomotor activity and tearfulness. In severe depression, patients’ affect is blunted or flat and they may have delusions.

Studies examining the utility of multiphasic screening and laboratory testing in psychiatric admissions failed to identify laboratory tests that could be recommended as “routine.” Most positive test results were associated with conditions, such as hypothyroidism, that were anticipated by information obtained from the medical history and a focused physical exam.

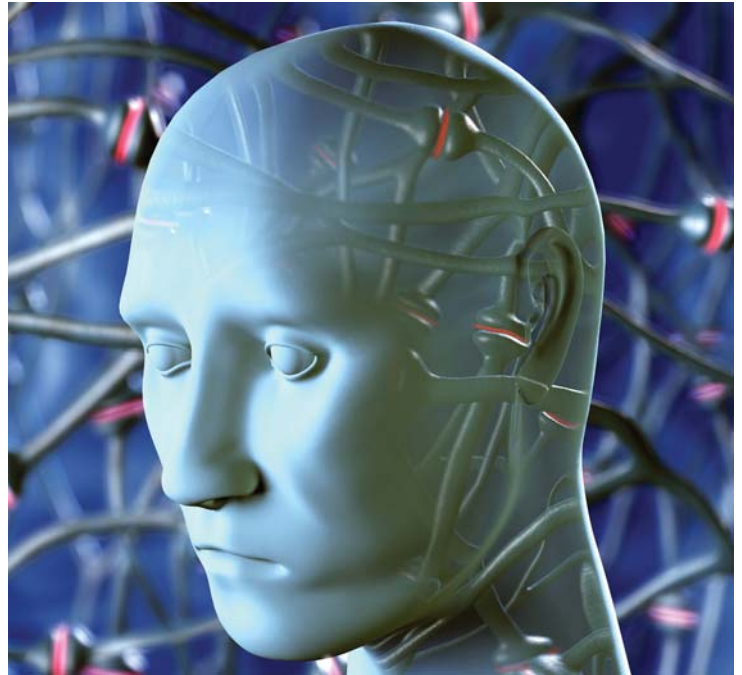
Non-Drug Treatment

Psychotherapy and depression

Non-drug therapy, at times in conjunction with drug therapy, can help many patients with depression.

Because psychotherapy and pharmacotherapy are equally effective for patients with mild to moderate depression, these patients should be offered a choice. Patients should be informed that medications produce remission faster than psychotherapy and that they may consider using both but recognize that there is limited available evidence showing added benefit.

In patients with a history of severe depression or current subsyndromal depression, antidepressant medication is superior to psychotherapy alone, but combination therapy with psychotherapy and antidepressants is more effective than either alone. The drug therapy can achieve complete remission while psychotherapy treats residual symptoms. Moreover, there is some evidence that psychotherapy may help prevent relapse in patients with recurrent depression.



Drug Treatment

Antidepressant drug therapy

Using drug therapy to treat patients for depression has a reachable goal: complete remission within six to 12 weeks and return to normal functioning. The keys are selecting the right drug for each patient, monitoring the patient and following up.

Initially, patients with major depression, dysthymic disorder or both (“double depression”) should be started on single-agent antidepressant drug therapy. The choice of a specific agent depends on its side effects since all agents are equally effective. Rates of withdrawal from clinical trials suggest that selective serotonin reuptake inhibitors (SSRIs) may be better tolerated than tricyclics and have less potential overdose lethality.

St. John’s Wort may be beneficial for patients who want to take something for minor depression or who are unwilling or unable to take conventional therapy for moderate depression. St. John’s Wort has had equivocal results when studied in randomized placebo-controlled trials. Optimum doses are not established, but many trials with positive findings have used standardized doses of 0.3% hypericin, 300 mg three times a day. Serious adverse effects with St. John’s Wort

are uncommon, but it is known that it activates the cytochrome P450 system and may reduce plasma concentration of certain coadministered drugs, such as protease inhibitors, cyclosporine, digoxin, theophylline, simvastatin, and warfarin. St. John's Wort is not indicated and has not been shown to be of benefit in patients with major depression.

Because physicians can use any of the approved antidepressant medications to treat major depressive disorder, dysthymic disorder or both—"double depression"—use the following parameters to guide your prescribing decisions:

- ◆ History of successful treatment with particular agent or of one used successfully with a first-degree relative treated for depression.
- ◆ Differences in the role of cytochrome P450 2D6 metabolism that may influence the risk of drug interaction.
- ◆ Differences in SSRI half-life that may influence risk of withdrawal if the medication is abruptly stopped.
- ◆ Risk of drug and food interactions with monoamine oxidase inhibitors (MAOIs).
- ◆ Potential lethality in overdose.
- ◆ Cost.
- ◆ Concern about pregnancy. Second generation antidepressants (e.g., SSRIs, bupropion, duloxetine, mirtazapine and venlafaxine) may be associated with an increased risk of fetal malformations (first trimester) and pulmonary hypertension (third trimester). The FDA issued an advisory that paroxetine should generally not be initiated in women who are in their first trimester of pregnancy or in those planning to become pregnant. If such women are already on paroxetine, they should consider discontinuing it or switching to another antidepressant. Despite the lack of FDA approval, the available data on the reproductive safety of antidepressant medications suggest relatively low teratogenic potential. The most extensive literature on reproductive safety exists for the tricyclic antidepressants and fluoxetine, which have shown no increased risk of teratogenicity after first-trimester exposure in both prospective and retrospective studies.

Physicians should also consider the impact of side effects. Rates of withdrawal from clinical trials suggest that SSRIs may be better tolerated than tricyclics, but all drugs have side effects. Dry mouth, constipation and dizziness are more common with tricyclics; nausea and headache are more common with SSRIs. MAOIs are associated with greater risk of adverse drug and food interactions.

Treat first episodes of depression to achieve complete remission, and continue treatment for four to nine months thereafter. Response to treat-

ment has been defined as a 50% reduction in depressive symptoms as measured by a case-finding tool such as the PHQ-9.

The duration of maintenance therapy may be longer if the precipitating event or other stressors persist, if there is a history of prior events or if depression lasted for a long time prior to starting therapy.

When to refer

Refer your patients to a psychiatrist if:

- ◆ Therapy with drugs you're familiar with fails.
- ◆ Therapy with different drug agents fails.
- ◆ Difficult-to-control side effects occur.
- ◆ Psychotic symptoms are present or primary psychotic disorder is suspected.
- ◆ Significant suicidal ideation or intent occurs or there's uncertainty regarding suicide risk.
- ◆ There's a history of possible or diagnosed bipolar affective disorder or a family history of bipolar disorder and symptoms suggesting mania are present.
- ◆ Depression and a complex comorbid mental condition (e.g., psychotic disorder, bipolar disorder, posttraumatic stress disorder, obsessive compulsive disorder) and substance abuse are present.
- ◆ Complex family or couple problems exist.

Begin patients with suicidal ideation—but without a plan or intent—on treatment and closely monitor them. Urgently refer patients with a suicide plan to a psychiatrist or emergency referral for hospitalization and psychiatric assessment, depending upon the clinical situation.

Follow-up

Up to half of patients experience side effects of depression treatment or stop therapy altogether, so it's important to monitor patients at regular intervals during initiation, titration to remission and maintenance pharmacotherapy. Moreover, although treatment-resistant depression is a common clinical problem, patients may respond better to one drug than another. Follow-up offers physicians a chance to find a better, timely solution.

See patients two and four weeks after starting therapy to assess acceptance of medication, reinforce educational messages and address adverse drug reactions and suicide risk. Assess patients again at six to eight weeks for response to therapy. At this point patients should complete a formal tool for severity assessment, such as the PHQ-9, and then be classified and treated as follows:

Complete response: Continue the same therapy modality for an additional four to nine months.

Partial response: Use a higher dose of the same agent, add a second agent or add psychotherapy.

No response: Switch to a different category of drug or to psychotherapy.

Once patients achieve remission, monitor them regularly and give additional counseling about medication adherence and risk of symptom recurrence.

Patients over 70 years of age with major depression who respond to an SSRI should be treated for two years to prevent recurrence. This continued medication treatment, along with psychotherapy, can prevent relapse.

Up to half of all patients will experience recurrent symptoms and will require long-term therapy. For the first recurrence, consider maintenance treatment for one to two times the interepisode interval. So, for example, if the second episode occurs 18 months after the first one, the treatment should be 18 to 36 months.

Because patients with three recurrences have a 90% chance of having another, consider life-time maintenance therapy for patients with three or more recurrences, or patients with a first recurrence and risk factors for further recurrences including:

- ◆ Family history of bipolar disorder.
- ◆ Recurrence within one year of successful treatment of previous episode.
- ◆ Young age of onset (e.g., adolescent).
- ◆ Severe (e.g., debilitating or suicidal attempt) and sudden onset of symptoms.

Patient Education

Patients must be counseled about antidepressant medication so that they adhere to the regimen, especially during the critical first month of treatment. Specifically, tell your patients to:

- ◆ Take their medicine daily.
- ◆ Anticipate a two- to four-week wait before feeling better.
- ◆ Continue taking the medication even if they're feeling better.
- ◆ Check with their physician before stopping the medication.
- ◆ Be aware of the potential symptoms of stopping the medication (e.g., dizziness, nausea, rhinitis and headaches).
- ◆ Know the medication's potential side effects.

Diagnostic instruments for depression

Primary Care Evaluation of Mental Disorders (PRIME-MD): A two-stage, modular instrument that assesses common mood, anxiety, eating, alcohol and somatoform disorders.

Patient Health Questionnaire (PHQ): A patient self-report version of the PRIME-MD with equivalent diagnostic accuracy that takes less than three minutes of physician time in 85% of patients.

Patient Questionnaire (PQ): A 25-item patient self-report that identifies patients for further assessment using the Clinician Evaluation Guide (CEG). PQ items may also be asked verbally by the physician or other personnel. Two PQ items are required for depression case-finding. The average CEG interview (addressing modules for all triggered disorders, not depression alone) takes an average of 8.5 minutes in the 80% of patients who screen positive

for at least one module.

PHQ-9: The mood module of the PHQ. It consists of items assessing the presence and severity of the nine symptoms of major depression. It is diagnostically accurate compared to physician-initiated assessment and can be used to follow severity of depressive symptoms over time. (The PHQ-9 is online at http://intermountainhealthcare.org/documents/51/2002_depression_phq9.pdf).

Brief PHQ: This includes the mood module portion of the PHQ and assesses for anxiety. It also contains a section exclusive to women with questions pertaining to menstruation, pregnancy and childbirth issues.

Symptom Driven Diagnostic System for Primary Care (SDDS-PC) is an alternative structured diagnostic tool that assesses multiple mental disorders that are common to

primary care: alcohol abuse or dependence, generalized anxiety disorder, major depression, obsessive compulsive disorder, panic disorder, and suicidal ideation.

SALSA: An alternative diagnostic strategy is the two-item (mood and anhedonia) case-finding questions with assessment of so-called SALSA score symptoms of depression:

- Sleep disturbance
- Anhedonia
- Low Self-esteem
- Appetite disturbance

Patients who report two of these four symptoms present nearly every day for at least two weeks are virtually identical with patients diagnosed using the five out of nine symptom algorithm. Over 97% of patients with major depression will have at least two of the SALSA symptoms.

Source: *PIER module on Depression.*



Depression

Web resources

For Patients

American Academy of Family Physicians

Depression: How Medicine Can Help
(<http://familydoctor.org/045.xml>)

American College of Physicians

Celebrating Life: A Guide to Depression for African Americans
(<http://www.doctorsforadults.com/images/healthpdfs/depressionbook.pdf>)

American College of Physicians

Feel Blue? Tired All the Time? Your Internist Can Help
(<http://www.doctorsforadults.com/images/healthpdfs/depression.pdf>)

American Psychiatric Association

A Basic Guide to Depression
(http://medem.com/MedLB/article_detail_lb.cfm?article_ID=ZZZDL37U2KC&sub_cat=128)

Medline Plus

Depression
(<http://www.nlm.nih.gov/medlineplus/ency/article/003213.htm>)

National Alliance for the Mentally Ill

What is Major Depression?
(http://www.nami.org/Template.cfm?Section=By_Illness&Template=/TaggedPage/TaggedPageDisplay.cfm&TPLID=54&ContentID=23039)

National Institute of Mental Health

Depression
(<http://www.nimh.nih.gov/publicat/depression.cfm>)

U.S. Food and Drug Administration

The Lowdown on Depression
(http://www.fda.gov/fdac/features/2003/103_dep.html)

National Cancer Institute

Depresión (PDQ®) (Spanish)
(<http://www.cancer.gov/espanol/pdq/cuidados-medicos-apoyo/depression/patient/>)

For Physicians

American Psychiatric Association

Practice guideline for the treatment of patients with major depression
(http://www.psych.org/psych_pract/treatg/pg/Depression2e.book.cfm)

U.S. Preventive Services Task Force

Screening for Depression (2002)
(<http://www.ahrq.gov/clinic/uspstf/uspstfdepr.htm>)
Screening for Suicide Risk (2004)
(<http://www.ahrq.gov/clinic/uspstf/uspstfssuic.htm>)

American College of Physicians

Outcomes of Minor and Subsyndromal Depression among Elderly Patients in Primary Care Settings
Annals of Internal Medicine Apr 2006; 144: 496-504
(<http://www.annals.org/cgi/content/full/144/7/496?>)

American College of Physicians

Depression by James L. Levensen, MD
(<http://pier.acponline.org/physicians/pdf/depressionbook.pdf>)