

Understanding the Vital Link:

Depression and Chronic Disease



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Needs Statement:

More than 19 million Americans suffer from depression, costing society \$44 billion annually in lost productivity. Major depression is now the leading cause of disability in the United States. At the same time, according to the Centers for Disease Control (CDC), there is growing recognition of the importance of both chronic disease and depressive disorders to the health of individuals and communities. And yet, per the US Preventative Services Task Force, primary care physicians miss more than half of all depression cases.

This vital gap can become a link to improving patient care in the United States when addressed by effective, focused, and case-based education – developed *by* primary care physicians *for* primary care physicians.

Per the CDC, chronic diseases — such as heart disease, cancer, and diabetes — are the leading causes of death and disability in the United States. These diseases account for 7 of every 10 deaths and affect the quality of life of 90 million Americans.

Depressive disorders assume an important role in the etiology, course, and outcomes associated with chronic disease. Multivariate community-based research and intervention fostering the detection and treatment of depressive disorders are needed, as is further examination of the role exerted by mental illnesses other than depression in the pathogenesis of chronic disease.

Patients with diabetes and chronic pain are especially prone to depression. For example:

- ❖ Per the NIMH, people with diabetes may be at greater risk for depression. In addition, individuals with depression may be at greater risk for developing diabetes.
- ❖ Major depression is thought to be four times greater in people with chronic back pain than in the general population (Sullivan, Reesor, Mikail & Fisher, 1992).
- ❖ Individuals with chronic physical complaints also have higher rates of lifetime major depression. In groups of patients with medically unexplained symptoms, such as chronic back pain and chronic dizziness, 66% of patients have a history of

recurrent major depression compared to less than 20% of control groups with medically explained symptoms (Atkinson *et al.* 1991; Katon and Sullivan 1990; Sullivan and Katon 1993).

- ❖ Co-morbidities of depression abound. Depression is most often related to alcohol or drug abuse, anxiety disorders, eating disorders, and a number of general medical conditions, including asthma, arthritis, stroke, coronary heart disease, cancer, HIV/AIDS, and hepatitis C.

Learning Outcomes:

At the conclusion of this activity, participants should be able to:

- ❖ Recognize true qualitative impact of depression on chronic diseases
- ❖ Evaluate depression as an independent risk factor of other chronic diseases
- ❖ Differentiate between remission and recovery, and treat depression to remission
- ❖ Implement improved practice management systems to support better treatment of patients with chronic disease and depression
- ❖ Incorporate important implications of cultural competencies into screening for and treating depression.

Recommendations	Evidence Strength
Patients with any chronic condition should be screened for depression, especially those with diabetes, cardiovascular disease, or chronic pain (Class B, D, M, R).	Class B: Cohort study. D: Cross-sectional study, case series, case report. M: Meta-analysis, systematic review, decision analysis, cost-effectiveness analysis. R: Consensus statement, consensus report, narrative review.
The VHA recommends that all stroke patients should receive a psychosocial assessment, psychosocial intervention, and referrals (QE: II-3; Overall Quality: Fair; R: B).	QE: II-3: Evidence obtained from multiple time series studies with or without intervention. Overall Quality: Fair: High-grade evidence linked to intermediate outcome or moderate grade evidence directly linked to health outcome. Grade (R): B: A recommendation that the intervention may be useful/effective.
The VHA strongly recommends that [stroke] patients with a diagnosed depressive disorder be given a trial of antidepressant medication, if no contraindication exists (QE: I; Overall Quality: Good; R: A).	QE: I: Evidence obtained from at least one properly randomized controlled trial. Overall Quality: Good: High-grade evidence directly linked to health outcome. Grade (R): A: A strong recommendation that the intervention is always indicated and acceptable.
Women with CVD should be evaluated for depression and refer/treat when indicated (Class IIa, Level B).	Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy. Level B: Limited evidence from single randomized trial or other non-randomized studies.
Health care professionals should be alert to the presence of depression in patients with COPD. The presence of anxiety and depression in patients with COPD can be identified using validated assessment tools (Grade D). Patients found to be depressed or anxious should be treated with conventional pharmacotherapy (Grade A). For antidepressant therapy to be successful, it needs to be supplemented by spending time with the patient explaining why depression needs to be targeted alongside the physical disorder (Grade C).	Grade A: Based on hierarchy I evidence. Grade C: Based on hierarchy III evidence or extrapolated from hierarchy I or II evidence. Grade D: Directly based on hierarchy IV evidence or extrapolated from hierarchy I, II, or III evidence (I: evidence from systematic reviews or meta-analysis of randomized controlled trials or evidence from at least one randomized controlled trial; II: evidence from at least one controlled study without randomization or evidence from at least one other type of quasi-experimental study; III: evidence from non-experimental descriptive studies; IV: evidence from expert committee reports or opinions and/or clinical experience of respected authorities).
Patients with coronary disease should be screened for anxiety and depression using a validated assessment tool (B). All cardiac patients in whom anxiety or depression is diagnosed should be treated appropriately (A).	Grade A: At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or a body of evidence including studies consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results. Grade B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+.
Health care professionals should be aware of the effects of depression on diabetes (Grade B). All people with diabetes should be screened for depression and offered appropriate therapy (Grade B).	Grade B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+.
Clinicians should use brief assessment tools routinely to ask cancer patients about pain, depression, and fatigue, and to initiate evidence-based treatments.	Evidence included presentations by experts; a systematic review of the medical literature provided by the Agency for Healthcare Research and Quality; and an extensive bibliography of cancer symptom management research papers, prepared by the National Library of Medicine. Scientific evidence was given precedence over clinical anecdotal experience.
It is recommended that screening for endogenous or prolonged reactive depression in patients with heart failure be conducted following diagnosis and at periodic intervals as clinically indicated. For pharmacologic treatment, SSRIs are preferred over TCAs, because the latter have the potential to cause ventricular arrhythmias, but the potential for drug interactions should be considered (Grade B).	Grade B: Cohort and case-control studies, post hoc, subgroup analysis, and meta-analysis, prospective observational studies or registries.
Consensus opinion is to treat depressed cardiac patients with a safe drug rather than watchful waiting since they would benefit from symptomatic relief of their depressive symptoms and there is a potential improvement in their cardiovascular risk profile. Although TCAs are effective against depression, they are associated with cardiovascular side effects including orthostatic hypotension, slowed cardiac conduction, antiarrhythmic activity, and increased heart rate. SSRIs by contrast are well tolerated and have a more benign cardiovascular profile and would be preferred initial agents for treatment of depression in individuals with cardiovascular disease (Grade D, M, R).	Grade D: Primary reports of new data collection: cross-sectional study, case series, case report. Class M: Reports that synthesize or reflect upon collections of primary reports: meta-analysis, systematic review, decision analysis, cost-effectiveness analysis. Class R: Reports that synthesize or reflect upon collections of primary reports: consensus statement, consensus report, narrative view.
Depression and pain symptoms commonly coexist, exacerbate or attenuate one another, and appear to share biological pathways and neurotransmitters. In those patients presenting with either pain or depressive symptoms, assess both domains. If co-morbidity is found, treat both conditions for optimal outcomes. Given that depression and pain symptoms appear to follow the same descending pathways of the central nervous system involving a functional deficiency of the neurotransmitters serotonin, norepinephrine, and dopamine, antidepressant medication is warranted, especially the dual-action tricyclic antidepressants such as amitriptyline or dual-action atypical antidepressant reuptake inhibitors such as venlafaxine or duloxetine. Combining pharmacologic treatment and cognitive-behavioral therapy appears to produce the most favorable treatment outcomes (Grade B, D, M, R).	Grade B: Primary reports of new data collection: cohort study. Grade D: Primary reports of new data collection: cross-sectional study, case series, case report. Class M: Reports that synthesize or reflect upon collections of primary reports: meta-analysis, systematic review, decision analysis, cost-effectiveness analysis. Class R: Reports that synthesize or reflect upon collections of primary reports: consensus statement, consensus report, narrative view.
Major depression is associated with an increased number of cardiac risk factors in patients with diabetes and a higher incidence of coronary heart disease; therefore, screening and treatment of depression in this group should be emphasized (Grade D).	Grade D: Primary reports of new data collection: cross-sectional study, case series, case report.

continued from page 4.

Website	Source
www.guideline.gov/summary/summary.aspx?doc_id=9344&nbr=005011	National Guideline Clearing-house
www.guideline.gov/summary/summary.aspx?doc_id=3846&nbr=003061	
www.guideline.gov/summary/summary.aspx?doc_id=4849&nbr=003490	
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www.guideline.gov/summary/summary.aspx?doc_id=9344&nbr=005011	

Contents

Pretest6
Introduction7
Impact of Depression Co-occurring With Specific Medical Illness8
Heart Disease8
Stroke9
Diabetes10
Cancer10
Respiratory Disease11
Chronic Pain11
Causality Between Depression and Co-morbid Medical Illness12
Behavioral/Lifestyle12
Biologic Association13
Metabolic Syndrome14
Detection of Co-morbid Depression in Primary Care15
Reasons for Undetected Depression15
Treatment of Co-morbid Depression in Patients With Medical Illness17
Heart Disease17
Stroke19
Diabetes19
Chronic Pain19
What PCPs Can Do20
Goals of Treatment20
Patient Education20
Practice Changes21
Reimbursement for Depression Treatment21
Summary23
Conclusions24
References24
Posttest30
Evaluation and Registration31

Pretest

Questions

1. In general, the more physical symptoms a patient presents, the greater the risk of a psychiatric disorder.
2. Co-morbid depression after a stroke increases mortality by:
3. Six months post myocardial infarction, co-morbid depression was associated with _____ increase in the risk of mortality.
4. The prevalence of depression in patients with diabetes is approximately _____ that of patients without diabetes.
5. Depression is recognized in approximately _____ of patients with diabetes.
6. Depression is appropriately treated in approximately _____ of patients with diabetes.
7. A recent study found that 22% of patients in primary care suffer from persistent debilitating pain and that these patients are four times more likely to develop depression.

Before Reading

- True
 - False
-
- 13%
 - 65%
 - Has no effect
-
- no
 - a 2-fold
 - a 4-fold
-
- equal to
 - double
 - triple
-
- 25%
 - 50%
 - 75%
 - 90%
-
- less than 25%
 - more than 50%
 - slightly more than 75%
-
- True
 - False

Introduction

Depression is a major health problem in the United States. Approximately 20.9 million American adults, or 9.5% of the US population aged 18 years and older have a mood disorder (major depressive disorder, dysthymic disorder, or bipolar disorder [see Box 1 for definitions]).¹ The lifetime prevalence of major depression in the general population is 13.2% to 17.1%, with a 12-month prevalence of 5.3% to 6.7%.¹⁻⁵

It is not surprising then that depression is the principal reason for 12.1 million office visits each year (primary care and specialist) and has an economic cost of \$44 billion annually.^{6,7} Clinical depression is a chronic, serious,

and costly mental illness, but it can be effectively treated in more than 80% of people with medication, psychotherapy, or a combination of both.⁸ The clinical paradox is that only one in three patients is accurately diagnosed, and only one in five patients with major depression receives adequate treatment.^{3,9}

The risk of depression is even higher in individuals with serious medical illnesses (eg, heart disease, stroke, cancer, diabetes, Parkinson's disease, Alzheimer's disease); the more severe the condition, the more likely the patient will experience depression.^{2,8-11} Conversely, depression is also a risk factor for developing some medical illnesses.⁸

Alone, depression can be incapacitating, but co-morbid depression and medical illness worsen outcomes for both.

Box 1. DSM IV criteria for depressive disorders

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

1. depressed mood most of the day, nearly every day, as indicated by either subjective report (eg, feels sad or empty) or observation made by others (eg, appears tearful)
2. markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)
3. significant weight loss when not dieting or weight gain (eg, a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day
4. insomnia or hypersomnia nearly every day
5. psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
6. fatigue or loss of energy nearly every day
7. feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
8. diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)
9. recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

Dysthymic disorder: Depressed mood for most of the day, for more days than not, as indicated either by subjective account or observation by others, for at least two years. *Note:* In children and adolescents, mood can be irritable and duration must be at least one year.

Minor depressive disorder: Episodes of at least two weeks of depressive symptoms but with fewer than the five items required for major depressive disorder.

Bipolar disorder: A clinical course that is characterized by the occurrence of one or more manic episodes or mixed episodes.

Manic episode: A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least one week (or any duration if hospitalization is necessary). During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:

1. inflated self-esteem or grandiosity
2. decreased need for sleep (eg, feels rested after only 3 hours of sleep)
3. more talkative than usual or pressure to keep talking
4. flight of ideas or subjective experience that thoughts are racing
5. distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli)
6. increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
7. excessive involvement in pleasurable activities that have a high potential for painful consequences (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

Mixed episode: The criteria are met both for a manic episode and for a major depressive episode (except for duration) nearly every day during at least a one-week period. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

APA. *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR)*. Washington, DC: APA; 2000:352.

Co-morbid depression is associated with greater role-function impairments, poor self-care, decreased ability to follow lifestyle recommendations, and poor adherence to medical treatment recommendations, thus hindering the treatment of other medical conditions.^{2,8,12,13} There is also evidence that depression can biologically affect the course of some medical illnesses and vice versa.¹⁴ Depression is associated with 50% to 100% higher medical costs in medical patients than others with the same condition, including emergency department (ED) visits, primary care visits, prescriptions, laboratory tests, hospital days, and mental health visits.^{2,15}

Here we discuss the lessons learned about the impact and treatment of depression in some common disease states (heart disease, stroke, diabetes, respiratory disease, chronic pain, cancer) to demonstrate why patients with co-morbid disease will benefit from the identification and treatment of depression. Practical information is presented to assist primary care physicians (PCPs) in identifying co-morbid depression and to develop a rationale for treatment. More detailed information about treating depression can be found in the **Recognition and Management of Depression** monograph at www.familydocs.org.

Impact of Depression Co-occurring With Specific Medical Illness

Heart Disease

Patients with depression are at approximately twice the risk of developing new heart disease.^{8,13,16} Clinical depression is a strong predictor for the development of coronary heart disease (CHD) events in healthy patients (OR: 2.69), but even subthreshold depressive symptoms are risk factors.¹⁷⁻¹⁹ The incidence of congestive heart failure (CHF) in depressed patients is also increased (16% vs 7% in non-depressed patients).^{19,20}

Once heart disease has developed, the prevalence of depression is also increased compared with the general population. The prevalence in CHF patients ranges from 20% to 40%;^{2,21-25} and up to 50% of patients recently hospitalized for coronary artery bypass graft (CABG) surgery experience depression.^{19,26} It occurs in 18% to 20% of people who have CHD but have not had a myocardial infarction (MI), and in up to 65% of patients who experience a first or recurrent acute MI each year (major depression in 15% to 22%).^{8,16,27-29} Younger women, who are more prone to depression in the community, are also more likely to have depression during hospitalization with an acute MI.³⁰ Depressive symptoms after an MI may be transient during hospitalization and subside shortly after discharge, persist for a longer time, or develop only after discharge.³¹ Of the approximately 20% of patients with major depression during hospitalization for MI, 35% have persistent depression at one month and an additional 6% have new depression at one month after discharge.³¹ However, more than half of the episodes of major depression associated with acute coronary syndromes (ACS) begin long before ACS and therefore were not caused by ACS.³²

Depression in cardiovascular populations is associated with a range of adverse outcomes independent of baseline heart disease severity. Among patients with an

acute MI, depressive symptoms predict cardiac mortality, recurrent events, rehospitalization, and worse health status, even in the absence of a clinical diagnosis of depression.^{13;16;19;29;30;33} Health care costs associated with readmissions and outpatient contacts during the year following an MI have been reported to be 41% higher for patients with mild to moderate depressive symptoms compared to no depressive symptoms.³⁴ After an MI, patients with clinical depression have a three- to five-fold greater risk of death within six months.^{8;9;16;17;19;30;35;36} Its prognostic role is at least equivalent to that of established indicators, such as left ventricular dysfunction, a history of acute MI, diabetes, smoking, hypertension, and obesity.^{8;9;16;17;19;30;35;36} Even minimal depressive symptoms, as well as transient depression after an MI, increase the risk for recurrent events, rehospitalization, and cardiac mortality compared to non-depressed patients.^{30;31;37;38} Moderate to severe depression before CABG surgery and/or persistent depression after surgery increases the risk for adverse cardiovascular outcomes and death after CABG more than two-fold.^{9;19;39}

In addition, depressive symptoms are strongly associated with health status in patients with heart disease, including symptom burden, physical limitation, and decreased quality of life (QOL) (Figure 1).⁴⁰ The association of depressive symptoms with health status at six months is at least as strong and consistent as traditional measures of

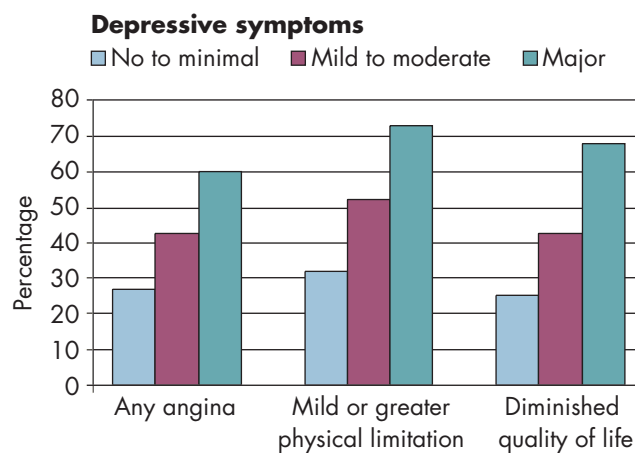
disease severity.³¹ Depressive symptoms are also an independent risk factor for lower functional improvement after CABG (Figure 2), and strongly predict short-term declines in health status in patients with established CHF.^{23;41} The negative effect of depression on functional status and mortality increases with the severity of depression (Figure 3).^{2;19;25;42;43} Depression in CHF is also associated with higher rates of secondary events, health care use, hospitalization, and ED visits.²⁵

Stroke

Depression is predictive for subsequent development of stroke in the general population, with a risk comparable to a 40-point increase in baseline systolic blood pressure.⁴⁴ Cheerfulness (extreme low level of depressive symptoms) is not protective against stroke; so it is depressed mood that increases the risk.⁴⁴ In an eight-year follow-up of Framingham Heart Study participants aged less than 65 years, the risk of developing stroke was four times greater in those with symptoms of depression.⁴⁵

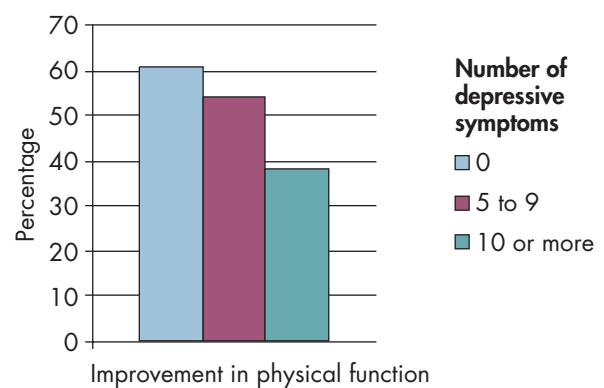
Major depression occurs in 10% to 27% of patients who experience a first or recurrent stroke, with an additional 15% to 40% experiencing some symptoms of depression within two months.^{2;8;27;46-49} Almost half of patients who experience depressive symptoms during this time will remain depressed at 18 months.⁴⁹ The severity of post-stroke depression may be related to the location of the brain injury.⁵⁰

Figure 1. Health status of heart disease patients stratified by depressive symptoms



Ruo B, et al. *JAMA*. 2003;290:215-21.

Figure 2. Changes in physical function 6 months after CABG surgery stratified by depressive symptoms



Mallik S, et al. *Circulation*. 2005;111:271-7.

Post-stroke depressive symptoms are associated with functional and cognitive impairment.^{49,51} Stroke patients with higher levels of depressive symptoms and/or a previous depressive episode use rehabilitation services less efficiently than those with fewer symptoms.⁵² Mood symptoms reported within one month of stroke are associated with increased 12- and 24-month mortality and depressive symptoms have been shown to increase risk of stroke mortality over a 29-year period (Figure 4).^{53,54}

Diabetes

Depression early in life appears to increase the risk of developing diabetes up to two-fold, even after adjusting for lifestyle factors and metabolic covariates, while the prevalence of depression ranges from 11% to 15% in patients with diabetes, approximately twice that of matched subjects without diabetes.^{2,9,13,55-59} A recent meta-analysis found an even higher prevalence in females with diabetes (23.8% vs 12.8% in males).⁶⁰ Although diabetes is strongly associated with depression, it is unclear whether diabetes itself increases the risk of developing depression.⁶¹

When depression accompanies diabetes, there is evidence of poorer glycemic control and more diabetic complications (eg, retinopathy, nephropathy, neuropathy, macrovascular changes, sexual dysfunction).^{2,55,62} Patients with major depression and diabetes are up to two times

more likely to have three or more CHD risk factors than patients without depression, and a higher incidence of CHD and adverse cardiac events.^{9,63,64} This is important because CHD mortality is increased two- to three-fold in patients with diabetes compared with the general population, and 70% to 80% of patients with diabetes die from CHD.^{2,63} Both minor and major depression are strongly associated with mortality (minor: OR 1.67; major: OR 2.30).⁶⁵

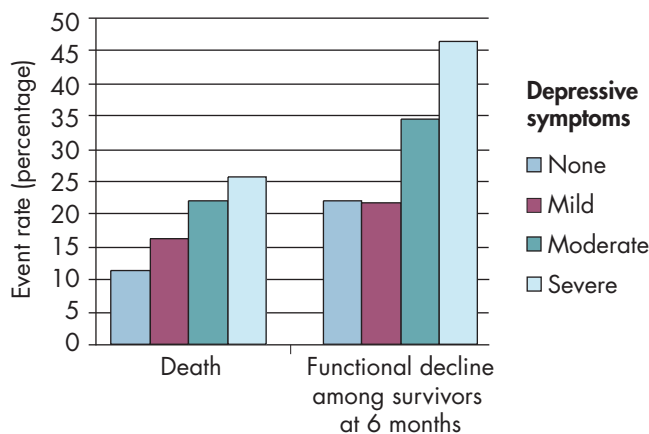
Diabetes patients with depression incur total health care expenditures three- to four-fold higher than for those not depressed.^{2,66} Depressive symptoms associated with diabetes significantly decrease health status and QOL, and increase the risk of functional disability, work loss, and cognitive dysfunction.^{2,61,67-69}

Cancer

Cancer develops more frequently in patients with chronic major depression, and adults with a history of cancer can also have a higher risk of depression.^{13,70,71} The prevalence of depression in cancer populations ranges from 1% to 42%, and increases with disease severity and symptoms such as pain and fatigue.^{2,70,72}

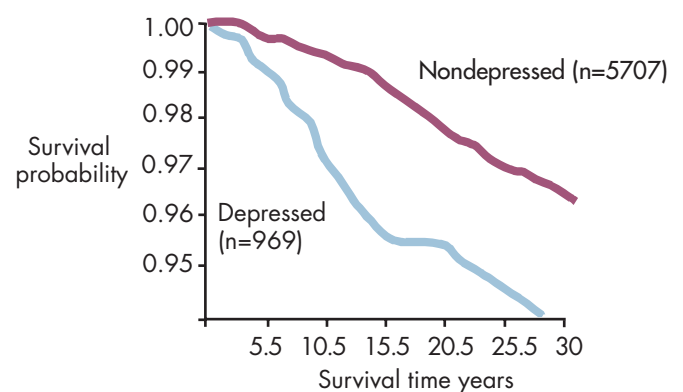
The prognosis for patients with cancer is worse in the presence of major depression, which predicts cancer progression and mortality.^{13,70,73} However, disentangling the deleterious effects of disease progression on mood is complicated by the fact that some symptoms of cancer mimic depression, and many medical treatments for

Figure 3. Risk of functional decline and death in patients with heart failure stratified by depressive symptoms



Vaccarino V, et al. *J Am Coll Cardiol.* 2001;38:199-205.

Figure 4. Depressive symptoms and increased risk of stroke mortality over a 29-year period



Everson SA, et al. *Arch Intern Med.* 1998;158:1133-8.

cancer are associated with development of depression, for example, interferon alpha.^{70,74}

Respiratory Disease

Up to 50% of asthma patients suffer from depressive symptoms.⁷⁵⁻⁷⁷ The prevalence of major depression is significantly higher for those who experience dyspnea, waking at night, and morning symptoms of asthma.⁷⁵ Patients with more depressive symptoms report a lower QOL than those with similar disease activity but fewer depressive symptoms.^{76,78} Asthma patients with psychologic dysfunction are more likely to have more frequent PCP visits (OR=5.9), ED visits (OR=5.3), exacerbations (OR=12.4), and hospitalizations (OR=4.8).⁷⁹

Patients with chronic obstructive pulmonary disease (COPD) are also at increased risk for developing depression, with prevalence estimates of up to 60%.^{2,80-84} Depression in COPD patients predicts increased respiratory and functional disabilities, reduced QOL, and higher mortality rates.^{2,81,85-88}

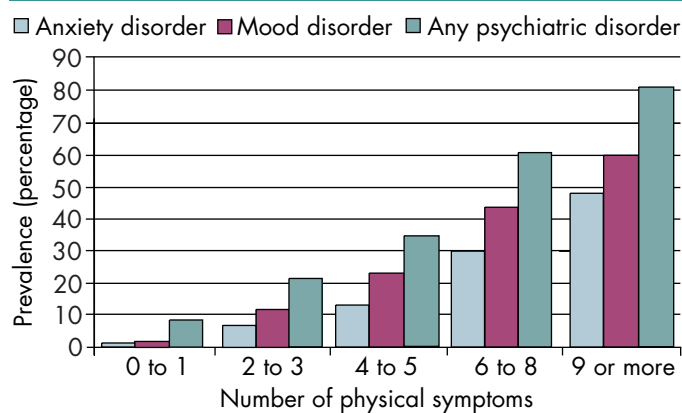
Chronic Pain

Depression and pain symptoms commonly coexist and exacerbate one another, and appear to share biologic pathways and neurotransmitters, perhaps involving serotonin, norepinephrine, or monoamine oxidase activity.^{9,89,90} The prevalence of pain symptoms in patients with depression is 43% to 65%, while the prevalence

rates vary across settings for concurrent major depression in pain cohorts; for example, 52% in pain clinics; 38% in psychiatric clinics; 56% in orthopedic clinics; and 27% in primary care clinics.^{9,90-93} A recent study found that 22% of patients in primary care suffer from persistent debilitating pain and that these patients are four times more likely to develop depression than the general population.^{9,94} The number of physical symptoms reported by primary care patients is highly predictive for depression or anxiety (Figure 5).⁹⁵

The depression-pain relationship is reciprocal, so the presence of depression in pain patients or of pain in depressed patients is associated with poorer functional status, disability, decreased QOL, and impaired social functioning than either alone.^{9,96} Depression with arthritis, for example, is a more robust predictor of disability than radiographic evidence of degenerative joint changes.⁹⁷⁻⁹⁹ Chronic pain can diminish the ability to engage in a variety of activities (eg, work, recreation, interaction with family and friends), which can cause a downward physical and emotional spiral leading to depression. Increasing pain severity, diffuse pain, pain that interferes with function, and pain refractory to treatment are associated with increased risk of depression, more depressive symptoms, and greater depression severity.⁹

Figure 5. Number of physical symptoms and risk of psychiatric disorder



Kroenke K, et al. *Arch Fam Med.* 1994;3:774-9.

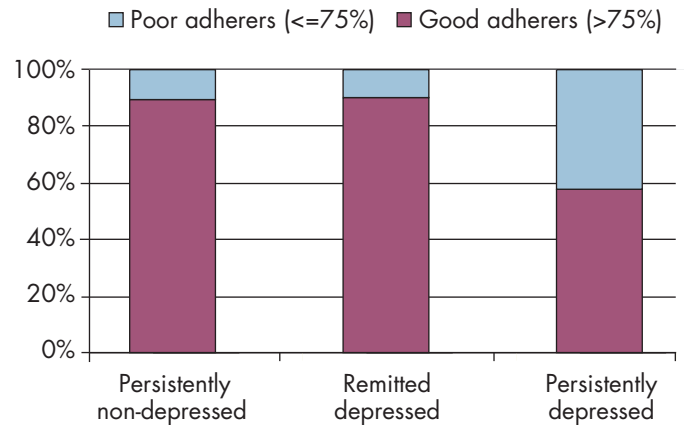
Causality Between Depression and Co-morbid Medical Illness

The causality between medical illness and depression appears to be bidirectional (Table 1).^{8-10;100;101} Multiple mechanisms link depression and chronic diseases; for example, certain drug treatments can cause depression; depression can also be a psychologic reaction to serious chronic disease.¹⁰² However, the relationship between psychosocial variables and medical illness commonly takes two forms: behavioral/lifestyle and biologic.^{102;103} The link is more likely to involve a combination of factors rather than any single pathway.³²

Behavioral/Lifestyle

There are a number of potential behavioral mechanisms by which depression may increase morbidity and mortality, functional impairment, and health care costs.^{9;13;19;104;105} Depression negatively impacts chronic medical illnesses through its maladaptive effect on adherence to medical regimens.^{9;13;77;103;105-108} Patients with depression have three times more non-adherence with other medical treatment,^{12;13} for example, 14% of depressed outpatients with CHD are not taking their medications vs 5% of those without major depression.¹⁰⁹ Adherence to even a medication with once-a-day dosing and minimal adverse effects is affected: following an acute MI 10.5% of non-depressed patients and 42.1% of persistently depressed patients were non-adherent with daily aspirin therapy (ie, 75% or fewer days) (Figure 6).¹⁰⁵

Figure 6. Adherence to aspirin therapy after ACS by depression state



Rieckmann N, et al. *Am Heart J.* 2006;152:922-7.

However, patients whose depressive symptoms remitted were as adherent as non-depressed patients.¹⁰⁵

Adherence not only includes taking medications as directed, but also adhering to self-care, health habits (eg, smoking, diet, overeating, sedentary lifestyle), and even return visits for medical care.^{13;15;110} For example, patients with depression following an acute MI are less likely to adhere to recommended behavior and lifestyle changes intended to reduce the risk of subsequent cardiac events.¹¹¹ High depression scores are associated with a nearly three-fold risk of smoking and increased likelihood of failing smoking cessation programs.^{103;112}

The vital link between depression and chronic disease is very evident in diabetes, where optimal outcomes require daily self-management, including eating a healthy diet, exercising, and regular glucose monitoring; and

Table 1. Association of depression with co-morbid medical illness

Medical disorders may:	Depression may:
▶ Contribute biologically to depression	▶ Contribute biologically to the medical disorder
▶ Cause people to become clinically depressed as a psychologic reaction to the prognosis, pain, and/or incapacity caused by the illness or its treatment	▶ Cause or exacerbate somatic symptoms (such as fatigue or pain)
▶ Result in depression from certain drug treatments for co-morbid illness (eg, interferon, corticosteroids)	▶ Affect health behavior (eg, poor diet, lack of exercise, unhealthy lifestyle, medication nonadherence)

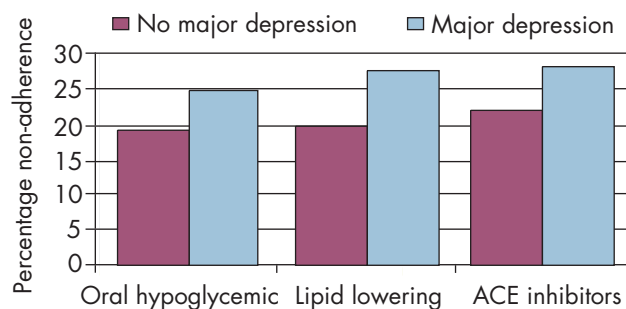
pharmacologic control of hyperglycemia, hypertension, and hyperlipidemia.⁵⁵ A study in primary care that examined the relationship between depression and diabetes self-management found that depression is associated with less physical activity, unhealthy diet, smoking, and lower adherence to medication (Figures 7 and 8).⁵⁵

Biologic Association

A growing body of evidence suggests that biologic mechanisms underlie a bidirectional link in which both the major depression and the medical illness fare worse when they are co-morbid than when they are separate.^{13;14;113} Certain illnesses (eg, stroke, Parkinson's disease, multiple sclerosis, some cancers) may cause depression via direct biologic mechanisms.¹⁰ Post-stroke depression is likely the result of specific changes in brain pathology and neurophysiology (eg, increased proinflammatory cytokine production resulting from brain ischemia in cerebral areas).¹¹⁴ Conversely, depression appears to decrease cerebrovascular reactivity, which is gaining importance as a prognostic factor for stroke risk, partly explaining the increased risk of stroke in depressed patients.¹¹⁵

Several hormonal systems may play a role in the pathophysiology of depression.¹¹⁶ They include dysregulation of the hypothalamic-pituitary-adrenal (HPA) system, hypothalamic-pituitary-gonadal and thyroid systems, as well as their interactions with immune and

Figure 8. Medication adherence in diabetes and depression

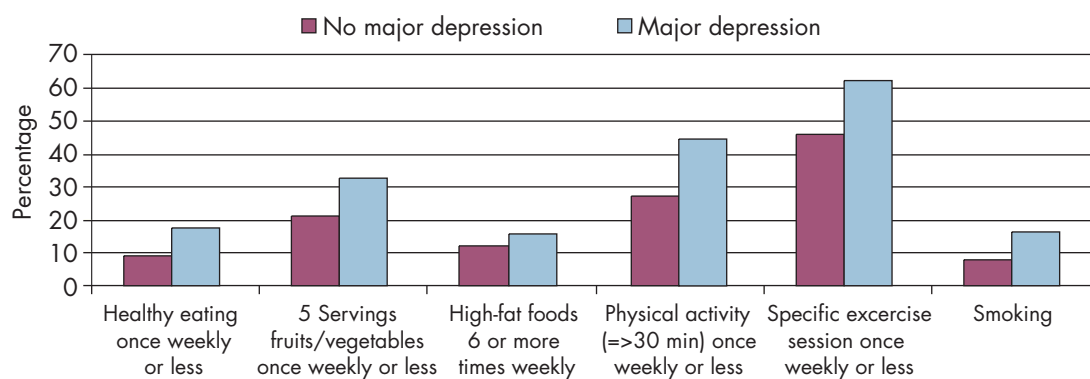


Lin EH, et al. *Diabetes Care*. 2004;27:2154-60.

other biologic and psychosocial processes.¹¹⁶ Enhanced activity of the HPA axis, involving elevated secretion of corticotrophin-releasing hormone, is a key neurobiologic alteration contributing to sleep alteration and the clinical presentation of major depression.¹¹⁷ Noradrenergic and serotonergic systems are also dysregulated in patients with depression, and depression can stimulate proinflammatory cytokines that influence a number of conditions.^{117;118}

The links between the psychologic and physiologic risk factors for cancer have been studied through psychoneuroimmunology.^{70;119} The persistent activation of the HPA axis in chronic stress response and in depression probably impairs the immune response, contributing to the development and progression of some cancer types.¹¹⁹ Compromised cellular and molecular immunologic factors in chronic stress and depression are associated with

Figure 7. Diabetes self-care and depression



Lin EH, et al. *Diabetes Care*. 2004;27:2154-60.

decreased cytotoxic T-cell and natural killer cell activities that affect processes such as immune surveillance, and are also associated with the events that modulate development of somatic mutations and genomic instability.¹¹⁹

Although it is common to attribute depression following ACS to psychologic and physiologic stress (ie, reactive), more than half of the episodes of major depression associated with ACS begin long before a cardiac event.³² How depression might contribute to ACS can be explained by the role of psychoneuroimmunologic pathways in the progression of CHD and its clinical manifestations as ACS.^{32;120} Adverse psychophysiologic effects include increased responsiveness of the sympathetic nervous system (ie, increased blood pressure and heart rate activity) and HPA axis (eg, hypercortisolemia) under conditions of mental stress.^{102;103} Other biologic explanations associated with depression, such as increased inflammatory processes (elevated C-reactive protein or cytokine levels), increased platelet dysfunction (heightened platelet aggregation or adhesiveness), and endothelial dysfunction, may also explain possible mechanisms for an increased CHD risk.^{9;32;63;102;121} However, no study has determined which — or what combination — of these mechanisms explains the association of depression with adverse cardiovascular outcomes.¹⁹

Metabolic Syndrome

The metabolic syndrome is a cluster of metabolic abnormalities, including disturbed glucose and insulin metabolism, hypertension, dyslipidemia, and centrally distributed obesity.¹²² The pathogenesis of the syndrome is complex and incompletely understood, but the interaction of obesity, a sedentary lifestyle, and dietary and genetic factors is known to contribute.¹²² The metabolic syndrome is associated with an increased risk of type 2 diabetes and CHD.¹²² The prevalence of the metabolic syndrome in non-diabetic adults is approximately 15%, but a recent study recorded a 36% prevalence in patients who had earlier been treated for depression, and a 58% prevalence among those with current major depression.¹²²

Depression may be linked to adverse health outcomes

through an association with the metabolic syndrome.^{122;123} Autonomic nervous system changes, dysregulation of the HPA axis, and altered inflammatory and hemostatic markers may explain this relationship between depression and the metabolic syndrome.¹²³

Regardless of whether depression is a cause, consequence, or marker for the metabolic syndrome, the association has important clinical ramifications.¹²³ Depressed individuals more often engage in deleterious health behaviors that may lead to the development of the metabolic syndrome and ultimately CHD, and they are less likely to comply with medical treatment, yet doing so is especially important in this group.¹²³ Therefore, even if depression is not associated with its development, it is likely that depression is associated with subsequent outcomes among those with the metabolic syndrome.¹²³

Detection of Co-morbid Depression in Primary Care

Nearly 74% of Americans who seek help for symptoms of depression will go to a PCP rather than a mental health professional.^{8,124} Because depression and medical disease commonly coexist and exacerbate one another, and in some disorders (eg, chronic pain) appear to share biologic pathways, patients with any chronic condition

should be screened for depression as part of routine care and both conditions treated for optimal outcomes.⁹ Several short, accurate, and easy-to-use instruments for detecting depression are available (Table 2).⁴ Brief instruments, including asking the patient two questions about the presence of depressed mood and anhedonia (“Over the past two weeks, have you felt down, depressed, or hopeless?” and “Over the past two weeks, have you felt little interest or pleasure in doing things?”), appear to perform as well as longer instruments.⁴

Despite the high prevalence, substantial impact, and prognostic importance of co-morbid depression, and that it is a treatable cause of pain, suffering, disability, and death, detection and treatment in the primary care setting

have been suboptimal.^{10;13;15;125-127} Usual care by PCPs fails to recognize 30% to 50% of depressed patients; for example, it is estimated that fewer than 50% of cardiac, diabetic, and asthmatic patients with major depression are diagnosed, and only about half of them are treated for depression.^{2;4;8;9;124;128;129} Older patients, who are at greater risk for co-morbid medical illness and tend to receive mental health care from a PCP, as well as minority patients, who are also more likely to obtain mental health care from a PCP, are therefore even less likely to be identified and treated effectively for depression.¹³⁰⁻¹³⁴

Reasons for Undetected Depression

Several reasons explain why depression is missed in primary care.¹⁰ It can be difficult to distinguish depressive symptoms such as sadness and loss of interest from a “realistic” response to stressful medical illness.¹⁰ Persistent low mood and lack of interest/pleasure in life cannot be accounted for by medical illness alone, but warning signs are often discounted by patients and clinicians who assume that feeling depressed is normal or inevitable for people with serious health conditions.^{8;10;135} Further complicating the picture is that many patients with clinically significant depressive symptoms have minor (subsyndromal or subthreshold) depression that does not

Table 2. Case-finding instruments to detect adult depression in primary care

Instrument	Items (n)	Time frame	Score range	Usual cut-point	Literacy	Administration time (min)
Beck Depression Inventory	21	Today	0-63	Mild, 10; moderate, 20; severe, 30	Easy	2-5
Center for Epidemiologic Study Depression Screen	20	Past week	0-60	16	Easy	2-5
General Health Questionnaire	28	Past few weeks	0-28	4	Easy	5-10
Medical Outcomes Study Depression Screen	8	Past week	0-1	0.06	Average	<2
Primary Care Evaluation of Mental Disorders	2	Past month	0-2	1	Average	<2
Symptom-Driven Diagnostic System-Primary Care	5	Past month	0-4	2	Easy	<2
Zung Self-Depression Scale	20	Recently	25-100	Mild, 50; moderate, 60; severe, 70	Easy	2-5

Pignone MP, et al. *Ann Intern Med.* 2002;136:765-76.

meet diagnostic criteria for major depression or dysthymic disorder.¹³⁶ The cumulative functional morbidity of these so-called lesser conditions exceeds that of major depression among the elderly.¹³⁶

The aspects of depression are multidimensional and include physical, emotional, and associated symptoms (Figure 9). In primary care, more than 50% of patients with depression report only somatic or physical symptoms, 60% of which are pain related, rather than the classic symptoms of sadness, hopelessness, or loss of pleasure in usual activities.^{9;137-141} This barrier particularly affects minority patients because in many cultures, for depression to become a problem for which a person seeks medical help, symptoms must include significant physical ailments.^{9;132;142} PCPs should suspect depression when multiple medical visits, multiple unexplained symptoms, fatigue, sleep disturbance, multiple worries, unexplained functional impairment, weight gain or loss, or changes in interpersonal relationships are noted.⁹

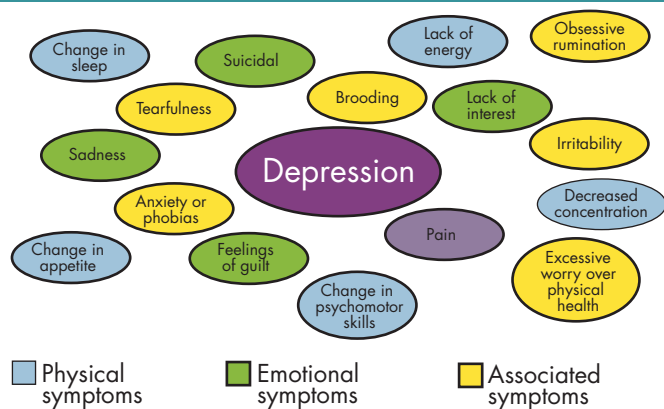
There can be confusion over whether physical symptoms of depression are due to an underlying medical condition, because many symptoms overlap.^{2;8} For example, weight loss, sleep disturbances, and low energy may occur in people with diabetes, thyroid disorders, some neurologic disorders, heart disease, cancer, and stroke; while apathy, poor concentration, and memory loss can occur with Parkinson's disease and Alzheimer's disease.⁸ In addition,

medications for Parkinson's disease, chronic hepatitis C, some cancers, and other medical problems can produce side effects similar to the symptoms of depression.⁸

Patients and PCPs may also have negative attitudes toward a diagnosis of depression; for example, depression may be seen as a moral failing, and patients may therefore be reluctant to report symptoms.^{143;144} Stigma associated with depression is more prevalent in minority and older patients; for example, African Americans tend to express more concern about stigma and spirituality.¹³² How patients perceive the communication with the PCP is particularly salient for depression because patients may not readily reveal their emotions or accept the diagnosis.¹⁴⁴ Certain behaviors, such as showing empathy, listening attentively, and asking questions about emotional issue, are associated with increased willingness by patients to share concerns.¹⁴⁴ If patients expect their PCP will not directly address emotional issues but will send them to a psychiatrist, patients may avoid emotional issues or may express them in physical terms.¹⁴⁴

Primary care patients with co-morbid medical illness often present with multiple problems and concerns, all of which cannot be addressed in a single, time-constrained visit.^{9;11;144-147} The detection and management of major depression represents an active choice from multiple physician-patient priorities including the treatment of acute physical illness, monitoring of chronic physical illnesses, and provision of preventive services.¹⁴⁸ The competing demands model suggests that physicians and patients bring an implicit agenda of issues to the primary care visit.¹⁴⁵ The attention depression receives during the visit is less associated with the severity of emotional symptoms than with the number or recency of other problems the patient presents.¹⁴⁸ Patient beliefs about depression (eg, whether the emotional problem is a legitimate medical concern, whether the PCP is a logical source of advice and care, and whether available treatments for depression are acceptable) also mediate the competition between physical and emotional problems.¹⁴⁵ Even if a patient's psychologic problems seem overwhelming to deal with during a short encounter, the PCP should still intervene,

Figure 9. Multidimensional aspects of depression



APA. Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR). Washington, DC: APA;2000:352. Ohayon MM, et al. *Arch Gen Psychiatry.* 2003;60:39-47.

which may require scheduling the patient to return for a longer visit and addressing disparate issues sequentially over a series of visits.¹⁴⁸

All patients benefit from continuity of care, coordination of care and communication among providers, and proactive patient monitoring.^{149,150} This would help to identify problems, provide problem-solving counseling, ensure engagement in treatment, and provide effective education to explain how the interaction between depression and co-morbid disease might result in adverse outcomes.¹⁵¹ PCPs are well positioned to provide integrated care for depression and co-morbid disease, but problems with the physician-patient relationship may be a barrier; for example, African American patients are more likely to rate their visits with white physicians as less participatory.¹³² Minority patients may also lack access to comprehensive primary care services. Instead they are more likely to receive health care in outpatient hospital clinics and in the ED, where they are less likely to receive the continuity of treatment provided in primary care that may allow better detection of depression.¹³²

Treatment of Co-morbid Depression in Patients With Medical Illness

Programs to improve care for depression in patients with co-morbid illness have been shown to decrease rates of depression and improve mood, QOL, and social and emotional functioning.^{2;10;81;112;152-160} Whether antidepressant treatment improves the prognosis for co-morbid conditions by improving adherence to medical treatment and self-care, facilitating appropriate use of health care resources, and affecting biologic systems, is more controversial.^{2;10;152;153} Some of the available evidence and recommendations for treating depression in four co-morbid conditions are presented here.

Heart Disease

The combination of a selective serotonin reuptake inhibitor (SSRI) with cognitive behavior therapy (CBT) is often the most effective treatment for depression in patients with CHD.¹⁶ Despite evidence that depression is a strong, dose-dependent, biologically plausible, temporal, independent risk factor for patients with CHD, no data yet conclusively support the hypothesis that antidepressant treatment can prevent cardiovascular events; the only evidence supporting such an effect comes from observational studies.^{9;19;29;161}

The Sertraline Antidepressant Heart Attack Randomized Trial (SADHART) to evaluate the safety of SSRIs for depressed patients with recent CHD found no difference in safety (change in left ventricular ejection fraction, increase in premature ventricular contractions, or prolongation of the QT interval) between the treatment and placebo groups.^{19;162} Although SADHART was not powered to evaluate cardiovascular events, investigators found a non-significant reduction in the composite endpoint (MI or CHD death) in the SSRI group.^{2;162} SSRI treatment of major depression following hospitalization for an ACS also appears to be cost-effective, with a trend toward significantly fewer psychiatric or cardiovascular hospitalizations compared with placebo.¹⁶³ After including

the costs of the SSRI, there was no increase in treatment costs associated with psychiatric and medical events compared with placebo.¹⁶³ Patients whose current episodes of major depression began before ACS, those with a history of major depression, and/or those whose episodes are severe benefited most from SSRI treatment.³²

Just as there are multiple mechanisms by which depression could increase cardiovascular disease, there are multiple mechanisms by which SSRIs could decrease risk.^{32;102} SSRIs may be directly cardioprotective by reducing platelet activation or altering abnormalities in heart rate variability or inflammatory markers.^{19;102;162;164} However, a larger randomized controlled trial (RCT) is needed to evaluate the potential benefits of SSRI medication on cardiovascular outcomes in patients with CHD.¹⁹

The Enhancing Recovery in Coronary Heart Disease (ENRICH) trial of CBT vs usual care following MI found no difference in event-free survival between the intervention and control groups, although CBT improved depressive symptoms and QOL.^{2;19} Control and intervention groups who had a high depression score or poor response to therapy had equal access to SSRIs, possibly diminishing the relative benefits of CBT.^{19;165} An observational secondary analysis of the ENRICH trial found that during the 29-month follow up, patients who received SSRIs had a statistically significant 42% reduction in a combined end-point of all-cause mortality or recurrent MI (RR: 0.57).^{38;102;165} In a commentary, Glassman observed:¹⁰²

Had the ENRICH study observed an uncontrolled 40% increase in mortality with antidepressant drug treatment, public advocates would be clamoring for review by the Food and Drug Administration, label changes, or even “black box” warnings.¹⁰² Yet this observation of a 40% decrease in life-threatening outcomes has been in the literature for almost three years with no systematic follow-up and minimal medical or psychiatric awareness. If treating MDD reduced mortality by only half of what the ENRICH study and SADHART suggest, it would save thousands of lives every year. At least as important, it would alter both the medical and public perception of depression, which has not changed despite

compelling evidence linking depression to an increase in vascular disease and death. If treating depression associated with acute coronary syndromes reduced medical deaths, it would require physicians to look for and recognize depression after MI, increasing the likelihood that they would recognize it in other settings as well. Acknowledging the implications of MDD for cardiac morbidity and mortality would validate depression as a systemic disease with implications for the entire body, and reduce the stigma of this diagnosis for medical professionals, the public, and the patients themselves.

Although the issue of whether or not treatment for depression will delay or prevent MI has not yet been demonstrated in RCTs, identifying depression in patients with heart disease is not difficult, and treatment alleviates depression.¹⁹ Consensus opinion is to evaluate CHD patients for depression and treat depressed CHD patients with a safe antidepressant drug rather than watchful waiting, since they would benefit from symptomatic relief of their depressive symptoms, have improved QOL, and could potentially improve their cardiovascular risk profile.^{9;19;166-168} For initial treatment of depression, the choice of psychotherapy, pharmacotherapy, or both depends on available resources and patient preferences.¹⁹ Tricyclic antidepressants (TCAs) are associated with cardiovascular side effects, but SSRIs are well tolerated and have a more benign cardiovascular profile, and so are the preferred initial agents for treating depression in individuals with CHD.^{9;19;38;161}

No study has examined whether treatment for depression improves outcomes in patients with CHF.^{19;169;170} However, it is still recommended that patients with CHF are screened for endogenous or prolonged reactive depression following diagnosis and at periodic intervals as clinically indicated.¹⁷¹ For pharmacologic treatment, SSRIs are preferred over TCAs because the latter could potentially cause ventricular arrhythmias, but the potential for drug interactions should be considered.¹⁷¹

Stroke

Antidepressant use among patients with post-stroke depression is associated with improvement in depressive symptoms.¹⁷² Recent studies have also demonstrated a correlation between depression and stroke recovery.³⁸ Treating post-stroke patients with antidepressants reduces morbidity and mortality, even in those with only minor depression.^{38;173-175} Patients whose post-stroke depression remitted with antidepressant treatment had significantly greater recovery in cognitive function over the course of treatment than patients whose mood disorders did not remit.⁵¹

Post-stroke patients with a depressive disorder should be given a trial of antidepressants if no contraindication exists.¹⁷⁶ Side effect profiles suggest that SSRIs or newer agents may be favored in this patient population.¹⁷⁶ Routine use of prophylactic antidepressants is not recommended in post-stroke patients.^{176;177}

Diabetes

Several trials have shown that antidepressants and CBT are effective in treating major depression in patients with diabetes.¹⁴⁹ Trials to improve depression have had mixed effects on diabetes outcomes.¹⁷⁸ In one study, enhanced depression care and outcomes were not associated with improved diabetes self-care behaviors.¹⁷⁸ Another disease management program for late-life depression in primary care, Improving Mood-Promoting Access to Collaborative Treatment (IMPACT), showed that improved depression care (education, problem-solving, or support for antidepressant management) in older adults with diabetes produced significantly greater improvements in depression severity, physical functioning, increases in exercise, and overall QOL compared with usual care, but did not affect A_{1c} levels.^{2;150} Another study found that SSRI treatment reduced the severity of depression in patients with diabetes and after only eight weeks also produced a trend toward better glycemic control.¹⁷⁹

There are large gaps in recognition and quality of depression care provided to patients with major depression and diabetes, but major depression is associated with an increased number of cardiac risk

factors in patients with diabetes and a higher incidence of CHD.^{9;180} Therefore, health care professionals should screen all patients with diabetes for depression and offer appropriate therapy.¹⁸¹

Chronic Pain

Depression and pain symptoms commonly coexist and exacerbate one another, and appear to share biologic pathways and neurotransmitters.⁹ Investigators assessing the effects of improving depression treatment in primary care settings for patients with arthritis and concurrent depression analyzed data from the IMPACT trial of collaborative care management of depression in older adults with coexisting arthritis.⁹⁹ In addition to reducing depressive symptoms, the intervention group experienced lower pain intensity and interference with activities of daily living; overall health and QOL were also enhanced relative to control patients at 12 months.⁹⁹

Given that depression and pain symptoms appear to follow the same descending pathways of the CNS, antidepressant medication is warranted, especially the dual-action atypical antidepressant reuptake inhibitors such as duloxetine or venlafaxine.⁹

What PCPs Can Do

Depressive symptoms are an independent modifiable risk factor in many chronic diseases.¹⁸² The successful management of depression is an important factor in how PCPs can affect the outcome of not only QOL for patients, but also medical illness.¹³ Health care professionals should be alert to the presence of depression in patients with chronic disease, routinely ask patients about depression, and initiate appropriate treatments based on the patient's preferences for psychotherapy or pharmacotherapy and as resources permit.^{132;183;184} Fewer than one quarter of patients treated for major depression in primary care receive treatment that meets quality standards for adequacy of dosage and duration of treatment.^{13;185} Appropriate treatment was less likely for men and those who were black, less educated, younger than 30 or older than 59 years.¹⁸⁵

Goals of Treatment

Depression is a highly recurrent and chronic disease — approximately 50% of people who experience a major depressive episode will have one or more further episodes in their lifetime.^{186;187} The goal of treatment is long-term remission of depressive symptoms. Up to one year of continuation phase treatment is recommended for virtually all depressed patients who respond to antidepressants, with a longer course of maintenance therapy recommended for those who have experienced multiple episodes.¹⁸⁸ Prolonged or lifelong pharmacotherapy has emerged as the main therapeutic tool to prevent relapse in depression.¹⁸⁶ Lifelong antidepressant treatment is particularly important within the context of a significant chronic disease because of the detrimental effect of relapse to a new depressive episode (eg, on self-care and treatment adherence in a patient with diabetes).

Many patients with co-morbid depression are not adequately treated; for example, only 2% of cancer patients in one study were receiving antidepressant medications.^{8;189;190} Even when adequate antidepressant

dosages are prescribed, treatment duration often falls short of recommendations,¹⁹¹ for example, 10% of COPD patients in one study did not have an adequate course of treatment due to dose, but 55% did not due to duration.^{81;192} Only one in five youths with co-morbid major depression and asthma received an adequate dosage and duration of antidepressant medication, and only one in six received a minimally adequate number of psychotherapy sessions (four or more).¹²⁹

One barrier to treatment of depression in patients with co-morbid chronic illness can be fear of drug-drug interactions. However, many software tools (eg, DrugIx, Eprocrates Rx Pro, Lexi-Drugs, mobileMICROMEDEX, Tarascon pocket Pharmacopoeia) are available to check for potential interactions at the point of care using personal digital assistants (PDAs) or handheld computers.^{193;194}

Patient Education

Patients with chronic diseases often cite aggravation of one condition by the symptoms of another and multiple medication regimens as barriers to self-management.¹⁸² For antidepressant therapy to be successful, it should be supplemented with patient education explaining why depression needs to be targeted alongside the physical disorder, explaining to patients about antidepressant onset of action and side effects, and assessing and addressing stigma toward mental health.^{9;132;184;195;196} More intensive efforts may be necessary early in the course of treatment to assure appropriate therapy of depressed patients with chronic disease.⁸¹ At each visit after initiation of depression management, check for adherence to pharmacotherapy or to referred psychotherapy and discuss adherence factors.^{9;132} An estimated 10% to 75% of patients are non-adherent with medications, with even higher rates among minority patients (eg, due to expectations, communication problems, or cost implications).^{9;197} It is also important that patients are carefully monitored for signs of suicidal tendencies when they begin antidepressant treatment because of concerns about the effect of SSRIs on the risk of suicide.¹⁹⁸⁻²⁰² It is important to remember that untreated depression is also

a major risk factor — in fact, the major risk factor — for suicide.²⁰³

Practice Changes

Patient visits in primary care are constrained by time, but simple methods to identify depression in patients with chronic illness can be used, for example, incorporating depression screening as a line item on chronic disease management flow sheets. Careful documentation in the medical record of the time spent on counseling and accurate use of CPT codes is necessary to obtain appropriate payment for the service. Integrating behavioral counseling into comprehensive disease management can help to enhance patient adherence and self-care, increase quality of care for the chronic disease, and make the office visit more efficient.

Disease management approaches can increase detection and improve the care of patients with depression.^{2,204} For example, in depressed primary care patients with histories of high medical utilization, a systematic depression management program increased adequate antidepressant treatment, decreased depression severity, and improved general health status with only small increases in health costs compared with usual care.^{2,205,206} A meta-analysis of depression management programs reported significant improvements in depression, physical functioning, health status, satisfaction with treatment, and adherence to treatment; as well as in the rate of detection of depression and adequacy of treatment with antidepressants.²⁰⁷ Depression-specific disease management programs typically include two key partners to implement the system changes: a care manager to assist the PCP in patient education, treatment, and treatment monitoring, and a mental health specialist to provide consultation and collaborative care with the PCP for more complex cases.^{2,136;207-211}

Given the large number of primary care patients with more than a single chronic condition and the potential advantages of coordinating care across multiple conditions, PCPs could increase efficiency and further support patient self-management by developing extended

care management interventions.¹⁴⁶ Group visits could be scheduled for interested patients with comparable chronic illnesses so that they can discuss self-managing their illnesses with others who are in similar situations.^{182,212} This also allows physicians to deliver extensive education and self-management instruction while possibly increasing financial productivity.²¹³ Group visits in adults with chronic diseases have been shown to reduce ED visits, hospitalizations, specialist visits, and primary care visits, while also improving patient and physician satisfaction.^{214,215}

Reimbursement for Depression Treatment

Incorporating behavioral counseling into comprehensive disease management and patient-directed care is not only essential to quality care, but also reimbursable. PCPs may diagnose and treat depression secondary to another diagnosis, but they should also know options for coding depression-related services when depression is the

Table 3. Psychiatric CPT codes

Code	Description
Diagnostic	
90801	Psychiatric diagnostic interview examination
90802	Psychiatric diagnostic interview examination using play equipment, physical devices, language interpreter or other mechanisms of communication
Therapeutic	
90804	20–30 minutes face to face with the patient
90805	20–30 minutes face to face with the patient with medical evaluation and management services
90806	45–50 minutes face to face with patient
90807	45–50 minutes face to face with patient with medical evaluation and management services
90862	Pharmacologic management, including prescription, use, and review of medication with no more than minimal medical psychotherapy. <ul style="list-style-type: none">▶ Medication management for a patient who is in psychotherapy with a non-physician colleague (eg, a psychologist)▶ Effective treatment of a patient's condition with psychotropic drugs alone▶ Management of a patient who has an organic type of disorder (eg, Alzheimer's) primarily with the use of medication

primary problem.^{216,217} Multiple diagnosis codes exist for depression, depending on the nature of the patient's depression, for example, the code for a single episode of acute depression is 296.2X, for a recurrent episode is 296.3X, and for depression not elsewhere classified or otherwise specified is 311. When a definitive diagnosis of depression cannot be made, the visit can also be coded using the patient's presenting symptoms, for example, 780.79, "Other malaise and fatigue."

If the service provided is primarily medical and does not include psychiatric services, submit the appropriate CPT code for office or outpatient medical evaluation and management (E/M) services (99201-99215).^{216,217} When the amount of time spent in counseling and coordination of care consumes more than one-half of the physician's face-to-face time with the patient, it is appropriate to code the service based on time. Alternatively, use prolonged services codes (99354-99355) in addition to the basic E/M service if the time spent with the patient is at least 30 minutes more than the typical time associated with the E/M code.

For psychotherapy or other psychiatric services, an appropriate CPT code from the psychiatry section (90801-90899) can be submitted (Table 3).^{216,217} These are not limited to mental health professionals, but some payers do not recognize PCPs as providers of primary mental health services and will not reimburse them for these codes. When payers do reimburse psychiatric services, careful code selection can help to ensure appropriate reimbursement for the physician's time. Psychiatry codes are either diagnostic or therapeutic; for example, 90801 describes a "psychiatric diagnostic interview examination." The therapeutic codes (beginning with 90804) describe individual psychotherapy, based on the setting in which the psychotherapy occurred, the type of psychotherapy provided, the amount of face-to-face time spent with the patient, and whether medical E/M services were provided on the same date. For example, code a 20- to 30-minute office visit for psychotherapy using 90804, or with medical E/M using 90805. CPT code 90862, typically used with a

mental disorders diagnosis code, is for "pharmacologic management, including prescription, use, and review of medication with no more than minimal medical psychotherapy."

Summary

- **Systematically screen** new and/or returning patients with any chronic disease for depressive symptoms.^{2,9}

Presentations for major depression include:⁹

- ▶ Multiple somatic complaints, weight gain/loss, mild dementia
- ▶ Multiple (more than five/year) medical visits; problems in more than one organ system, with the absence of sufficient physical findings to explain the symptoms
- ▶ Fatigue
- ▶ Work or relationship dysfunction/changes in interpersonal relationships
- ▶ Sleep disturbances
- ▶ Dampened affect
- ▶ Poor behavioral follow-through with activities of daily living or prior treatment recommendations
- ▶ Volunteered complaints of stress or mood disturbance

The USPSTF found that asking the following two simple questions is effective:⁴

1. Over the past two weeks, have you felt down, depressed, or hopeless?
2. Over the past two weeks, have you felt little interest or pleasure in doing things?

- **Positive screening results** should trigger full **diagnostic** interviews that use standard criteria from the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) to determine the presence or absence of major depression.^{2,218} Consider using a standardized instrument to document baseline symptoms and severity to assist in evaluating response and remission.⁹

- **Treat** depression at an adequate dosage of antidepressant medication for an adequate duration and/or with psychotherapy. The goal of treatment is remission.² Prolonged or lifelong therapy should be considered for patients with serious co-morbid

illnesses.¹⁸⁶ Provide and document engagement education with the patient about the nature of the disease and risks/benefits of treatment options.⁹

- **Assess** ongoing response to treatment by measuring patients' depressive symptoms at the beginning of treatment and within one, three, six, and 12 months of initiating treatment.² More frequent assessments soon after treatment begins are also needed in light of the FDA advisory regarding antidepressant medications and suicidality.^{2,198-202} Use a system to assure ongoing contacts with the patient (scheduled follow-up appointments, phone calls, and some way to react and/or reach out if the patient drops out of treatment).⁹
- **Co-manage** patients' depression with a care manager, and/or behavioral health specialist, when necessary.² A social worker, marriage or family therapist, advanced practice nurse, or clinical psychologist assigned to assist in depression care management can significantly improve outcomes.²

Conclusions

While many health plans view behavioral health as a “carve-out” and not reimbursable for PCPs, it remains their duty to identify the common, confounding psychopathologies, make appropriate referrals, and evaluate progress at subsequent visits.

Compelling evidence links depression to an increase in morbidity and mortality for a number of chronic diseases. Screening for depression as a medical risk factor in patients with chronic disease should be as much a standard of care as measuring blood pressure, blood lipid levels, or blood sugar levels. Early diagnosis with appropriate treatment can reduce patient discomfort, morbidity, and health care costs.

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Posttest

Questions

1. In general, the more physical symptoms a patient presents, the greater the risk of psychiatric disorder.
 - True
 - False
2. Co-morbid depression after a stroke increases mortality by:
 - 13%
 - 65%
 - Has no effect
3. Six months post myocardial infarction, co-morbid depression was associated with _____ increase in the risk of mortality.
 - no
 - a 2-fold
 - a 4-fold
4. The prevalence of depression in patients with diabetes is approximately _____ that of patients without diabetes.
 - equal to
 - double
 - triple
5. Depression is recognized in approximately _____ of patients with diabetes.
 - 25%
 - 50%
 - 75%
 - 90%
6. Depression is appropriately treated in approximately _____ of patients with diabetes.
 - less than 25%
 - more than 50%
 - slightly more than 75%
7. A recent study found that 22% of patients in primary care suffer from persistent debilitating pain and that these patients are four times more likely to develop depression.
 - True
 - False

After Reading

Evaluation

How well do you think the educational objectives were addressed?

Rating Scale: 4 = Fully addressed 3 = Mostly addressed 2 = Partially addressed 1 = Not addressed
Please fill in the circles completely.

	4	3	2	1
Recognize true qualitative impact of depression on chronic diseases	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Evaluate depression as an independent risk factor of other chronic diseases	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Differentiate between response and remission, and treat depression to remission	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Implement improved practice management systems to support better treatment of patients with chronic disease and depression	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Incorporate important implications of cultural competencies into screening for and treating depression	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Please rate the following education components.

Rating scale: 4 = Strongly agree 3 = Agree 2 = Disagree 1 = Strongly disagree
Please fill in the circles completely.

The enduring material...	4	3	2	1
Was understandable and easy to follow	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Presented information appropriate to the topic	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Were supported by figures and tables that were clear and understandable	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Used examples that were informative and appropriate	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Was free of bias	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

List 2-3 activities you plan to implement in your practice to address depression.

- 1.
- 2.
- 3.

CAFP may follow-up with participants on implementation of these activities.

Registration

Name: _____

Address: _____

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I certify that I have completed this activity as designated. Signature: _____

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