# Identify and Treat Depression for Reduced Cardiac Risk and Improved Outcomes

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★ ***CME Credit***

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For over 40 years, coronary artery disease (CAD) has been the leading cause of death in the United States. Death from CAD in the U.S. has declined by 23% since 2000 through modification of biologic cardiac risk factors (hypertension, elevated cholesterol, and smoking) and improvements in the treatment of CAD.[1] Measurable risk factors, unfortunately, do not completely predict cardiac risk. Depression is a common, poorly identified, and inadequately treated independent risk factor for future cardiac events.

## Depression Can Be Triggered by a Major Cardiac Event

In hospitalized patients who have experienced acute myocardial infarction (AMI), depression is 3 times more common than in the general community.[2] Fifteen to twenty percent of post-AMI patients meet criteria for major depression,[3-5] with estimates highest in younger women.[6] Estimates of the prevalence of depression are similar in patients who are hospitalized for AMI, acute coronary syndromes, angioplasty, coronary artery bypass surgery, and valve surgery.[7] Higher rates of depression have been reported in women and in patients hospitalized with congestive heart failure (CHF).[7,8] In community-based studies, the prevalence of depression in the general population is reported between 4.8%[9] and 6.6%.[10] It is 9.3% in patients living with CAD, which is comparable to the 7.9%–17% rate seen in those living with other chronic medical conditions.[9]

## Depression Is an Independent Risk Factor for Coronary Artery Disease

Eight longitudinal studies (including 15,613 patients followed for 153,031 patient-years) have robustly shown that depression, measured by various scales and by self-reporting, increases the risk of first cardiac event (relative risk, 1.5–4.8) in patients without a history of CAD.[11] Among 8,000 healthy Finnish adults without CAD, depression increased the relative risk of cardiac death by 2.05 over 6.6 years of follow-up.[12]

## Depression Increases All-Cause Death and Cardiac Complications in Patients with Coronary Artery Disease

Multiple studies have examined the mortality rates of CAD patients who have depression.[13,14] Despite methodologic differences, including sample sizes, endpoint definition, criteria for depression, and variable lengths of follow-up, most studies report a 2-fold increase in all-cause death for patients with depression in the 1 to 2 years after AMI.[2,7,8,15,16] Frasure-Smith and colleagues[17] reported a 4-fold increased risk of death at 6 months for patients with depression that had been diagnosed 5 to 15 days after AMI and had persisted at 18 months. The Enhancing Recovery in Coronary Heart Disease[18] (ENRICHD) trial compared a subgroup of 359 depressed patients after AMI to 408 nondepressed patients and reported a late (>12-mo) increased relative risk (2.8) of all-cause death in the depressed patients.[18,19] Depression after AMI that is complicated by CHF is an independent predictor of all-cause death (at 2 yr, 29% vs 18%, $P=0.004$) and of cardiovascular death or hospitalization (42% vs 33%, $P=0.016$). In a well-designed case-control study, 2,228 clinically depressed patients after AMI were at increased risk of sudden cardiac death (odds ratio [OR], 1.43;

95% confidence interval, 1.18–1.73) when compared with 4,164 control patients.[20] The sudden cardiac death risk persisted after adjustment for confounding factors (including antidepressant use) and actually rose with increasing depressive symptom severity, suggesting the presence of a "dose-response" relationship between depression severity and cardiac events (OR 1.3 for less severe depression vs an OR of 1.77 for severe depression, $P$ <0.001 for trend).

### Pathophysiologic Links between Depression and Coronary Artery Disease Risk Can Be Direct or Indirect

Depression contributes both to direct and indirect mechanisms that increase the risk of adverse events in patients with CAD. Biomarkers that have been shown to predict cardiac events and promote atherosclerosis (C-reactive protein, interleukin-6, tumor necrosis factor, fibrinogen, adrenaline, urinary catecholamines, intracellular adhesion molecule-1, and platelet factor 4) are elevated in depressed patients with CAD and provide a direct biological link to inflammatory cardiac events. Indirectly, depression augments the risk of CAD development and progression by increasing or continuing unhealthful lifestyle choices: continued smoking, inactivity, poor diet, and social isolation.[19,21-24] Depression is associated with poor adherence to prescribed medications[25] and with a 3-fold rise in noncompliance with medical treatment regimens.[26]

### Screening for Depression Is Recommended in All Cardiac Patients

A nationwide survey of cardiologists revealed that 49% were unaware that depression was an independent risk factor for CAD and that 71% failed to inquire about depression in over half of their patients.[27] Because cardiologists are often the point-of-care physician after acute cardiac events, they doubtless have a responsibility to screen for depression. A simple 2-question assessment, the Patient Health Questionnaire-2 (PHQ-2) (Fig. 1), has been validated to identify currently depressed patients. The PHQ-2 has been endorsed as a screening tool in cardiac patients by the American Heart Association, the American Psychiatric Association, and others.[11,28] A response score of 3 or more to the PHQ-2 indicates the need for a follow-up, 5-minute, 9-question screening test (Fig. 2) that provides a provisional depression diagnosis and a severity score with reasonable sensitivity and specificity. A score greater than 10 suggests a high probability of depression, and scores greater than 20 are associated with severe functional impairment. Patients with scores over 10 should be referred for more comprehensive evaluation and treatment.

### Treatment of Depression Includes Pharmacologic Treatment and Behavioral Therapy

Although behavioral therapy might be effective in the long run, it has not been shown to be beneficial for treating depression in acute cardiac patients because

## Patient Health Questionnaire-2 (PHQ-2)

*Over the past 2 weeks, have you often been bothered by any of the following:*

1. Little interest or pleasure in doing things.
    a. Not at all
    b. Several days
    c. More than half the days
    d. Nearly every day

2. Feeling down, depressed, or hopeless?
    a. Not at all
    b. Several days
    c. More than half the days
    d. Nearly every day

Score responses as follows: a=0; b=1; c=2; d=3.
If the total score is 3 or more, follow up using the PHQ-9, a 9-item, self-administered questionnaire (Fig. 2).

***Fig. 1*** *The Patient Health Questionnaire-2 (PHQ-2) is a simple 2-question assessment that has been validated to identify currently depressed patients.*

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**PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)**

| Over the last 2 weeks, how often have you been bothered by any of the following problems? (Use "✓" to indicate your answer) | Not at all | Several days | More than half the days | Nearly every day |
|---|---|---|---|---|
| 1. Little interest or pleasure in doing things | 0 | 1 | 2 | 3 |
| 2. Feeling down, depressed, or hopeless | 0 | 1 | 2 | 3 |
| 3. Trouble falling or staying asleep, or sleeping too much | 0 | 1 | 2 | 3 |
| 4. Feeling tired or having little energy | 0 | 1 | 2 | 3 |
| 5. Poor appetite or overeating | 0 | 1 | 2 | 3 |
| 6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down | 0 | 1 | 2 | 3 |
| 7. Trouble concentrating on things, such as reading the newspaper or watching television | 0 | 1 | 2 | 3 |
| 8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual | 0 | 1 | 2 | 3 |
| 9. Thoughts that you would be better off dead or of hurting yourself in some way | 0 | 1 | 2 | 3 |

FOR OFFICE CODING: 0 + _____ + _____ + _____
=Total Score: _____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

| Not difficult at all | Somewhat difficult | Very difficult | Extremely difficult |
|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ |

***Fig. 2*** *The Patient Health Questionnaire-9 (PHQ-9) is a 5-minute, 9-question screening test that is administered in response to a PHQ-2 response score of 3 or higher. The PHQ-9 provides a provisional diagnosis of depression and a severity score that imparts reasonable sensitivity and specificity. A score greater than 10 suggests a high probability of depression, and scores greater than 20 are associated with severe functional impairment. Patients with scores over 10 should be referred for a more comprehensive evaluation and treatment plan.*

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of the need for immediate results. Selective serotonin reuptake inhibitors (SSRIs) are the preferred treatment for depression in patients with CAD, whereas tricyclic antidepressants and monoamine oxidase inhibitors are contraindicated due to their adverse cardiotoxic effects. Two SSRIs, sertraline and citalopram, have been shown in randomized clinical trials to be safe and efficacious in CAD patients with moderate or severe depression.[29,30] Treatment (nonrandomized) of depression with an SSRI in patients with AMI enrolled in the Enhancing Recovery in Coronary Heart Disease Patients study yielded a 42% reduction in death or recurrent myocardial infarction when compared with depressed patients not treated with an antidepressant.[31] Although there are as yet no randomized antidepressant trials proving that treatment of depression improves cardiac outcome in patients with CAD, treatment has been shown to be safe and might improve depressive symptoms, adherence to treatment, and medication compliance.

## Summary

*Why do we stay in prison when the door is wide open?*
– Jalal ad-Din Rumi

Depression is an independent risk factor for the development of CAD. Patients with CAD have a high rate of depression, which worsens their prognosis. Screening CAD patients with the 2-question PHQ-2 to identify those at greatest risk of depression is strongly recommended, as is referring patients for further evaluation and possible treatment when depression has been identified by the PHQ-9. Treating depression is likely to improve cardiovascular outcomes.

The PHQs are in the public domain and free to use. To download and for more information, visit www.phqscreeners.com.

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