

# Assessment and Treatment of Depression in Patients With Cardiovascular Disease: National Heart, Lung, and Blood Institute Working Group Report

KARINA W. DAVIDSON, PhD, DAVID J. KUPFER, MD, J. THOMAS BIGGER, MD, ROBERT M. CALIFF, MD, ROBERT M. CARNEY, PhD, JAMES C. COYNE, PhD, SUSAN M. CZAJKOWSKI, PhD, ELLEN FRANK, PhD, NANCY FRASURE-SMITH, PhD, KENNETH E. FREEDLAND, PhD, ERIKA S. FROELICHER, RN, PhD, ALEXANDER H. GLASSMAN, MD, WAYNE J. KATON, MD, PETER G. KAUFMANN, PhD, RONALD C. KESSLER, PhD, HELENA C. KRAEMER, PhD, K. RANGA R. KRISHNAN, MD, FRANÇOIS LESPÉRANCE, MD, NINA RIECKMANN, PhD, DAVID S. SHEPS, MD, MSPH, AND JERRY M. SULS, PhD

**Objective:** The National Heart, Lung, and Blood Institute convened an interdisciplinary working group of experts to develop recommendations for the assessment and treatment of depression in patients with coronary heart disease (CHD). **Method:** Consensus of experts. **Results:** Our current recommendations are that the Beck Depression Inventory-I be employed for epidemiological studies of depression and CHD, that the Patient Health Questionnaire 2-item version be employed for screening for trial eligibility, that the Depression Interview and Structured Hamilton (DISH) be employed for diagnostic ascertainment for trial inclusion, and that the Hamilton rating scale, which is part of the DISH, be employed for both depression symptom reduction and the remission criterion in any trial. We further recommend that a randomized controlled trial be undertaken to determine whether selective serotonin reuptake inhibitors, psychotherapy, or combined treatment can reduce the risk of CHD events and mortality associated with depression in CHD patients. **Conclusions:** This report summarizes the recommendations made by the working group and discusses the rationale for each recommendation, the strengths and weaknesses of alternative approaches to assessment and treatment, and the implications for future research in this area. **Key words:** depression, cardiovascular diseases, assessment, treatment, consensus, recommendations.

**ACS** = acute coronary syndrome; **BDI** = Beck Depression Inventory; **CBASP** = Cognitive Behavioral Analysis System of Psychotherapy; **CBT** = cognitive behavior therapy; **CIDI** = Composite International Diagnostic Interview; **CHD** = coronary heart disease; **CVD** = cardiovascular disease; **DISH** = Depression Interview and Structured Hamilton; **ENRICH** = Enhancing Recovery in Coronary Heart Disease; **HAM-D** = Hamilton Rating Scale for Depression; **IDS-SR** = Inventory of Depressive Symptomatology, self-report; **IMPACT** = Improving Mood—Promoting Access to

Collaborative Treatment; **IPT** = interpersonal therapy; **MI** = myocardial infarction; **NHLBI** = National Heart, Lung, and Blood Institute; **PHQ** = Patient Health Questionnaire; **RCT** = randomized controlled trial; **SADHART** = Sertraline Antidepressant Heart Attack Randomized Trial; **SCID** = Structured Clinical Interview for DSM-IV; **SSRI** = selective serotonin reuptake inhibitor; **STAR\*D** = Sequenced Treatment Alternatives to Relieve Depression.

## INTRODUCTION

On August 10 and 11, 2004, the National Heart, Lung, and Blood Institute (NHLBI) convened an interdisciplinary working group of experts in cardiology, psychology, psychiatry, nursing, epidemiology, clinical trial methodology, and biostatistics to develop recommendations concerning the assessment and treatment of depression in patients with coronary heart disease (CHD). The objective of the working group was a) to review the diagnosis and measurement of depression and evaluate the applicability of depression instruments in CHD patients for research purposes; b) to review the efficacy and safety of interventions for treating depression in CHD patients; and c) to recommend research needed to reduce morbidity and mortality associated with depression in this population.

This report summarizes the recommendations made by the working group and discusses the rationale for each recommendation, the strengths and weaknesses of alternative approaches to assessment and treatment, and the implications for future research in this area. Comments from the scientific community on an earlier version of this report, which was posted on the NHLBI Web site, have been incorporated into this document.

## Background

Depression is associated with an increased risk of cardiac events in cardiovascular disease (CVD) patients and is known to increase the cost of patient care and decrease the quality of life.

From the Department of Medicine, Columbia University College of Physicians and Surgeons, New York, NY (K.W.W.<sup>1</sup>, J.T.B.,<sup>1</sup> A.H.G.<sup>2</sup>); Cardiovascular Institute (K.W.W.<sup>1</sup>) and Department of Psychiatry (K.W.W.,<sup>1</sup> N.R.<sup>1</sup>), Mount Sinai School of Medicine, New York, NY; Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA (D.J.K.,<sup>2</sup> E.F.<sup>2</sup>); Behavioral Medicine and Prevention Research Group, National Heart, Lung, and Blood Institute, Bethesda, MD (S.M.C.,<sup>2</sup> P.G.K.<sup>1</sup>); Duke Clinical Research Institute, Duke University Medical Center, Durham, NC (R.M.C.<sup>2</sup>); Department of Psychiatry, Behavioral Medicine Center, Washington University School of Medicine, St. Louis, MO (R.M.C.,<sup>2</sup> K.E.F.<sup>1</sup>); Department of Psychiatry, University of Pennsylvania School of Medicine, Philadelphia, PA (J.C.C.<sup>1</sup>); Department of Psychiatry and School of Nursing, McGill University, Montreal; the Montreal Heart Institute Research Center, Montreal; Centre Hospitalier de l'Université de Montreal Research Center, Montreal; Department of Psychiatry, University of Montreal, Montreal, Quebec, Canada (N.F.-S.<sup>1</sup>); School of Nursing, University of California San Francisco, San Francisco, CA (E.S.F.<sup>2</sup>); Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle, WA (W.J.K.<sup>2</sup>); Department of Health Care Policy, Harvard Medical School, Boston, MA (R.C.K.<sup>1</sup>); Department of Psychiatry and Behavioral Science, Stanford University, Stanford, CA (H.C.K.<sup>1</sup>); Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine, Durham, NC (K.R.R.K.<sup>1</sup>); Department of Psychiatry, University of Montreal, Montréal, Quebec, Canada (F.L.<sup>2</sup>); Division of Cardiovascular Medicine, University of Florida, and Malcom Randall VA Medical Center, Gainesville, FL (D.S.S.<sup>2</sup>); Department of Psychology, University of Iowa, Iowa City, IA (J.M.S.<sup>1</sup>).

<sup>1</sup>Depression Assessment Panel.

<sup>2</sup>Depression Treatment Panel.

Address correspondence and reprint requests to Karina W. Davidson, PhD, Department of Medicine, Columbia University College of Physicians and Surgeons, 622 W 168th St, PH9 Center, Room 941, New York, NY 10032. E-mail: kd2124@columbia.edu

Received for publication January 12, 2006; revision received April 3, 2006.

DOI: 10.1097/01.psy.0000233233.48738.22

Even at low levels of severity, depressive symptoms are associated with increased risk for the incidence and recurrence of acute coronary syndromes (ACSs), as well as all-cause mortality in patients with known heart disease. Moreover, prospective epidemiologic studies have shown that depression is associated with an increase in risk independent of other known medical prognostic markers in this population.

The use of diverse measures of depression in observational studies makes quantitative systematic reviews difficult. However, the fact that the preponderance of evidence supports a strong relationship between depression and morbidity and mortality due to CHD in studies using more than 25 different depression assessment instruments demonstrates the robustness of this relationship to variation in instrumentation.

Greater standardization of nomenclature and of diagnosis and assessment of depression would contribute significantly to scientific progress because it would allow formal comparison across studies and rigorous cumulation of findings. The term *depression* is not used consistently across studies. The design of observational and treatment studies in this field would be facilitated by consistent standards for assessment and diagnosis. Moreover, the efficacy of different treatment studies could be compared more easily if the measures of depression were identical or similar or if their relationship to one another were better understood.

Because at any given time, up to 20% of patients with heart disease meet the DSM-IV (*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*) criteria for major depression (1), identifying better treatments for depression in this population could lead to improved medical, financial, and psychosocial outcomes for a substantial segment of the US population. Although cognitive behavior therapy (CBT), interpersonal therapy (IPT), and other behavioral therapies, either alone or in combination with selective serotonin reuptake inhibitors (SSRIs), have been shown to be effective in treating depression, their efficacy in altering the course of CVD has not been demonstrated. In the ENRICH (Enhancing Recovery in Coronary Heart Disease) (2) and SADHART (Sertraline Antidepressant Heart Attack Randomized Trial) (3) studies, post hoc subgroup analyses showed a possible cardiovascular benefit for patients treated with SSRIs. In SADHART, treatment with sertraline reduced platelet activation beyond that achieved by other antiplatelet regimens, including clopidogrel (4,5). In ENRICH, secondary analyses showed that those patients in the treatment arm whose depression improved or who were treated with sertraline had reduced mortality (6,7). Thus, whether treatment of depression with either SSRIs or CBT can reduce morbidity or mortality in CHD patients remains unclear and can only be determined in future randomized controlled trials (RCTs).

Since the ENRICH and SADHART studies were launched in the 1990s, new approaches to treating depression have been developed for patients with a variety of medical conditions, including those with diabetes mellitus, those presenting at primary care clinics, and those with chronic pain. Evaluation of the treatments developed in these clinical trials

and subsequent research on depression treatments in medically ill patients suggest that a careful review is needed to determine whether treatment options exist that are more suited for patients with medical comorbidities. Given the chronic, recurring nature of depression symptoms and the frequent co-occurrence of depression with CVD, it is especially important to identify safe and effective treatments for patients with depression and CVD.

## RECOMMENDATIONS FOR ASSESSMENT

Our recommendations are intended to promote development of more uniform assessment of depression in CVD patients. Toward that end, we made separate recommendations for different research purposes (see Table 1). These recommendations will be modified as needed on an ongoing basis based on comments from the research community, and updated recommendations will be presented when appropriate.

These recommendations are intended to apply only to research, including clinical trials, epidemiologic studies, and studies of mechanisms. Recommendations for clinical application are beyond the scope of our mandate and will be more appropriate when sufficient research results have accrued. However, we recognize that the initial screening of patients for depression can be done by primary care providers or clinical research coordinators with minimal training or by patients themselves using a self-administered assessment. If there were agreement on a screening tool, it would be simpler and less expensive to recruit CVD patients for depression treatment trials, and it would be simpler to put trial results into practice.

We strongly recommend that when diagnostic instruments are administered, well-trained individuals be employed, with attention to implementing quality-control procedures, such as audiotaping interviews for review. Each of the measures discussed below is described in an Appendix that can be found on the National Institutes of Health Web site (8). Finally, efforts to develop more accurate measures of post-myocardial infarction (MI) depression are encouraged, as there is an overlap in depression and cardiac disease symptoms.

### Epidemiologic Studies of CHD Patients

We recommend 2 self-report measures. The widespread use and well-understood properties of the first edition of the Beck Depression Inventory (BDI) (9) make it the leading self-report instrument used in epidemiologic studies. In the near future, new psychometric data on the second edition of BDI (10) will become available for CHD samples, and it will become clearer whether and in what situations the second edition should replace the first edition. We also recommend the use of the Inventory of Depressive Symptomatology, self-report version (IDS-SR) (11).

For epidemiologic research that requires diagnostic measures of depression and for which the time and resources to diagnose depression are available, we recommend the Depression Interview and Structured Hamilton (DISH) (12) or the Composite International Diagnostic Interview (CIDI) (13).

# ASSESSMENT AND TREATMENT OF DEPRESSION

TABLE 1. Summary of Recommendations for Assessing Depression by Study Type<sup>a</sup>

	Epidemiologic Studies	Screening for Trial Inclusion	Diagnostic Ascertainment for Trial Inclusion	Depression Severity Rating During a Trial
Screening				
Depressed mood and anhedonia from Patient Health Questionnaire (PHQ-2)		X		
Self-report				
Beck Depression Inventory, first edition (BDI)	X	X		X
Beck Depression Inventory, second edition (BDI-II)	<sup>b</sup>			<sup>b</sup>
Inventory of Depressive Symptoms (IDS-SR)	X			X
Other rating				
Inventory of Depressive Symptoms, Clinician Rated (IDS-CR)				<sup>b</sup>
Hamilton Rating Scale for Depression, 17 item (HAM-D-17)				X
Montgomery-Asberg Depression Rating Scale				<sup>b</sup>
Clinical interview				
Depression Interview and Structured Hamilton (DISH)	X		X	
Center for International Diagnostic Interview (CIDI)	X		X	

<sup>a</sup>Bold Xs are the primary recommendations. We have no current recommendations for assessing depression history or defining depression remission.

<sup>b</sup>Future research is recommended to determine usefulness of these measures.

The CIDI is favored primarily because it was designed for use in epidemiologic studies (i.e., it is highly structured and efficient and was designed for use by lay interviewers who have undergone required training) and because it has been used in some of the largest and most important studies in the recent history of psychiatric epidemiology (14,15). Although the high prevalence of depression reported in the National Comorbidity Survey (NCS) (16) raised concerns about the CIDI, we are not aware of an existing instrument that is superior. It is noteworthy that blinded clinical reappraisal interviews with a gold standard semistructured research diagnostic interview in the most recent NCS had good concordance with the CIDI and yielded a prevalence estimate comparable to that of the CIDI.

### Screening Candidates for Eligibility in Randomized Controlled Trials

The 2-item screening tool from the Patient Health Questionnaire (PHQ-2) is recommended to identify currently depressed patients within a CVD population. Should one or both of the items of the PHQ-2 be positive for depression, all 9 PHQ items (PHQ-9) should be administered. Although the BDI can also be used as a screening instrument, it is not a diagnostic instrument; a total score of 10 or higher is the most widely used cutoff when using the BDI-I for screening purposes. The BDI was found to be an accurate screening tool for DSM-IV major depressive disorder in patients after MI (17). The PHQ-9 and BDI can also be used to record depression severity in CVD trials that do not involve depression as a primary end point.

### Diagnostic Ascertainment of Depression for RCTs

After considerable discussion, we concluded that DISH and CIDI have substantial advantages for diagnosing depressed patients for inclusion in RCTs. Although the Structured Clinical Interview for DSM-IV (SCID) was considered for this purpose, some limitations were noted, including heavy burdens on the interviewer and participant, unknown reliability for medically ill patients, and the need for lengthy and continuous training. A significant advantage of DISH is that, in addition to assisting with the diagnosis of major and minor depression and dysthymia, it yields a score on Williams' structured version of the 17-item Hamilton Rating Scale for Depression (HAM-D-17). A significant advantage of the CIDI, in comparison, is that it yields a score on Rush's structured version of the 16-item Inventory of Depressive Symptoms (Q-IDS-SR) (18). We note that DISH and CIDI interviews are not reliable or useful without appropriately training interviewers and audio recording of interviews for quality control.

### Rating Depression Severity During RCTs

We recommend using observer ratings of depression, as well as self-reports. Currently, the first edition of BDI is recommended as the self-report instrument of choice. However, as already noted for clinical epidemiologic studies, new data on the psychometric properties of the second edition of BDI in CHD samples may support its future use in RCTs. Despite the widely recognized limitations of HAM-D-17, we recommend using this scale to rate depression severity in clinical trials based on its acceptability to the US Food and Drug Administration and its use in previous

trials. When possible, HAM-D-17 may be supplemented with one of the more psychometrically sophisticated measures, such as the IDS-CR. Further research is needed to determine whether the IDS-CR and the Montgomery-Asberg Depression Rating Scale are appropriate for stand-alone use in the CVD population. In addition to training and quality control, we emphasize that masking or blinding assessment staff to treatment condition is critical to ensure the internal validity of the trial assessments. Centralized telephone rating should be considered in multicenter trials.

#### **Ascertainment of Depression Treatment Success in RCTs**

We did not make recommendations concerning the amount of symptom reduction in the proposed measures that would constitute a successful response to depression treatment. We recommend that remission of depression (e.g., a HAM-D-17 score <7) be specified as one of the outcome measures for any clinical trial, whether the study is of treatment efficacy for depression or of medical outcomes, and that the percentage of participants with remitting symptoms be compared between randomized arms. A criterion for success based on differences in depression scores between randomized arms of a trial also should be specified. We request comments from the broader clinical research community on the criterion to be used to evaluate the success of depression treatments in usual care versus placebo control groups, including estimates of responses to depression treatment that are considered clinically meaningful for medically ill populations.

#### **Summary**

Our current recommendations are that the BDI-I be employed for epidemiological studies, the PHQ-2 be employed for screening for trial eligibility, the DISH interview be employed for diagnostic ascertainment for trial inclusion, and the Hamilton rating scale, which is part of the DISH, be employed for both depression symptom reduction and the remission criterion. These recommendations may change as data accrue on the usefulness of these and other depression measures, but research requires assessment that is not burdensome to the participant and that is useful for cross-study comparison; these measures best provide such utility at this time.

#### **Research Needs**

Considerable discussion focused on research needed to inform future recommendations. A large validation study in which a number of assessment measures are employed simultaneously was thought to be ideal. Such a study should include a sufficient number of men, women, and minority groups, with oversampling as needed, to ascertain differences between subgroups, as well as concurrent validity and psychometric properties. The limitations of many of the measures, including the ability to differentiate between somatic and cognitive symptoms, the association with other negative affective states and psychiatric comorbidity, and the validity of self-report instruments in elderly frail medically ill patients, require further evaluation. The time frame used for each measure (e.g., de-

pressive symptoms experienced in the last week, in the last month, or before the acute coronary event) should also be considered. Critical design issues, such as whether each respondent would be administered only one of the measures or would receive multiple measures in a randomly rotated order of administration, were not discussed but would need to be resolved before launching such a methodological study.

#### **RECOMMENDATIONS FOR TREATMENT**

The observational evidence base for an association between depression and cardiovascular morbidity and mortality has become larger and more consistent during the past decade. In addition, because CVD and depression are the 2 most prevalent causes of death and disability worldwide (19), it is important to increase research efforts to develop effective interventions when these disorders occur together.

A major focus of our discussion was the question of safe and effective treatment for depression in CHD patients. We evaluated the efficacy of pharmacologic and psychotherapeutic interventions for depression generally and their application specifically to treatment of depressive symptoms in CHD patients.

#### **Treatment Options for Depression in CHD Patients**

A considerable amount of literature shows that several efficacious treatment options exist for treating clinical depression in the general population. During the past 25 years, the therapy targeted to a DSM-IV diagnosis of major depression, as well as chronic depression (dysthymia), has received considerable attention. The first generation of antidepressants (the tricyclics and monoamine oxidase inhibitors) was shown to benefit the majority of patients with clinical depression, but there were also adverse effects. In addition, their safety profile for CHD patients was poor. These issues were alleviated by the introduction of the next generation of antidepressants, particularly the SSRIs, whose safety in CHD patients is superior. The safety of serotonin-norepinephrine reuptake inhibitors for CHD patients remains unknown. The majority of patients with clinical depression in medical or primary care settings are currently treated with SSRIs or serotonin-norepinephrine reuptake inhibitors.

Pharmacotherapy is not considered the only acceptable treatment for mild to moderately severe clinical depression. Psychotherapeutic interventions such as IPT and CBT also have been found to be effective. For chronic depression, a variant on CBT known as the Cognitive Behavioral Analysis System of Psychotherapy (CBASP) has been evaluated recently in several clinical trials (e.g., 20). Although monotherapy or targeted psychotherapy has been the major component of first-line treatment, many patients do not achieve complete remission of symptoms, and combined treatments are common. These combined treatments have been called either augmentation or sequencing strategies and have included the combination of two or more medications or the combination of a pharmacologic intervention and targeted psychotherapy. Augmentation strategies have also included other classes of psychotropic drugs, including lithium and, more re-

## ASSESSMENT AND TREATMENT OF DEPRESSION

cently, low doses of the class of medications known as atypical antipsychotics.

A large, multistep clinical trial of outpatients with nonpsychotic major depressive disorder, Sequenced Treatment Alternatives to Relieve Depression (STAR\*D) (21), is testing an algorithm involving several first-line antidepressants combined with cognitive therapy. Collaborative case management was a key component of the treatment algorithm for the Improving Mood—Promoting Access to Collaborative Treatment (IMPACT) clinical trial for late-life depression in primary care (22). Other treatment strategies are commonly used for treating subsyndromal depression, and the efficacy of new treatments for severe or treatment-resistant depression is currently being explored. For RCTs, the treatment algorithm should be specified carefully so that a full range of options can be implemented systematically to ensure that depression in patients with CHD is safely and effectively treated.

Although these approaches to treatment emerged primarily from treatment trials for acute depression, recurrence is common in clinical depression, and prevention of recurrence is important. For treatment strategies for both acute and chronic depression, functional outcome measures, including quality of life, should be added to the usual depressive symptom outcome measures. We began with the premises that currently available algorithms for treating depression in non-CHD patients should be evaluated for treating depression in CHD patients and that assessments of medical outcomes can be added to examine the impact of the depression treatment on reduction of cardiac risk factors and cardiac events.

Post hoc exploratory subgroup analyses from the SADHART and ENRICHD trial suggest that patients with more severe depression and those with a history of depression may have better depression outcomes after treatment (3); moreover, SSRI can provide a beneficial effect on platelets (4,5). Finally, subgroup analysis showed that patients in the treatment arm of ENRICHD whose depression was treated successfully had decreased mortality (6). The results of all subgroup analyses must be viewed as hypothesis-generating and require testing in a future randomized clinical trial. We discussed the following issues raised by the ENRICHD and SADHART studies relevant to treating CHD patients:

- **Timing of the intervention:** A strategy of initiating treatment of depression in the immediate post-MI period and limiting treatment to this period (e.g., first 6 months after MI) may have limited potential because patients are medically unstable and their depression status is highly labile (depression is often more severe immediately after the event and may be a transient reaction to the MI itself). This can result in enrollment of individuals whose depression may remit spontaneously in the weeks and months after the event. These may not be the best patients in whom to test the hypothesis that reducing depression will reduce the risk of mortality and morbidity in patients with ACS. However, to the extent that pharmacotherapy may provide cardiovascular ben-

efit directly, rather than through reduction of depressive symptoms, initiating treatment early may be preferable. Further data are needed to clarify this issue.

- **Duration of the intervention:** In the ENRICHD trial, treatment was delivered for 6 months, included specific strategies for relapse prevention, and was extended only for pharmacotherapy. The discontinuation of psychotherapy at 6 months may have contributed to diminishing differences in depression status between the treatment and usual care groups over time. Longer treatment may be particularly important if the effect of depression on event-free cardiovascular survival is being investigated. It is likely that treatment should be delivered for a longer period than in the SADHART and ENRICHD studies, especially to prevent and address recurrences. Several cardiovascular therapies do not result in survival differences between treatment and control groups for 6 to 12 months. Examples include trials of angiotensin-converting enzyme inhibitors in high-risk patients without heart failure (23) and trials of implantable cardioverter defibrillator therapy in MI patients with reduced left ventricular ejection fractions (24).
- **Responsiveness of the patient population to treatment:** In clinical trials of patients presenting with ACS rather than depression, and with enrollment based on in-hospital screening for depression, patients may not appreciate the importance of their mood disorder. This observation raises an important motivational issue that may influence adherence to treatment. Studies of depression treatments in other medical populations (such as patients with diabetes mellitus or congestive heart failure) that involve patients motivated to treat their depression and that offer patients a choice between initial treatment options have reported clinically meaningful improvement in depression (25,22). These factors should be considered in establishing eligibility criteria and in the design of clinical trials.

Based on the data reviewed, we agreed that depression treatments found to be effective in non-CHD populations (CBT, SSRIs, and combined treatments) will likely also reduce depression in CHD patients. Given that depression can be treated safely and effectively in CHD patients and that a large and consistent body of evidence shows that depression is associated with an approximate three-fold increase in relative risk for CVD mortality and morbidity compared with nondepressed patients, we conclude that an RCT is needed to determine whether SSRI, psychotherapy, or combined treatment can reduce the risk of CVD events and mortality associated with depression in CHD patients.

### Recommendations for Research

After considering various options, we recommend that an RCT be planned in detail. The trial should involve multiple centers so that a sufficient number of patients are recruited and should specify clearly defined treatment algorithms with adequate follow-up to include a sufficient number of cardiac events. Depressed CHD patients should be at moderate cardiac

risk (e.g., low ejection fraction) and should be recruited from cardiology and primary care settings and assigned randomly to either a stepped-care depression treatment arm or a usual cardiac care arm. The intervention should be of sufficient duration and intensity to ensure a difference in depressive symptoms between the randomized arms. Results of such a trial would provide important information concerning the clinical care of depressed CHD patients.

## REFERENCES

- Krishnan KRR, Delong M, Kraemer H, Carney RM, Spiegel D, Gordon C, McDonald W, Dew MA, Alexopoulos G, Buckwalter K, Cohen PD, Evans D, Kaufmann PG, Olin J, Otey E, Waincott C. Comorbidity of depression with other medical illnesses in the elderly. *Biol Psychiatry* 2002;52:559–88.
- Berkman LF, Blumenthal J, Burg M, Carney RM, Catellier D, Cowan MJ, Czajkowski SM, DeBusk R, Hosking J, Jaffe A, Kaufmann PG, Mitchell P, Norman J, Powell LH, Raczynski JM, Schneiderman N. Effects of treating depression and low perceived social support on clinical events after myocardial infarction: the Enhancing Recovery in Coronary Heart Disease Patients (ENRICH) Randomized Trial. *JAMA* 2003;289:3106–16.
- Glassman AH, O'Connor CM, Califf RM, Swedberg K, Schwartz P, Bigger JT Jr, Krishnan KR, van Zyl LT, Swenson JR, Finkel MS, Landau C, Shapiro PA, Pepine CJ, Mardekian J, Harrison WM, Barton D, McLvor M; Sertraline Antidepressant Heart Attack Randomized Trial (SADHART) Group. Sertraline treatment of major depression in patients with acute MI or unstable angina. *JAMA* 2002;288:701–9.
- Serebruany VL, Suckow RF, Cooper TB, O'Connor CM, Malinin AI, Krishnan KR, van Zyl LT, Lekht V, Glassman AH; Sertraline Antidepressant Heart Attack Randomized Trial. Relationship between release of platelet/endothelial biomarkers and plasma levels of sertraline and N-desmethylsertraline in acute coronary syndrome patients receiving SSRI treatment for depression. *Am J Psychiatry* 2005;162:1165–70.
- Serebruany VL, Glassman AH, Malinin AI, Nemeroff CB, Musselman DL, van Zyl LT, Finkel MS, Krishnan KR, Gaffney M, Harrison W, Califf RM, O'Connor CM; Sertraline AntiDepressant Heart Attack Randomized Trial Study Group. Platelet/endothelial biomarkers in depressed patients treated with the selective serotonin reuptake inhibitor sertraline after acute coronary events: the Sertraline AntiDepressant Heart Attack Randomized Trial (SADHART) Platelet Substudy. *Circulation* 2003;108:939–44.
- Carney RM, Blumenthal JA, Freedland KE, Youngblood M, Veith RC, Burg MM, Cornell C, Saab PG, Kaufmann PG, Czajkowski SM, Jaffe AS. Depression and late mortality after myocardial infarction in the Enhancing Recovery in Coronary Heart Disease (ENRICH) study. *Psychosom Med* 2004;66:466–74.
- Taylor CB, Youngblood ME, Catellier D, Veith RC, Carney RM, Burg MM, Kaufmann P, Shuster J, Mellman T, Blumenthal JA, Krishnan R, Jaffe AS, for the ENRICH Investigators. Effects of antidepressant medication on morbidity and mortality in depressed post-MI patients. *Arch Gen Psychiatry* 2005;62:792–8.
- Appendix: Summary of Instruments. National Heart, Blood, and Lung Institute Working Group, Assessment and Treatment of Depression in Patients with Cardiovascular Disease. NHLBI Web site. Available at: <http://www.nhlbi.nih.gov/meetings/workshops/depression/instruments.htm>. Accessed June 10, 2005.
- Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:561–71.
- Beck AT, Steer RA, Brown GK. Manual for Beck Depression Inventory II (BDI-II). San Antonio, TX: Psychology Corporation; 1996.
- Rush AJ, Giles DE, Schlessner MA, Fulton CL, Weissenburger J, Burns C. The Inventory for Depressive Symptomatology (IDS): preliminary findings. *Psychiatry Res* 1986;18:65–87.
- Freedland KE, Skala JA, Carney RM, Raczynski JM, Taylor CB, Mendes de Leon CF, Ironson G, Youngblood ME, Krishnan KR, Veith RC. The Depression Interview and Structured Hamilton (DISH): rationale, development, characteristics, and clinical validity. *Psychosom Med* 2002;64:897–905.
- Kessler RC, Ustun TB. The World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *Int J Methods Psychiatr Res* 2004;13:93–121.
- Kessler RC, Demler O, Frank RG, Olfson M, Pincus HA, Walters EE, Wang P, Wells KB, Zaslavsky AM. Prevalence and treatment of mental disorders, 1990 to 2003. *N Engl J Med* 2005;352:2515–23.
- Kessler RC, Berglund P, Borges G, Nock M, Wang PS. Trends in suicide ideation, plans, gestures, and attempts in the United States, 1990–1992 to 2001–2003. *JAMA* 2005;293:2487–95.
- Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, Wittchen HU, Kendler KS. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. *Arch Gen Psychiatry* 1994;51:8–19.
- Strik JJ, Honig A, Lousberg R, Denollet J. Sensitivity and specificity of observer and self-report questionnaires in major and minor depression following myocardial infarction. *Psychosomatics* 2001;42:423–8.
- Rush AJ, Trivedi MH, Carmody TJ, Ibrahim HM, Markowitz JC, Keitner GI, Kornstein SG, Arnow B, Klein DN, Manber R, Dunner DL, Gelenberg AJ, Kocsis JH, Nemeroff CB, Fawcett J, Thase ME, Russell JM, Jody DN, Borian FE, Keller MB. Self-reported depressive symptom measures: sensitivity to detecting change in a randomized, controlled trial of chronically depressed, nonpsychotic outpatients. *Neuropsychopharmacology* 2005;30:405–16.
- Murray CJL, Lopez AD. Quantifying the burden of disease and injury attributable to 10 major risk factors. In: Murray CJL, Lopez AD, eds. *The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability from Diseases, Injuries and Risk Factors in 1990 and Projected to 2020*. Cambridge MA: Harvard University Press; 1996.
- Schatzberg AF, Rush AJ, Arnow BA, Banks PL, Blalock JA, Borian FE, Howland R, Klein DN, Kocsis JH, Kornstein SG, Manber R, Markowitz JC, Miller I, Ninan PT, Rothbaum BO, Thase ME, Trivedi MH, Keller MB. Chronic depression: medication (nefazodone) or psychotherapy (CBASP) is effective when the other is not. *Arch Gen Psychiatry* 2005;62:513–20.
- Trivedi MH, Rush AJ, Wisniewski SR, Nierenberg AA, Warden D, Ritz L, Norquist G, Howland RH, Lebowitz B, McGrath PJ, Shores-Wilson K, Biggs MM, Balasubramani GK, Fava M. Evaluation of outcomes with citalopram for depression using measurement-based care in STAR\*D: implications for clinical practice. *Am J Psychiatry* 2006;163:28–40.
- Unutzer J, Katon W, Callahan CM, Williams JW Jr, Hunkeler E, Harpole L, HOFFING M, Della Penna RD, Noel PH, Lin EH, Areal PA, Hegel PT, Tang L, Belin TR, Oishi S, Langston C. Collaborative care management of late-life depression in the primary care setting: a randomized controlled trial. *JAMA* 2002;288:2836–45.
- Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients: the Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med* 2000;342:145–53.
- Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, Daubert JP, Higgins SL, Brown MW, Andrews ML. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med* 2002;346:877–83.
- Katon WJ, Von Korff M, Lin EH, Simon G, Ludman E, Russo J, Ciechanowski P, Walker E, Bush T. The Pathways Study: a randomized trial of collaborative care in patients with diabetes and depression. *Arch Gen Psychiatry* 2004;61:1042–9.