

# Treatment of Depression After Coronary Artery Bypass Surgery

## A Randomized Controlled Trial

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**Context:** There has been little research on the treatment of depression after coronary artery bypass surgery.

**Objective:** To test the efficacy of 2 nonpharmacological interventions for depression after coronary artery bypass surgery compared with usual care.

**Design:** A 12-week, randomized, single-blind clinical trial with outcome evaluations at 3, 6, and 9 months.

**Setting:** Outpatient research clinic at Washington University School of Medicine, St Louis, Missouri.

**Patients:** One hundred twenty-three patients who met the DSM-IV criteria for major or minor depression within 1 year after surgery.

**Intervention:** Twelve weeks of cognitive behavior therapy or supportive stress management. Approximately half of the participants were taking nonstudy antidepressant medications.

**Main Outcome Measure:** Remission of depression, defined as a score of less than 7 on the 17-item Hamilton Rating Scale for Depression.

**Results:** Remission of depression occurred by 3 months in a higher proportion of patients in the cognitive be-

havior therapy (71%) and supportive stress-management (57%) arms than in the usual care group (33%) ( $\chi^2=12.22$ ,  $P=.002$ ). Covariate-adjusted Hamilton scores were lower in the cognitive behavior therapy (mean [standard error], 5.5 [1.0]) and the supportive stress-management (7.8 [1.0]) arms than in the usual care arm (10.7 [1.0]) at 3 months. The differences narrowed at 6 months, but the remission rates differed again at 9 months (73%, 57%, and 35%, respectively;  $\chi^2=12.02$ ,  $P=.003$ ). Cognitive behavior therapy was superior to usual care at most points on secondary measures of depression, anxiety, hopelessness, stress, and quality of life. Supportive stress management was superior to usual care only on some of the measures.

**Conclusions:** Both cognitive behavior therapy and supportive stress management are efficacious for treating depression after coronary artery bypass surgery, relative to usual care. Cognitive behavior therapy had greater and more durable effects than supportive stress management on depression and several secondary psychological outcomes.

**Trial Registration:** clinicaltrials.gov Identifier: NCT00042198

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APPROXIMATELY 1 IN EVERY 5 patients meets the DSM-IV criteria for a major depressive episode during recovery from coronary artery bypass graft (CABG) surgery,<sup>1,2</sup> and at least as many experience milder forms of depression.<sup>3,4</sup> Depression around the time of surgery predicts postoperative complications, longer physical and emotional recovery, worse quality of life, and increased rates of cardiac events and mortality.<sup>5-10</sup> In addition, perceived cognitive impairment after CABG surgery is worse in depressed than nondepressed patients with comparable profiles on objective neuropsychological tests.<sup>11</sup>

There has been little research on the treatment of post-CABG depression. The

short-term effects of alprazolam on anxiety and depression were evaluated in a small, placebo-controlled trial nearly 20 years ago,<sup>12</sup> but no randomized, controlled antidepressant trials that specifically targeted post-CABG patients with clinical depression have been published. A recent randomized trial of a brief, home-based nursing intervention vs standard care for emotional distress after CABG surgery found no between-group differences in self-reported depression or anxiety symptoms in the sample as a whole, though there were significant differences 6 months after surgery in a subgroup with high levels of anxiety or depression at baseline.<sup>13</sup>

The purpose of this study was to test the efficacy of 2 nonpharmacological interven-

tions for depression during the first year after CABG surgery. It is the first randomized, controlled clinical trial to evaluate these treatments for post-CABG depression. Cognitive behavior therapy (CBT) was selected because it is well established as an efficacious treatment for depression in other patient populations<sup>14,15</sup> and because it was used to treat depression after acute myocardial infarction in a large, multicenter, randomized clinical trial, the Enhancing Recovery in Coronary Heart Disease (ENRICHD) study.<sup>16,17</sup>

We also tested a supportive stress-management intervention. Supportive stress management was evaluated, because stressful experiences can contribute to the onset and maintenance of depressive episodes<sup>18-20</sup> and because stress management has shown promise in previous studies as a treatment for depression in both psychiatric<sup>21</sup> and cardiac<sup>22-24</sup> patients. Most cardiac rehabilitation programs include a brief stress-management component, typically delivered in a group format, but these interventions tend to yield only modest improvements in depression and anxiety.<sup>22</sup> Consequently, we tested an intervention that was more intensive than the stress-management modules that are usually included in cardiac rehabilitation, that more specifically focused on coping with depressogenic and anxiogenic stressors, and that was delivered within the context of a supportive therapeutic relationship.

## METHODS

### PATIENTS

Patients aged 21 years or older who had undergone CABG surgery within the past year at a Washington University-affiliated hospital (Barnes-Jewish, Christian, or Missouri Baptist Hospitals) in St Louis, Missouri, were screened for eligibility by study recruiters. Patients were excluded from participation for severe psychiatric comorbidities, such as schizophrenia or bipolar disorder, active alcoholism or substance abuse, severe cognitive impairment, noncardiac illnesses with a poor 1-year prognosis, being too medically ill or living too far away to participate, being unable to communicate in English, or for receiving ongoing psychotherapeutic services. Current use of an antidepressant medication was not an exclusion criterion, as long as the patient had been taking a therapeutic dose for at least 6 weeks. Potentially eligible patients who provided written informed consent were then screened for depression. Those who scored 10 or higher on the Beck Depression Inventory (BDI)<sup>25</sup> and who met *DSM-IV* criteria for a current major or minor depressive episode, as determined by the Depression Interview and Structured Hamilton (DISH),<sup>26</sup> were enrolled in the trial. The self-described race and ethnicity of enrollees were classified according to the standard National Institute of Health categories in fulfillment of National Institute of Health reporting requirements. The study was approved by the Human Research Protection Office at Washington University Medical Center, St Louis, Missouri. Enrollment began in December 2001 and ended in August 2005; the follow-up was completed in December 2005.

### STUDY DESIGN

This study was a randomized, single-blind, parallel-group, controlled clinical trial that compared the efficacy of CBT or supportive stress management for depression after CABG surgery with usual care. A target sample size estimate of 43 patients per group was based on 80% power to detect a treatment-

control difference of 4 points on the Hamilton Rating Scale for Depression (HAM-D) at 3 months. Patients who met the eligibility criteria for participation underwent baseline testing at an outpatient research clinic at Washington University School of Medicine and were then randomly assigned to 12 weeks of individual CBT, individual supportive stress-management, or usual care for depression. The CBT and supportive stress-management interventions were provided in addition to, not as a replacement for, any antidepressant medications that the participants may have been receiving from their physicians. The interventions were compared with usual care rather than with a pill placebo or an attention control condition, because antidepressants are being prescribed by primary care and other physicians to a growing proportion of cardiac patients with depression as part of usual care.<sup>27,28</sup> Furthermore, our main aim was to determine whether these interventions are superior to usual medical care for depression after CABG surgery, not to ascertain the extent to which their benefits may be attributable to attention, placebo, or other nonspecific effects.

We used a SAS program (SAS Institute, Cary, North Carolina) to generate a random allocation sequence with block sizes of 3 and 6. Group assignments were concealed in sealed envelopes and revealed to the study coordinator immediately after the participant completed all of the baseline assessments.

## TREATMENT PROCEDURES

### Cognitive Behavior Therapy

Cognitive behavior therapy was provided in weekly, individual, 50- to 60-minute sessions by 1 of 3 therapists (2 clinical psychologists and a clinical social worker) with training and experience in CBT. Although twice-weekly sessions were permitted for up to 4 weeks for patients with severe depression or for crisis intervention, it was seldom necessary to exercise the option to increase the frequency of sessions. Brief telephone contacts between treatment sessions were also allowed as needed. Each case was reviewed in a weekly supervision meeting with 1 of the investigators (K.E.F.).

The treatment manuals were standard CBT texts.<sup>29,30</sup> Some of the standard cognitive-behavioral techniques were modified for cardiac patients.<sup>31</sup> For example, it was necessary to ensure that behavioral activation plans were medically safe. The patient's physician was consulted to resolve any questions about medical safety.

The study protocol did not specify a fixed, session-by-session treatment sequence. As in the ENRICHD trial,<sup>16,32</sup> however, the earlier sessions usually emphasized target problem identification, problem solving, and behavioral activation, and later sessions emphasized cognitive techniques, including challenging distressing automatic thoughts and changing dysfunctional attitudes. The last 2 sessions also emphasized consolidation of the self-therapy and relapse-prevention skills that were promoted throughout the intervention.

### Supportive Stress Management

Supportive stress management was also provided in weekly, individual, 50- to 60-minute sessions by 1 of 3 therapists (2 clinical social workers and a counseling psychologist) with training and experience in counseling and stress-management interventions. As with CBT, brief telephone contacts were permitted between treatment sessions as needed, and twice-weekly sessions were allowed when needed, but the frequency was once per week in most cases. Each case was reviewed in a weekly supervision meeting with 1 of the investigators (R.M.C.).

The intervention was delivered in the setting of a supportive therapeutic relationship with the objective of improving the

patient's ability to cope with stressful life events and daily stressors. During the initial session, the therapist explained that stress has been linked in prior research to both depression and heart disease, that the ability to cope with stress depends on skills that can be improved through training and practice, and that this can be helpful in overcoming depression. The patient was asked to describe recent stressful experiences and to discuss their impact, with emphasis on depression symptoms.

During the following sessions, the patients were given systematic instruction with guided practice in progressive relaxation training<sup>33,34</sup> and other techniques, including controlled breathing and relaxing imagery.<sup>35</sup> The techniques were modified as needed to accommodate painful medical conditions or orthostatic hypotension. The patients were asked to practice them daily and to maintain a practice log. As they gained proficiency in relaxation skills, they were asked to apply them to stressful or distressing situations in daily life. At each session, they were asked to describe these experiences, their use of relaxation techniques to cope with them, and the effect this had on their mood. If the patient reported any difficulties in applying or benefiting from the techniques, part of the session was devoted to addressing these barriers.

### QUALITY ASSURANCE AND PATIENT SAFETY MONITORING

A patient safety monitoring committee met regularly to review worsening depression or anxiety, suicidal ideation, and adverse events. The committee included a psychiatrist and 3 clinical psychologists, one of whom also had extensive experience in cardiac nursing. A cardiologist investigator was also consulted as needed to address medical safety issues. There were no study-related serious adverse events.

The therapists in both arms completed checklists after every session to assess adherence to their respective treatment protocols. They also completed the Treatment Process Scale, a measure developed for this study, after each session. The 11 items on the Treatment Process Scale are rated from 0 to 6 (total score range, 0-66); each item addresses a particular aspect of the case from the therapist's perspective. For example, 1 of the items assesses the therapist's view of the quality of the therapeutic relationship.

Ninety-four percent of the treatment sessions were audiotaped. Researchers randomly selected a recording for each patient from sessions 2, 3, or 4, and another from 1 of the last 3 sessions, excluding the final session. The tapes were rated by 4 advanced doctoral students in clinical psychology who had received intensive training in the study interventions and therapy-rating procedures. Each tape was independently rated by 2 raters on (1) the Cognitive Therapy Scale<sup>36,37</sup>; (2) the Cognitive Therapy subscale of the Collaborative Study Psychotherapy Rating Scale (CSPRS) (Hollon et al, unpublished data, 1988)<sup>38</sup>; and (3) the Stress Management Scale, which was developed for this study. The Stress Management Scale is a 7-item rating scale that closely resembles the Cognitive Therapy Scale, except it evaluates the components of the supportive stress-management intervention. The items are rated from 0 (poor) to 6 (excellent) and assess the therapist's performance in the following domains: (1) socialization to the stress-management intervention, (2) review of previous homework, (3) in-session assessments, (4) relaxation training, (5) overcoming barriers to improvement, (6) review of stressful events, and (7) applications of stress-management skills to daily life. Total scores on the Cognitive Therapy Scale range from 0 to 42. The ratings were averaged across raters and sessions, yielding 1 score per patient on the Cognitive Therapy Scale, the CSPRS, and the Stress Management Scale. High Cognitive Therapy Scale and CSPRS scores and low Stress Management

Scale scores were predicted for the CBT arm and the opposite was predicted for the supportive stress-management arm. This pattern would indicate that the therapists were adhering to their respective treatment protocols and that the interventions differed from one another as intended.

Participants in both intervention arms were asked to complete a modified Beck Institute Patient Session Feedback form after each session. It was modified to incorporate the Empathy Scale,<sup>39</sup> a measure of the patient's perception of the quality of the therapeutic relationship. The Empathy Scale has been shown to predict depression improvement in CBT.<sup>40</sup>

### OUTCOME MEASURES

The primary outcome measure was HAM-D score,<sup>41</sup> derived from DISH.<sup>26</sup> Remission of depression was defined as a HAM-D score less than 7. The BDI<sup>25</sup> was used as a secondary measure of depression, and a BDI score of less than 7 was used as a secondary definition of remission. Additional secondary outcome measures included the Beck Anxiety Inventory,<sup>42</sup> the Beck Hopelessness Scale,<sup>43</sup> the Perceived Stress Scale,<sup>44</sup> and the Medical Outcomes Study Short-Form 36-item Health Survey (SF-36).<sup>45</sup> An experimental measure, the Heart Surgery Questionnaire (HSQ), was developed for this study to assess perceived psychological impact of CABG surgery. The HSQ asks the patient to rate how he or she has been feeling during the past month compared with how he or she recalls having felt during the month prior to heart surgery. Each item is rated on a scale of 1 (much less) to 5 (much more). It includes four 5-item subscales derived via factor analysis from a pool of items drawn from interviews with participants after CABG in previous studies: vitality, dysphoric mood, irritability, and perceived cognitive impairment. The subscales are internally consistent (Cronbach  $\alpha=0.83, 0.71, 0.77, \text{ and } 0.73$ , respectively).

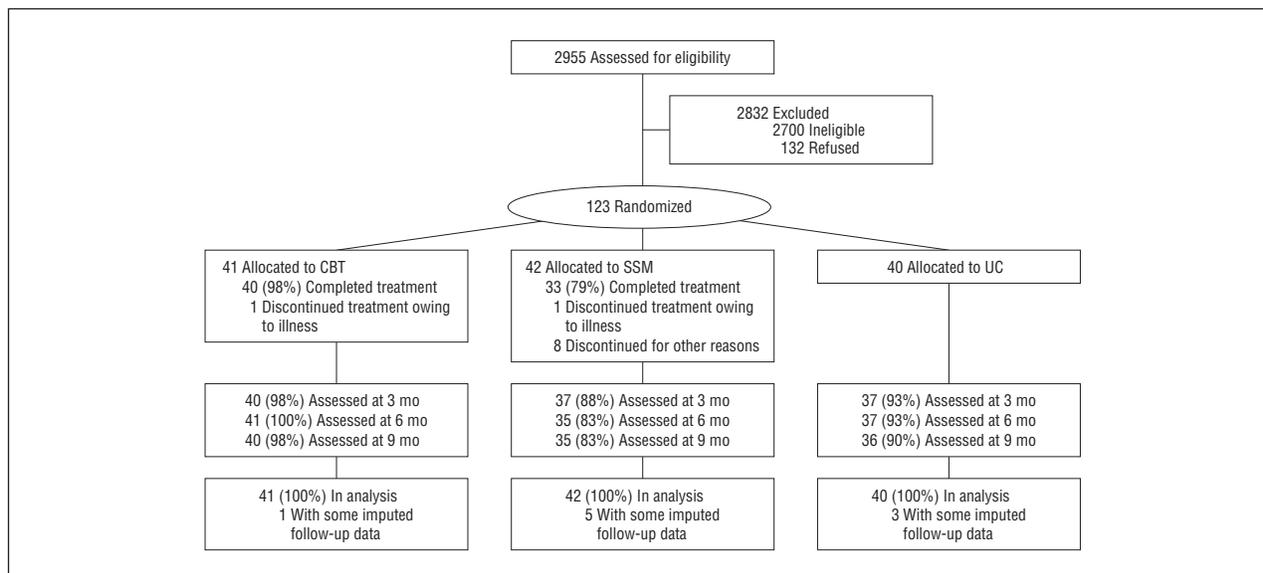
Several objective neuropsychological tests that are often used to assess cognitive impairment after CABG surgery<sup>46</sup> were also administered at baseline. These included the Digit Symbol test,<sup>47</sup> part B of the Trailmaking Test,<sup>48</sup> a paragraph recall test,<sup>49</sup> and the Short Blessed Test (orientation, memory, and concentration).<sup>50,51</sup>

The DISH and the entire test battery were repeated at the end of the 12-week treatment phase. Most of the tests were re-administered at 6- and 9-month follow-up assessments; the HSQ and the neuropsychological tests were administered at baseline and 12 weeks only. The outcome assessors were masked to the participants' group assignments. The study recruiters and outcome assessors had prior training and experience with the DISH, and their interviews were supervised during the study by 2 of the investigators (K.E.F. and J.A.S.). They received additional training in the administration of the neuropsychological battery from 1 of the investigators (K.E.F.).

### STATISTICAL ANALYSIS

There were no missing data on the baseline variables used in this article. Data on 1 or more outcome measures were missing for 7%, 8%, and 10% of the participants at the 3-, 6-, and 9-month assessments, respectively. These data were plausibly missing at random. The SAS Proc MI multiple-imputation procedure was used to impute missing data. Owing to nonmonotonicity, the Markov Chain Monte Carlo method<sup>52</sup> was first used to produce a monotone missing pattern. The standard parametric method was then used to impute the remaining values. The imputation model included all variables used in the outcome analyses.

$\chi^2$  Tests and 1-way analyses of variance were used for univariate comparisons of patient characteristics, and 2-tailed *t* tests were used for between-group comparisons of quality assurance measures. Statistical significance was defined as  $P < .05$ .



**Figure 1.** Flowchart of participants through each stage of the trial. CBT indicates cognitive behavior therapy; SSM, supportive stress management; and UC, usual care.

The outcome analyses conformed to the intention-to-treat principle. A  $\chi^2$  test with 2 *df* was used in the primary analysis to determine whether or not HAM-D remission rates differed among the groups at each follow-up point; 1-*df* tests were then used for pairwise comparisons. The same approach was used in a secondary analysis of remission based on BDI scores. Cox proportional hazards regression was used to determine whether there were differences between the 2 active treatment arms in time to remission of depression, by analyzing the scores of BDIs that were administered weekly by the therapists, along with the baseline and 3-month measures.

Mixed models (SAS Proc Mixed; SAS Institute Inc) with first-order autoregressive and variance components covariance structures were used to analyze between-group differences in HAM-D scores and in the secondary outcomes that were measured at 4 points. The random effects account for individual differences in the baseline level (random intercepts) and in the trajectory of change over time (random slopes) in the outcome variable. Type III tests of fixed effects were used to examine the effects of group, time, group  $\times$  time interaction, and antidepressant use. A significant group  $\times$  time interaction indicates that the course of change over time in the outcome differs among the 3 groups. Antidepressant use was modeled as a time-dependent covariate, with a value of 1 assigned to each interval during which the patient was taking an antidepressant, and 0 to all other intervals. Tukey-adjusted planned contrasts examined pairwise differences at each follow-up point. Some of the secondary outcomes (the neuropsychological tests and the HSQ) were measured only at baseline and 3 months. These analyses were similar to the mixed models we previously described except that the compound symmetry covariance structure was specified. A planned subgroup analysis was conducted to determine whether the effects of treatment differed between patients with major vs minor depression at baseline.

## RESULTS

### SAMPLE

**Figure 1** shows that of 2955 patients who were screened for eligibility, 2700 (91.3%) were excluded and 132 (4.5%) refused to participate. The most common principal reasons for exclusion were transportation barriers, including

excessive distance from the medical center ( $n=1213$ ), and absence of depression ( $n=1114$ ). A total of 123 patients were enrolled. The median time from surgery to study enrollment was 92 days; 50% were enrolled within 3 months of surgery, 20% between 3 and 6 months, 21% between 6 and 9 months, and 10% between 9 and 12 months. Forty-two of the participants (34%) met the *DSM-IV* criteria for a minor depressive episode at enrollment, and 81 (66%) met the criteria for a major depressive episode. Onset of 35 of the depressive episodes (28%) occurred prior to surgery and 88 (72%) occurred after surgery. Eighty-three of the participants (68%) also had a history of at least 1 major depressive episode. The enrolled patients were randomly assigned to CBT ( $n=41$ ), supportive stress management ( $n=42$ ), or usual care ( $n=40$ ).

**Table 1** presents the demographic and medical characteristics of the participants by group. The proportion of African American participants randomly assigned to the supportive stress-management arm was higher than expected ( $P=.01$ ). There were no other significant differences in the characteristics of the groups. Intervention completion rates were 98% in the CBT arm and 79% in the supportive stress-management arm ( $P=.01$ ). One participant dropped out of CBT owing to medical illness; 9 dropped out of supportive stress management because of logistical barriers ( $n=5$ ), plateau of perceived benefits of treatment ( $n=4$ ), or psychiatric complications ( $n=1$ ). Participants in CBT also attended more sessions (mean [standard deviation (SD)], 11 [2]) than participants in the supportive stress-management group (8 [3]) ( $P<.001$ ). The 3-month (posttreatment) evaluation was completed by 40 of the CBT (98%), 37 of the supportive stress-management (88%), and 37 of the usual care (93%) participants ( $P=.25$ ). There were no significant differences among the groups in the proportions of patients who took nonstudy antidepressants during the trial (CBT, 54%; supportive stress management, 52%; usual care, 45%;  $P=.70$ ).

**Table 1. Demographic and Clinical Characteristics at Enrollment of Patients Who Underwent Coronary Artery Bypass Surgery**

Characteristic	No. (%)			$\chi^2$	P Value
	CBT (n=41)	SSM (n=42)	UC (n=40)		
Sex					
F	23 (56)	21 (50)	17 (43)	1.50	.47
M	18 (44)	21 (50)	23 (57)		
Race					
White	36 (88)	28 (67)	36 (90)	9.05	.01
African American	5 (12)	14 (33)	4 (10)		
Age, mean (SD), y	62 (11)	59 (10)	61 (9)	$t_{120} = 1.59$	.08
Married or has a partner	22 (54)	25 (60)	18 (45)	1.75	.42
Education					
<High school	7 (17)	23 (56)	11 (27)	$\chi^2 = 6.21$	.18
High school graduate	6 (14)	16 (38)	20 (48)		
>High school	8 (20)	13 (33)	19 (47)		
Currently working	24 (59)	22 (52)	22 (55)	0.32	.85
Annual household income $\geq$ \$30 000 <sup>a</sup>	19 (51)	19 (48)	21 (54)	0.32	.85
History of myocardial infarction	23 (56)	21 (50)	18 (45)	1.00	.61
History of coronary angioplasty	14 (34)	15 (36)	16 (40)	0.32	.85
Previous coronary artery bypass surgery	7 (17)	4 (10)	4 (10)	1.37	.50
Current $\beta$ -blocker therapy	29 (71)	29 (69)	26 (65)	0.32	.85
Hypertension	32 (78)	34 (81)	29 (73)	3.38	.18
Diabetes	22 (54)	21 (50)	16 (40)	1.09	.58
Current smoker	4 (10)	5 (12)	4 (10)	0.12	.94
Current <i>DSM-IV</i> depressive episode <sup>b</sup>					
Minor depression	15 (37)	12 (29)	15 (38)	0.89	.64
Major depression	26 (63)	30 (71)	25 (62)		

Abbreviations: CBT, cognitive behavior therapy; SSM, supportive stress management; UC, usual care.

<sup>a</sup>Data available for 116 patients.

<sup>b</sup>Determined by the Depression Interview and Structured Hamilton interview.

**Table 2. Depression Remission at 3, 6, and 9 Months After Coronary Artery Bypass Surgery<sup>a</sup>**

Depression Scale	No. (%) of Patients Scoring Below Cutoff for Remission			$\chi^2$	P Value
	CBT (n=41)	SSM (n=42)	UC (n=40)		
HAM-D					
3 mo <sup>b,c</sup>	29 (71)	24 (57)	13 (33)	12.22	.002
6 mo	28 (68)	20 (48)	21 (53)	3.91	.14
9 mo <sup>b,c</sup>	30 (73)	24 (57)	14 (35)	12.02	.003
Sustained <sup>b</sup>	23 (56)	17 (41)	9 (23)	9.55	.009
BDI					
3 mo <sup>b,c</sup>	29 (71)	22 (52)	11 (28)	15.24	<.001
6 mo <sup>b</sup>	28 (68)	20 (48)	17 (43)	6.10	.047
9 mo <sup>b</sup>	27 (66)	20 (48)	12 (30)	10.43	.005
Sustained <sup>b,c</sup>	21 (51)	14 (33)	6 (15)	11.95	.003

Abbreviations: BDI, Beck Depression Inventory; CBT, cognitive behavior therapy; HAM-D, Hamilton Rating Scale for Depression; SSM, supportive stress management; UC, usual care.

<sup>a</sup>Sustained remission was defined as being in remission at all 3 follow-up assessments. The overall *P* value is for the 2 *df* test of differences among groups at the indicated follow-up time. The planned contrasts are 1-*df* tests of pairwise differences between groups.

<sup>b</sup>Cognitive behavior therapy was not equal to UC in planned contrast.

<sup>c</sup>Supportive stress management was not equal to UC in planned contrast.

## REMISSION OF DEPRESSION

As shown in **Table 2**, remission rates on the HAM-D were significantly higher in the CBT and supportive stress-management groups than in the usual care group at 3 and 9 months. The effect sizes, expressed as number needed to treat,<sup>53</sup> were 2.6 (95% confidence interval [CI], 2.4-2.8) for CBT vs usual care, 4.1 (95% CI, 3.9-4.3) for supportive stress management vs usual care, and 7.4 (95% CI,

7.2-7.6) for CBT vs supportive stress management. This suggests, for example, that 1 additional remission could be expected for every 2.6 patients treated with CBT instead of usual care. Sustained remission, defined as a HAM-D score less than 7 at all 3 follow-up points, occurred in 56%, 41%, and 23% of the CBT, supportive stress-management, and usual care participants, respectively (*P* = .009). Compared with usual care, BDI remission rates were superior in the CBT group at all follow-up times and in the supportive

**Table 3. Secondary Outcomes in Patients Who Underwent Coronary Artery Bypass Surgery<sup>a</sup>**

Measure	Covariate-Adjusted Least-Squares Mean (SE)			Group		Time		Group × Time		AD	
	CBT (n=41)	SSM (n=42)	UC (n=40)	F Test	P Value	F Test	P Value	F Test	P Value	F Test	P Value
<b>HAM-D</b>											
Baseline	19.3 (1.0)	20.8 (1.0)	18.5 (1.0)	$F_{2,123} = 3.43$	.04	$F_{3,214} = 194.59$	<.001	$F_{6,213} = 6.07$	<.001	$F_{1,437} = 1.49$	.22
3 mo <sup>b,c</sup>	5.5 (1.0)	7.8 (1.0)	10.7 (1.0)								
6 mo	6.6 (1.0)	8.5 (1.0)	8.3 (1.0)								
9 mo <sup>b</sup>	5.5 (1.0)	7.7 (1.0)	10.3 (1.0)								
<b>BDI</b>											
Baseline	22.3 (1.3)	23.7 (1.3)	20.8 (1.4)	$F_{2,123} = 3.88$	.02	$F_{3,219} = 122.40$	<.001	$F_{6,218} = 7.35$	<.001	$F_{1,435} = 0.06$	.81
3 mo <sup>b,c,d</sup>	5.4 (1.3)	9.3 (1.4)	13.8 (1.4)								
6 mo	7.8 (1.3)	10.6 (1.4)	10.7 (1.4)								
9 mo <sup>b</sup>	6.7 (1.3)	9.9 (1.4)	12.9 (1.4)								
<b>Beck Anxiety Inventory</b>											
Baseline	14.6 (1.4)	18.6 (1.4)	15.0 (1.4)	$F_{2,125} = 2.65$	.07	$F_{3,213} = 39.94$	<.001	$F_{6,213} = 3.04$	.007	$F_{1,457} = 0.03$	.87
3 mo <sup>b</sup>	6.0 (1.4)	9.3 (1.4)	11.0 (1.5)								
6 mo <sup>b</sup>	8.1 (1.4)	11.0 (1.4)	12.7 (1.5)								
9 mo <sup>b,c</sup>	9.1 (1.4)	10.1 (1.5)	14.2 (1.5)								
<b>Beck Hopelessness Scale</b>											
Baseline	7.2 (0.8)	9.6 (0.8)	8.2 (0.8)	$F_{2,280} = 9.98$	<.001	$F_{3,71} = 11.76$	<.001	$F_{6,70} = 0.93$	.48	$F_{1,448} = 0.07$	.79
3 mo <sup>b</sup>	3.5 (0.8)	4.9 (0.9)	6.4 (0.9)								
6 mo <sup>b</sup>	3.5 (0.8)	5.5 (0.8)	6.6 (0.9)								
9 mo <sup>b</sup>	3.5 (0.8)	5.5 (0.9)	7.5 (0.9)								
<b>Perceived Stress Scale</b>											
Baseline	22.7 (1.2)	24.8 (1.2)	22.8 (1.2)	$F_{2,126} = 3.16$	.046	$F_{3,242} = 63.05$	<.001	$F_{6,241} = 3.12$	.006	$F_{1,437} = 3.11$	.08
3 mo <sup>b</sup>	12.8 (1.2)	15.5 (1.2)	17.4 (1.2)								
6 mo	14.4 (1.2)	16.7 (1.2)	17.5 (1.2)								
9 mo <sup>b,c</sup>	14.0 (1.2)	14.6 (1.2)	18.6 (1.2)								
<b>SF-36 physical score</b>											
Baseline	34.1 (1.5)	35.0 (1.5)	33.9 (1.5)	$F_{2,127} = 1.12$	.33	$F_{3,244} = 8.99$	<.001	$F_{6,243} = 1.02$	.41	$F_{1,460} = 0.48$	.49
3 mo	38.0 (1.5)	38.7 (1.5)	35.8 (1.5)								
6 mo	36.2 (1.5)	38.7 (1.5)	37.3 (1.5)								
9 mo	37.6 (1.5)	39.9 (1.5)	36.9 (1.6)								
<b>SF-36 mental score</b>											
Baseline	34.3 (1.9)	34.4 (1.9)	34.8 (1.9)	$F_{2,133} = 4.58$	.01	$F_{3,231} = 63.13$	<.001	$F_{6,230} = 2.81$	.01	$F_{1,431} = 0.01$	.91
3 mo <sup>b</sup>	52.5 (1.9)	48.6 (2.0)	43.3 (1.9)								
6 mo <sup>b</sup>	49.7 (1.9)	47.3 (2.0)	42.1 (2.0)								
9 mo <sup>b,c</sup>	49.1 (1.9)	47.8 (2.0)	42.4 (2.0)								

(continued)

stress-management group at 3 months. These effects correspond to numbers needed to treat of 2.3 (95% CI, 2.1-2.5) for CBT vs usual care, 4.0 (95% CI, 3.8-4.2) for supportive stress management vs usual care, and 5.5 (95% CI, 5.2-5.7) for CBT vs supportive stress management. Sustained remission, based on a BDI score less than 7 at all 3 follow-up points, occurred in 51%, 33%, and 15% of patients in the CBT, supportive stress-management, and usual care groups, respectively ( $P = .003$ ).

Median time to remission on the BDI was 36 days in the CBT arm and 43 days in the supportive stress-management arm. In a Cox proportional hazards regression analysis, however, there was no significant difference between these groups in time to remission.

#### CONTINUOUS DEPRESSION SCORE OUTCOMES

As shown in **Table 3** and **Figure 2**, change in HAM-D scores differed among groups. At the 3-month, end-of-treatment assessment, HAM-D scores were significantly lower in both the CBT and the supportive stress-management

groups compared with the usual care group. There were no differences among the groups at 6 months, but CBT was again superior to usual care at 9 months. Cognitive behavior therapy was superior to usual care and supportive stress management on the BDI at 3 months and to usual care at 9 months. Supportive stress management was also superior to usual care at 3 months, but not at subsequent times. Planned subgroup analyses revealed nonsignificant group × depression diagnosis × time interactions on the HAM-D ( $P = .06$ ) and the BDI ( $P = .08$ ), suggesting that the effects of active treatment were similar regardless of whether major or minor depression was present at baseline. However, post hoc tests revealed that within the usual care arm, patients with minor depression at baseline tended to improve over time, but those with major depression tended to remain depressed.

#### OTHER SECONDARY OUTCOMES

As shown in **Table 3**, CBT was superior to usual care on the Beck Anxiety Inventory, Beck Hopelessness Scale, Perceived Stress Scale, and the SF-36 mental component

**Table 3. Secondary Outcomes in Patients Who Underwent Coronary Artery Bypass Surgery<sup>a</sup> (continued)**

Measure	Covariate-Adjusted Least-Squares Mean (SE)			Group		Time		Group × Time		AD	
	CBT (n=41)	SSM (n=42)	UC (n=40)	F Test	P Value	F Test	P Value	F Test	P Value	F Test	P Value
HSQ Vitality											
Baseline	10.7 (0.7)	10.8 (0.7)	11.1 (0.7)	$F_{2,120} = 1.62$	.20	$F_{1,118} = 103.49$	<.001	$F_{2,118} = 4.58$	.01	$F_{1,205} = 2.09$	.15
3 mo <sup>b,c</sup>	16.9 (0.7)	16.4 (0.7)	14.1 (0.7)								
HSQ Dysphoric Mood											
Baseline	16.9 (0.6)	17.1 (0.6)	17.2 (0.6)	$F_{2,121} = 2.42$	.09	$F_{1,120} = 87.21$	<.001	$F_{2,119} = 2.40$	.10	$F_{1,198} = 9.91$	.002
3 mo <sup>b</sup>	11.5 (0.6)	12.7 (0.6)	14.3 (0.7)								
HSQ Irritability											
Baseline	16.9 (0.6)	17.7 (0.6)	17.5 (0.6)	$F_{2,123} = 2.34$	.10	$F_{1,121} = 88.09$	<.001	$F_{2,120} = 2.50$	.09	$F_{1,213} = 9.48$	.002
3 mo <sup>b</sup>	12.3 (0.6)	13.3 (0.7)	15.0 (0.7)								
HSQ Cognitive Impairment											
Baseline	17.6 (0.6)	18.2 (0.6)	17.5 (0.6)	$F_{2,121} = 1.80$	.17	$F_{1,119} = 43.40$	<.001	$F_{2,119} = 4.77$	.01	$F_{1,210} = 3.05$	.08
3 mo <sup>b,c</sup>	13.8 (0.6)	14.7 (0.6)	16.6 (0.7)								
Short Blessed Test											
Baseline	3.8 (0.5)	3.5 (0.5)	3.0 (0.5)	$F_{2,118} = 0.87$	.42	$F_{1,113} = 0.01$	.93	$F_{2,112} = 0.01$	.99	$F_{1,236} = 0.05$	.82
3 mo	3.7 (0.5)	3.5 (0.5)	3.0 (0.5)								
Digit Symbol Test											
Baseline	49.1 (2.7)	50.7 (2.5)	50.1 (2.7)	$F_{2,115} = 0.55$	.58	$F_{1,96} = 23.37$	<.001	$F_{2,94} = 2.47$	.09	$F_{1,154} = 0.24$	.62
3 mo	51.6 (2.7)	56.7 (2.6)	53.4 (2.7)								
Paragraph recall											
Baseline	13.3 (0.7)	14.8 (0.7)	13.5 (0.7)	$F_{2,115} = 2.15$	.12	$F_{1,110} = 15.83$	<.001	$F_{2,109} = 0.02$	.98	$F_{1,196} = 0.09$	.77
3 mo	11.5 (0.7)	12.2 (0.7)	11.9 (0.7)								
Part B of the Trailmaking Test, s											
Baseline	149.5 (8.8)	140.0 (8.4)	143.4 (8.9)	$F_{2,114} = 0.43$	.65	$F_{1,99} = 15.62$	<.001	$F_{2,97} = 0.08$	.93	$F_{1,206} = 0.05$	.83
3 mo	130.6 (8.7)	118.3 (8.8)	125.8 (8.9)								

Abbreviations: AD, antidepressant; BDI, Beck Depression Inventory; CBT, cognitive behavior therapy; HAM-D, Hamilton Rating Scale for Depression; HSQ, Heart Surgery Questionnaire; SF-36, Short-Form 36-item Health Survey; SSM, supportive stress management; UC, usual care.

<sup>a</sup>The *P* values are for type 3 fixed effects of group, time, group × time interaction, and antidepressant use, based on a mixed model. For the planned contrasts, the significance threshold is *P* < .05 per comparison.

<sup>b</sup>Cognitive behavior therapy was not equal to UC in planned contrast.

<sup>c</sup>Supportive stress management was not equal to UC in planned contrast.

<sup>d</sup>Cognitive behavior therapy was not equal to SSM in planned contrast.

score. Supportive stress management was superior to usual care at 9 months on the Beck Anxiety Inventory, the Perceived Stress Scale, and the SF-36 mental component score. Neither CBT nor usual care affected the SF-36 physical component score. Neither intervention had an effect on any of the objective neuropsychological tests, yet both were superior to usual care in decreasing perceived cognitive impairment on the HSQ. Compared with usual care, both interventions also yielded higher scores on the HSQ Vitality subscale, and CBT yielded lower scores on the HSQ Dysphoric Mood and Irritability subscales.

Change in score correlations were examined to clarify the discrepancy between the objective and subjective neuropsychological outcomes. Change in HSQ Perceived Cognitive Impairment did not correlate with any objective neuropsychological measure, but it correlated strongly with change in HAM-D ( $r_{112} = 0.57, P < .001$ ), BDI ( $r_{112} = 0.48, P < .001$ ), Beck Anxiety Inventory ( $r_{112} = 0.40, P < .001$ ), Beck Hopelessness Scale ( $r_{112} = 0.36, P < .001$ ), and SF-36 mental component ( $r_{112} = -0.55, P < .001$ ) scores.

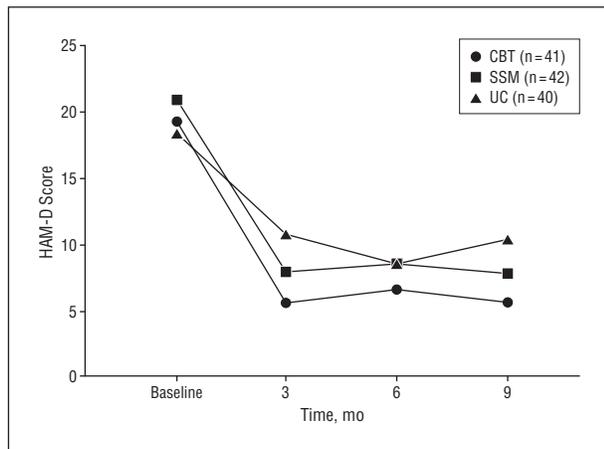
Nonstudy antidepressant use did not affect the depression outcomes, as assessed by the HAM-D and the BDI, but it did have significant effects on dysphoric and irritable mood according to the HSQ. It did not affect any of the other secondary outcomes.

## TREATMENT PROCESS MEASURES

There were higher scores in the CBT than in the supportive stress-management arm on the Cognitive Therapy Scale (mean [SD], 55.5 [5.4] vs 27.7 [4.7],  $P < .001$ ) and the CSPRS Cognitive Therapy subscale (147.6 [15.3] vs 62.8 [8.0],  $P < .001$ ). In contrast, scores were higher in the supportive stress-management (34.1 [7.4]) than in the CBT (6.8 [4.9]) arm on the Stress Management Scale ( $P < .001$ ). The groups did not differ on the Burns Empathy Scale, a measure of the patient's perception of the quality of the therapeutic relationship (supportive stress management, 14.9 [2.0]; CBT, 15.0 [0.6];  $P = .71$ ). They also did not differ by scores on the Treatment Process Scale, a measure of the therapist's perception of the therapeutic relationship and of the therapy process (supportive stress management, 45.5 [11.4]; CBT, 43.9 [5.2];  $P = .41$ ).

## COMMENT

This study was the first randomized, controlled trial for depression after coronary bypass surgery. We found that CBT was superior to usual care with respect to improvement in depression, defined as higher remission rates ac-



**Figure 2.** Hamilton Rating Scale for Depression (HAM-D) scores at baseline, posttreatment (3 months), and at 6- and 9-month follow-ups. Both treatment arms were superior to usual care (UC) at 3 and 9 months in Tukey-adjusted planned contrasts. CBT indicates cognitive behavior therapy; SSM, supportive stress management.

cording to the HAM-D and lower 3-month HAM-D scores. There were no differences between CBT and usual care in depression outcomes at 6 months, but these groups differed once again at 9 months. Sustained remission during the 3-, 6-, and 9-month assessments was also significantly more common in the CBT and supportive stress-management arms than in the usual care arm. The results were similar on the BDI. Minor depression tended to improve in patients who received only usual care but more slowly and to a lesser extent than in the CBT arm. In contrast, major depression tended to improve in the CBT arm but not among patients who received only usual care. Furthermore, the gains achieved in CBT were largely maintained throughout the 9 months, but relapse was relatively common in the usual care arm by 9 months. Cognitive behavior therapy was also superior to usual care on most secondary psychological outcomes, including anxiety, hopelessness, perceived stress, and the mental (but not the physical) component of health-related quality of life. On most of these measures, differences between CBT and usual care were found at all 3 follow-up assessments.

The supportive stress-management outcomes were encouraging, but not as favorable as those in the CBT arm. Supportive stress management was superior to usual care on the HAM-D at 3 months as well as on the BDI, but significant differences were not found at 6 or 9 months. Supportive stress management was also superior to usual care at 9 months with respect to anxiety, perceived stress, and the mental component of health-related quality of life, but there were no between-group differences at 3 or 6 months.

The groups did not differ by Burns Empathy Scale or Treatment Process Scale scores. The scores on these measures were relatively high, suggesting that the participants and therapists in both active treatment arms were generally pleased with the quality of the therapeutic relationship. This commonality may help to explain why both interventions were efficacious, despite the differences between them. On the other hand, more supportive stress-management than CBT participants dropped

out of the intervention, and the mean number of sessions was smaller in the supportive stress-management than the CBT arm. The patients who dropped out of supportive stress management tended to do so after about 4 to 6 sessions. In some cases, patients reported that they felt sufficiently confident in their stress-management skills that they expected additional sessions to yield diminishing benefits. This suggests that it might be better to reduce the length of supportive stress management to 4 to 6 weeks. Alternatively, a supportive stress-management module could be incorporated into a more comprehensive cognitive behavioral intervention.

Approximately half of the patients in all 3 arms were taking nonstudy antidepressants. Antidepressant use did not have detectable effects on the depression outcomes, though it was associated with improvements in dysphoric and irritable mood, as measured by the HSQ. These results must be considered with caution, because the antidepressant therapy was not determined by random assignment and because it was represented in the outcome analysis only as a binary indicator of use vs nonuse without regard to the dosage, type of antidepressant, or patient adherence. Nevertheless, these findings suggest the need for further investigation of the efficacy of antidepressant therapy for post-CABG depression.

The average participant's neuropsychological test scores were consistent with very mild cognitive impairment at baseline and slight improvement during 3 months. Neither intervention had any discernible effects on objective neuropsychological test performance, yet patients in both the CBT and supportive stress-management arms had lower perceived cognitive impairment at 3 months than those in the usual care group. Furthermore, improvement in perceived cognitive impairment correlated with improvement in depression but not with change in neuropsychological functioning. This raises 2 possibilities. One is that treatment for depression may help patients feel better about their cognitive functioning after CABG surgery, even if it does not actually improve. The other is that depression affects cognitive functioning after CABG surgery in ways that are not captured by the neuropsychological tests used in this study. Either way, improvement in perceived cognitive functioning is a collateral benefit of treatment for post-CABG depression. It should also be noted that recent controlled studies have raised doubts about whether the CABG operation itself is responsible for any of the neurocognitive decline that has been observed after bypass surgery.<sup>54-56</sup>

Transportation barriers were the primary reason for exclusion in approximately 40% of the patients who were screened for eligibility. Many patients have to travel far to undergo CABG surgery at major regional medical centers, and they are unable to return for weekly psychotherapy sessions. In several recent cognitive behavioral intervention trials, some or all of the sessions were conducted by telephone.<sup>17,57-61</sup> This is a promising strategy for patients who live too far away or are too ill to travel to an outpatient clinic for weekly sessions.

This study had several limitations. First, it was slightly underpowered for comparisons between the active treatment and control arms, and there was insufficient statistical power for comparisons of the 2 active treatment

arms. Cognitive behavior therapy was more consistently superior to usual care on most measures than was supportive stress management, but a larger trial would be needed to establish whether CBT is clearly superior to supportive stress management. Second, as in most behavioral trials, double-blinding was not possible. However, the outcome assessors were masked to the patient's baseline data and group assignment. Third, the outcomes were not measured continuously. It is possible that undetected relapses of depression or other clinically relevant developments may have occurred in the intervals between the 3-, 6-, and 9-month assessments. Consequently, it is possible that some of the patients who were classified as having a sustained remission of depression might have experienced brief, undetected relapses in the intervals between the follow-up evaluations. Finally, owing to logistical constraints, the protocol did not include maintenance therapy sessions. The 6- and 9-month outcomes might have been better if maintenance sessions had been included.

In conclusion, this randomized, controlled trial showed that CBT was an efficacious treatment for depression in patients with a recent history of coronary bypass surgery. Supportive stress management was also superior to usual care for depression in these patients, but it had smaller and less durable effects than CBT. Nonstudy antidepressant medications, obtained in approximately half of the participants in all 3 arms of the trial, had no significant effect on depression outcomes. Cognitive behavior therapy was superior to usual care on other psychological outcomes, including anxiety, hopelessness, and perceived stress. Neither intervention affected objective neuropsychological performance, but perceived cognitive functioning improved as depression improved.

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