Telephone-Delivered Collaborative Care for Treating Post-CABG Depression: A Randomized Controlled Trial

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Telephone-Delivered Collaborative Care for Treating Post-CABG Depression
A Randomized Controlled Trial

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CORONARY ARTERY BYPASS graft (CABG) surgery is one of the most common and costly medical procedures performed in the United States.1 Its main indications are the relief of angina and improvement in quality of life.2 Yet as many as half of post-CABG patients report depressive symptoms in the perioperative period,3 are more likely to experience a decreased health-related quality of life (HRQL) and functional status,4 continued chest pains,5,6 and increased rates of rehospitalization and death following CABG surgery independent of cardiac status, medical comorbidity, or the extent of surgery.7,11

Although the mechanism whereby depression affects post-CABG outcomes remains unknown,12 widely generalizable strategies to detect and effectively treat post-CABG depression are of great interest. Several treatment trials for depression have been conducted in cardiac populations, but most achieved less than anticipated benefits with regard to reducing mood symptoms13-19 or cardiovascular morbidity.13,16,19,20 Moreover, none used the proven effective collaborative care approach21 recently recommended by a National Institutes of Health expert consensus panel.22

Unlike earlier interventions that used a single antidepressant,3,15,17,18 counseling modality,20 or antidepressant in combination with counseling for treating cardiac patients with depression,14,19 collaborative care emphasizes a flexible real-world treatment package that involves active follow-up by a nonphysician care manager who adheres to evidence-based...

Context Depressive symptoms commonly follow coronary artery bypass graft (CABG) surgery and are associated with less positive clinical outcomes.

Objective To test the effectiveness of telephone-delivered collaborative care for post-CABG depression vs usual physician care.

Design, Setting, and Participants Single-blind effectiveness trial at 7 university-based and community hospitals in or near Pittsburgh, Pennsylvania. Participants were 302 post-CABG patients with depression (150, intervention; 152, usual care) and a comparison group of 151 randomly sampled post-CABG patients without depression recruited between March 2004 and September 2007 and observed as outpatients until June 2008.

Intervention Eight months of telephone-delivered collaborative care provided by nurses working with patients’ primary care physicians and supervised by a psychiatrist and primary care physician from this study.

Main Outcome Measures Mental health–related quality of life (HRQL) measured by the Short Form-36 Mental Component Summary (SF-36 MCS) at 8-month follow-up; secondary outcome measures included assessment of mood symptoms (Hamilton Rating Scale for Depression [HRS-D]), physical HRQL (SF-36 PCS), and functional status (Duke Activity Status Index [DASI]); and hospital readmissions.

Results The intervention patients reported greater improvements in mental HRQL (all P < .02) (SF-36 MCS: \( \Delta \), 3.2 points; 95% confidence interval [CI], 0.5-6.0), physical functioning (DASI: \( \Delta \), 4.6 points; 95% CI, 1.9-7.3), and mood symptoms (HRS-D: \( \Delta \), 3.1 points; 95% CI, 1.3-4.9) and were more likely to report a 50% or greater decline in HRS-D score from baseline (50.0% vs 29.6%; number needed to treat, 4.9 [95% CI, 3.2-10.4]) than usual care patients (P < .001). Men with depression were particularly likely to benefit from the intervention (SF-36 MCS: \( \Delta \), 5.7 points; 95% CI, 2.2-9.2; P = .001). However, the mean HRQL and physical functioning of intervention patients did not reach that of the nondepressed comparison group.

Conclusion Compared with usual care, telephone-delivered collaborative care for treatment of post-CABG depression resulted in improved HRQL, physical functioning, and mood symptoms at 8-month follow-up.

Trial Registration clinicaltrials.gov Identifier: NCT00091962

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treatment protocols, supports patients with timely education about their illness, considers patients’ prior treatment experiences and current preferences, teaches self-management techniques, actively involves primary care physicians in their patients’ care through regular exchanges of real-time information, proactively monitors treatment responses and suggests adjustments when indicated, and facilitates comanagement or transfer of care to local mental health specialists when patients do not respond to treatment, have clinically complicated cases, or upon request by the patient or primary care physician.23,24

This report presents the main findings from Bypassing the Blues, the first randomized trial of a collaborative care strategy for treating depression following an acute cardiac event.

METHODS

Patients

We screened post-CABG patients for depression prior to hospital discharge at 2 university-affiliated and 5 community hospitals in metropolitan Pittsburgh, Pennsylvania. We implemented a protocol approved by the institutional review board of the University of Pittsburgh, each participating hospital, and an independent data and safety monitoring board appointed by our funding agency.25 From March 2004 to September 2007, trained nurse recruiters identified medically stable patients who had recently undergone CABG surgery and obtained their signed informed consent to undergo screening procedures for this study.

Nurse recruiters administered the 2-item Patient Health Questionnaire (PHQ-2)26 and considered an affirmative answer to either item as a positive depression screen.27 We required patients to have a Folstein Mini-Mental State Examination28 score of 24 or greater as evidence of mental competence to provide consent; have no current alcohol dependence or other substance abuse disorder; not be in treatment with a mental health specialist, express active suicidality, or have a history of psychotic illness or bipolar disorder; be discharged home or to short-term rehabilitation; and to speak English, have no communication barriers, and have telephone access. Upon verification of these eligibility requirements, nurses from the study obtained the patients’ signed informed consent permitting us to contact them following hospital discharge to confirm protocol eligibility prior to randomization. Via oral and via mail communication, we encouraged all PHQ-2 screen–positive patients to contact their primary care physician to discuss this clinical finding.

Mood symptoms commonly follow CABG procedures and may represent the normal sequelae of surgery (eg, fatigue, sleeplessness).29 To confirm that patients were still protocol eligible 2 weeks after hospital discharge, we administered the PHQ-9 via telephone.30 Patient scores of 10 or greater confirmed the prior PHQ-2 screen results and indicated at least a moderate level of depressive symptoms.27

Assessments and Outcome Measures

Nurse recruiters collected information on patients’ self-reported race (according to categories provided by research staff)31 and sociodemographic characteristics, and conducted a detailed medical record review of comorbid medical conditions, extent of surgery, and medication use. Following confirmation of protocol eligibility at 2 weeks and at 2-, 4-, and 8-month follow-up, blinded telephone assessors administered the 36-item Short Form (SF-36)32,33 to determine general mental (Mental Health Component Scale [MCS]) and physical (Physical Health Component Scale [PCS]) HRQL; the 12-item Duke Activity Status Index (DASI)34 to determine disease-specific physical functioning; and the 17-item Hamilton Rating Scale for Depression (HRS-D) to track mood symptoms.35

Minimally clinically important changes have been defined as improvements of 3 or more points or 0.25 effect size improvements36,37 on these measures,34,38 and a meaningful recovery from depression as a 50% or greater reduction from baseline symptoms.39 We selected the SF-36 MCS as our primary outcome measure because it assesses a wider domain of functioning and is more extensively used as an outcome measure among cardiac patients than the HRS-D or any other mood questionnaire. We also administered the PRIME-MD mood and anxiety modules to determine the presence of major depression and an anxiety disorder, respectively.40

Following the 2-week baseline assessment and after each of the 3 follow-up contacts, we mailed participants a $20 check for their time ($80/patient).

Assessors inquired about any hospitalizations patients experienced since their last assessment. In the event of hospitalizations or death, relevant medical records, death certificates, or both were sought and forwarded to 2 physicians for independent review and classification (end point classification committee). When not in complete agreement, the event was discussed at a meeting and adjudicated by consensus. We also abstracted and quantified process measures of depression care from the electronic registry used by our care managers to document treatment.23

Randomization Procedure

Following confirmation of protocol eligibility and completion of the 2-week assessment, we randomized patients with depression to the intervention group or the usual care group in a 1:1 ratio in blocks of 4 according to a computer-generated random assignment sequence stratified by hospital site, prepared in advance by our statistician (S.M.), entered into the computer-assisted telephone interview program used by our assessors, and concealed until after the 2-week telephone call. A nurse or project coordinator from the study then informed patients of their treatment assignment and notified their primary care physician.

Nondepressed Comparison Group

We randomly sampled approximately 1 PHQ-2 screen–negative patient who was not using an antidepressant and met all other protocol eligibility criteria for every 2 randomized post-CABG study patients with depression, stratified by par-
ticipating hospital and sex, and oversampled by race. Later, the patient was required to score less than 5 on the 2-week PHQ-9 to continue participation.

**Intervention**

As described elsewhere, a nurse care manager telephoned intervention patients to review their psychiatric history, provide basic psychoeducation about depression and its effect on cardiac disease, and describe treatment options. Treatment options included providing a workbook to enhance patients' knowledge and ability to self-care for depression, initiation or adjustment of antidepressant pharmacotherapy prescribed under their primary care physician's direction; watchful waiting for mildly elevated mood symptoms; or referral to a local mental health specialist (psychologist or psychiatrist).

**Case Review**

After the initial contact, the nurse care manager presented the patient's clinical information to the study psychiatrist (C.F.R.) and internist (B.L.R.) at a weekly case review session focused on newly randomized patients and those with severe mood symptoms. The data included an overview of each patient's clinical course including serial PHQ-9 scores, pharmacotherapy usage, workbook chapters covered, mental health specialist referral status, and additional details to inform decision making (eg, prior antidepressant use and individual PHQ-9 item scores).

Following a case discussion, the clinical management team formulated treatment recommendations consistent with each patient's prior experiences, current treatment preferences, and insurance coverage. The nurse conveyed these recommendations to the patient via telephone and to the patient's primary care physician for consideration via fax, telephone, or mail depending on the urgency, and updated the study team about the patient's progress at the next case review session.

**Antidepressant Pharmacotherapy**

Selective serotonin reuptake inhibitor (SSRI) antidepressants are considered safe for use in cardiac patients, with no evidence indicating superior efficacy for treatment-naive patients. Therefore, for those lacking a history of prior SSRI use or brand preference, we typically recommended citalopram because it has limited drug interactions with other medications, requires few dosage adjustments, and is available in generic form. For patients with depression already using an SSRI, we advised a dosage increase or a switch to another SSRI if they were taking the maximum amount. We generally recommended 2 SSRI trials before switching to a serotonin norepinephrine reuptake inhibitor or bupropion, ie, other antidepressants with low cardiovascular toxicity.

Primary care physicians prescribed and approved all adjustments to their patients' pharmacotherapy and we dispensed no medications. However, the nurses offered to telephone antidepressant prescriptions to patients' pharmacies under the primary care physicians' verbal orders to promote adherence with our treatment recommendations.

**Mental Health Referral**

We advised referral to a local mental health specialist in the event of poor treatment response, severe psychopathology, complex psychosocial problems, or patient preference. The care manager offered to assist by identifying a clinician within the patient's insurance network, facilitating the initial appointment, or both. Following the date of the scheduled visit, the nurse contacted the patient to confirm the appointment was kept and telephoned monthly to monitor mood symptoms and promote adherence with follow-up appointments.

**Follow-up**

During the acute phase of treatment, the care manager telephoned patients every other week to review lesson plans, monitor antidepressant pharmacotherapy, administer the PHQ-9 to assess treatment response, encourage follow-up with the primary care physician and mental health specialist, and inform the patient of new treatment recommendations generated at the weekly case review sessions. Depending on the patient's treatment choice(s), symptoms, and motivation, these telephone contacts lasted 15 to 45 minutes and continued for 2 to 4 months. The patient subsequently transitioned to the continuation phase of care during which the care manager made contact every 1 to 2 months until completion of the 8-month intervention.

**Usual Care**

For ethical reasons, we informed usual care patients of their depression status, as well as their primary care physicians. However, we provided no treatment advice unless we detected suicidality on a follow-up assessment.

**Blinding**

Telephone assessors were blinded to patients' randomization and baseline depression status and they precautioned patients at the beginning of each call not to divulge their treatment assignment. Given the nature of our intervention, neither patients nor their primary care physicians were blinded to the treatment assignment.

**Data and Safety Monitoring**

We programmed our data management system to identify intervention patients in whom the blinded HRS-D scores increased by 25% or more above their 2-week baseline score; and comparison participants who scored 10 or more on the HRS-D. If indicated following a review, we wrote to the primary care physician and offered to identify local mental health specialists and provide additional depression treatment advice. Whenever staff detected suicidality, they were instructed to immediately contact a study psychiatrist to determine the level of threat and convey treatment advice to the patient and respective primary care physician.

**Statistical Analyses**

Women may derive less benefit from CABG surgery than men, and women with depression exposed to a psychosocial

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3790 Patients post-CABG signed HIPAA consents

733 Not approached for study participation
418 Time constraint
57 Deceased/medical complications
258 Other

3057 Approached for study participation

572 Refused screening

2485 Completed the PHQ-2

1387 Had a positive PHQ-2 screen result

119 Excluded
24 Refused consent
96 ineligible
45 MMSE score < 24
24 Receiving mental health treatment
15 Alcohol abuse
5 Bipolar disorder
3 Substance abuse
3 Communication barrier

1098 Had a negative PHQ-2 screen result

800 Excluded
647 Randomly excluded
58 Refused consent
95 ineligible
85 Prior MDD treatment
7 MMSE score < 24
1 Substance abuse
1 Receiving mental health treatment
1 Communication barrier

1268 Consented to participate in study

127 Not interested in study participation
35 Medical complications
6 Ineligible

1100 Completed 2-wk PHQ-9

763 Ineligible PHQ-9 score
352 Scored 5-9
411 Scored 0-4

2037 Had PHQ-9 score ≥ 10

385 Excluded
28 Not interested in study participation
7 Medical complications

302 Completed baseline assessment

302 Patients with depression randomized

150 Randomized to the intervention group
152 Randomized to receive usual care

150 Randomized to intervention group
152 Randomized to receive usual care

2-mo Assessment
121 Assessed
15 Unable to contact
7 Refused assessment
7 Dropped out

2-mo Assessment
136 Assessed
9 Unable to contact
6 Refused assessment
1 Dropped out

4-mo Assessment
123 Assessed
11 Unable to contact
8 Refused assessment
8 Cumulative drop-outs

4-mo Assessment
135 Assessed
8 Unable to contact
7 Refused assessment
2 Cumulative drop-outs

8-mo Assessment
126 Assessed
9 Unable to contact
9 Refused assessment
9 Cumulative drop-outs
1 Deceased

8-mo Assessment
126 Assessed
13 Unable to contact
9 Refused assessment
4 Cumulative drop-outs
0 Deceased

150 Included in primary analysis

151 Assigned to comparison group (without depression)

151 Assigned to comparison group
160 Had PHQ-9 score < 5
9 Excluded
4 Not interested in study participation
5 Other

151 Completed baseline assessment

2-mo Assessment
130 Assessed
9 Unable to contact
5 Refused assessment
2 Dropped out

4-mo Assessment
142 Assessed
4 Unable to contact
2 Refused assessment
2 Cumulative drop-outs
1 Deceased

8-mo Assessment
141 Assessed
2 Unable to contact
3 Refused assessment
2 Cumulative drop-outs
3 Cumulative deceased

151 Included in primary analysis

CABG indicates coronary artery bypass graft; HIPAA, Health Insurance Portability and Accountability Act; MDD, major depressive disorder; MMSE, Mini-Mental State Examination; PHQ, Patient Health Questionnaire. Overall, 13% of patients (60/453) did not complete their 8-month telephone assessment. Missed assessments for any reason did not differ by randomization or baseline depression status. Reasons for withdrawal among randomized patients were mostly at patients' request or loss of follow-up.
intervention following myocardial infarction may experience less positive cardiac outcomes than women exposed to a control condition. Therefore, we powered our trial to conduct an intent-to-treat analysis within each sex on the SF-36 MCS, our primary outcome measure. The trial was not powered for a treatment by sex analysis. We hypothesized our intervention would produce a 0.5 or greater effect size improvement on the SF-36 MCS vs usual care at 8-month follow-up.

### Table 1. Baseline Sociodemographic, Clinical, and Mental Health Characteristics by Randomization Status and Baseline Depression Status

<table>
<thead>
<tr>
<th></th>
<th>With Depression (n = 150)a</th>
<th>Usual Care (n = 152)a</th>
<th>P Value</th>
<th>Without Depression (n = 151)b</th>
<th>P Valueb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>64 (10.8)</td>
<td>64 (11.2)</td>
<td>.44</td>
<td>66 (9.6)</td>
<td>.03</td>
</tr>
<tr>
<td>Men</td>
<td>54 (81)</td>
<td>63 (96)</td>
<td>.11</td>
<td>63 (95)</td>
<td>.38</td>
</tr>
<tr>
<td>White race</td>
<td>88 (132)</td>
<td>93 (142)</td>
<td>.13</td>
<td>81 (122)</td>
<td>.005</td>
</tr>
<tr>
<td>&gt;High school education</td>
<td>57 (86)</td>
<td>54 (82)</td>
<td>.55</td>
<td>52 (78)</td>
<td>.42</td>
</tr>
<tr>
<td>Married</td>
<td>64 (96)</td>
<td>69 (105)</td>
<td>.41</td>
<td>69 (104)</td>
<td>.84</td>
</tr>
<tr>
<td>Working, part-time or full-time</td>
<td>41 (61)</td>
<td>32 (49)</td>
<td>.07</td>
<td>38 (57)</td>
<td>.37</td>
</tr>
<tr>
<td>SF-36 MCS, mean (SD)c</td>
<td>43.2 (11.2)</td>
<td>42.8 (11.8)</td>
<td>.72</td>
<td>61.5 (5.8)</td>
<td>&lt;.001d</td>
</tr>
<tr>
<td>SF-36 PCS, mean (SD)c</td>
<td>31.3 (7.0)</td>
<td>30.2 (7.1)</td>
<td>.19</td>
<td>37.4 (7.4)</td>
<td>&lt;.001d</td>
</tr>
<tr>
<td>Duke Activity Status Index, mean (SD)c</td>
<td>7.1 (5.8)</td>
<td>7.7 (7.6)</td>
<td>.41</td>
<td>13.2 (6.4)</td>
<td>&lt;.001d</td>
</tr>
<tr>
<td>Perceived Social Support Scale, mean (SD)c</td>
<td>70.0 (10.6)</td>
<td>68.5 (11.2)</td>
<td>.36</td>
<td>73.2 (12.2)</td>
<td>&lt;.001d</td>
</tr>
<tr>
<td>Hypertension</td>
<td>87 (131)</td>
<td>80 (122)</td>
<td>.10</td>
<td>81 (122)</td>
<td>.43</td>
</tr>
<tr>
<td>Diabetes</td>
<td>40 (60)</td>
<td>45 (68)</td>
<td>.40</td>
<td>39 (59)</td>
<td>.50</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>85 (128)</td>
<td>77 (117)</td>
<td>.06</td>
<td>74 (112)</td>
<td>.09</td>
</tr>
<tr>
<td>Stroke</td>
<td>8 (12)</td>
<td>8 (12)</td>
<td>.97</td>
<td>5 (8)</td>
<td>.30</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>21 (32)</td>
<td>23 (35)</td>
<td>.72</td>
<td>9 (14)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Chronic renal insufficiency</td>
<td>13 (19)</td>
<td>7 (10)</td>
<td>.07</td>
<td>11 (16)</td>
<td>.74</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>49 (73)</td>
<td>44 (67)</td>
<td>.42</td>
<td>45 (68)</td>
<td>.79</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>28 (42)</td>
<td>20 (31)</td>
<td>.12</td>
<td>21 (31)</td>
<td>.38</td>
</tr>
<tr>
<td>Percent ejection fraction, mean (SD), N</td>
<td>51 (12.3)</td>
<td>50 (12.6)</td>
<td>.28</td>
<td>51 (13.0)</td>
<td>.92</td>
</tr>
<tr>
<td>Tobacco use in past year</td>
<td>25 (37)</td>
<td>30 (45)</td>
<td>.59</td>
<td>14 (21)</td>
<td>.005d</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>39 (59)</td>
<td>34 (52)</td>
<td>.36</td>
<td>28 (42)</td>
<td>.06</td>
</tr>
<tr>
<td>Aspirin</td>
<td>84 (126)</td>
<td>80 (121)</td>
<td>.32</td>
<td>81 (123)</td>
<td>.93</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>81 (122)</td>
<td>77 (117)</td>
<td>.35</td>
<td>82 (124)</td>
<td>.37</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>14 (21)</td>
<td>17 (26)</td>
<td>.46</td>
<td>12 (18)</td>
<td>.30</td>
</tr>
<tr>
<td>Lipid-lowering medication</td>
<td>73 (109)</td>
<td>67 (102)</td>
<td>.29</td>
<td>78 (118)</td>
<td>.05</td>
</tr>
</tbody>
</table>

Abbreviations: ACE, angiotensin-converting enzyme; CABG, coronary artery bypass graft; SF-36 MCS, Medical Outcomes Study Short Form Mental Component Scale; SF-36 PCS, Physical Component Scale; PHQ, Patient Health Questionnaire.

a Data are reported as No. (%) unless otherwise indicated.
bP value indicates depressed vs nondepressed patients.
cHigher scores indicate better health-related quality of life.
dHigher scores remain significant after using Hochberg method for multiple comparisons.
eHigher scores indicate more severe symptoms.
fPanic, generalized anxiety, or anxiety not otherwise specified.
We selected this time point to allow a therapeutic alliance to develop between patients and their care managers and sufficient time for several therapeutic trials, if necessary, of antidepressant pharmacotherapy and counseling to take effect. Randomizing 150 men (or women) with depression would provide 83% power to detect a medium effect size difference of 0.5 or greater using a 2-tailed α = .05 and assuming 10% attrition, and 80% power to detect an effect size of 0.3 or greater using our full sample (N = 300).

We compared baseline sociodemographic, clinical, and functional status measures by randomization and baseline depression status using t tests for continuous data, χ² analyses for categorical data, and controlling for multiple comparisons using the Hochberg method. To calculate changes in score and effect sizes on all randomized patients with depression with 95% confidence intervals (CIs), we used a repeated measures mixed-effect model with treatment, time (4 time points), and sex; all 2- and 3-factor interaction terms with subject intercepts were treated as a random effect to account for individual differences at randomization; and time was treated as a fixed-effect categorical variable. We used the restricted maximum likelihood inferential procedure to fit our mixed models under missing-at-random and unstructured covariance matrix assumptions; multiple imputation techniques to calculate missing 8-month HRS-D scores; χ² tests to compare differences in the proportions of patients who achieved a remission; and the number needed to treat using the reciprocal of the difference in response rates. Cumulative event rates were calculated using Kaplan-Meier survival analyses with log-rank χ² tests for determining statistical significance. All P values were 2-tailed with significance levels of .05 or less, and all statistical tests of outcomes measures were 2-group comparisons involving only randomized patient groups with depression. All analyses were performed using SAS statistical software (SAS Institute Inc, Cary, North Carolina) using the Proc Mixed function for calculation of effect size changes and scores.

**RESULTS**

Of the 2485 post-CABG patients consenting to our PHQ-2 depression screening procedure, 56% (1387) had positive screen results prior to hospital discharge.
Patients in the intervention and usual care groups were similar on all baseline clinical, sociodemographic, and surgical criteria (Table 1). However, compared with patients without depression, patients with depression tended to be slightly younger and were more likely to be nonwhite, have chronic obstructive pulmonary disease, use tobacco, and to report prior treatment for depression, and lower levels of HRQL and physical functioning (all \( P \leq .03 \)). Compared with depressed men, women with depression also reported higher rates of comorbid anxiety and prior depression treatment.

**Clinical Outcomes**

From baseline to 8-month follow-up, intervention patients achieved significant clinical improvements on the SF-36 MCS (3.2 points; 95% CI, 0.5-6.0; \( P = .02 \)) with an effect size of 0.30 (95% CI, 0.17-0.52; \( P = .01 \)) and also on our key secondary outcome measures compared with patients receiving usual post-CABG care (Table 2 and eFigure 1 [http://www.jama.com]). We detected no differences in outcomes by recruitment site from baseline to 8-month follow-up when comparing intervention patients with patients receiving usual post-CABG care. While these improvements became evident at 2-month follow-up (eFigure 2 [http://www.jama.com]), the mean level of HRQL and physical functioning for intervention patients never attained that of our comparison group of patients without depression. Overall, 50% (75/150) of intervention patients reported a 50% or greater reduction in mood symptoms from baseline to 8-month follow-up vs 29.6% (45/152) of patients in usual care, and the number needed to treat to produce 1 additional treatment response was 4.9 (95% CI, 3.2-10.4; Table 3).

**Clinical Outcomes by Sex**

At 8-month follow-up, men randomized to our intervention group (post-CABG patients with depression) reported a 5.7-point improvement (\( P = .001 \)) on the SF-36 MCS and improvements on our other key secondary measures (Table 2 and eFigure 1 [http://www.jama.com]). Overall, 60.5% (49/81) of men in the intervention group vs 33.3% (32/96) of men in the usual care group reported a 50% or greater reduction in HRS-D score from baseline to 8-month follow-up, while 37.7% (26/69) vs 23.2% (13/56) of women reported so (Table 3). Although we found a significant sex \( \times \) treatment interaction on the SF-36 PCS (\( F = 5.25, \) degrees of freedom = 1302, \( P = .02 \)), we did not identify any other sex \( \times \) treatment or 3-way (sex \( \times \) treatment \( \times \) time) interactions on our other outcome measures.

**Rehospitalizations**

By 8-month follow-up we identified 207 readmissions including 85 (41%) for cardiovascular causes (eTable 1 [http://www.jama.com]). Overall, 33% of intervention patients, 32% of usual care patients, and 25% of comparison patients were rehospitalized (eFigure 3 [http://www.jama.com]).

**Processes of Care Management**

Of the 150 patients in our 8-month intervention group, 83% had 3 or more telephone care manager contacts by 4-month follow-up and the median number of contacts was 10 (range, 0-28; eTable 2 [http://www.jama.com]). Although the number of contacts did not differ by sex, men were more likely to use the workbook (91% [74/81] vs 78% [54/69]; \( P = .02 \)), and women were more likely to use pharmacotherapy (59% [41/69] vs 43% [35/81]; \( P = .05 \)). Rates of self-reported pharmacotherapy use increased from baseline levels at all follow-up points; however, these rates were higher in intervention patients than in usual care ones. Furthermore, rates of mental health specialist care were low and did not differ by randomization status (eg, 4% in intervention patients vs 6% in usual care patients at 8-month follow-up).

**COMMENT**

Bypassing the Blues is the first clinical trial of a collaborative care strategy for treating depression following an acute cardiac event. We found collaborative care for treating post-CABG depression to improve mental HRQL and physical functioning and reduce mood symptoms at 8-month follow-up. The internal and external validity of our findings are strengthened by multiple design elements including a randomized study design with blinded assessments of outcomes; patient recruitment from both academically affiliated and community hospitals; use of a time-efficient depression case-identification strategy recommended by the American Heart Association; telephone delivery of our intervention; consideration of patients’ treatment preferences; and a stipulation that patients obtain antidepressant pharmacotherapy from their primary care physician and mental health specialist counseling at prevailing costs.

The observed effect size improvement on self-report measures such as the HRS-D...
is at the upper end reported by a meta-analysis of 37 collaborative care trials for primary care patients with depression (effect size, 0.25; 95% CI, 0.18-0.31) and resembles the effect size obtained from more intensive forms of psychotherapy and pharmacotherapy. The effectiveness of our treatment strategy also compares favorably to the effect size improvements in HRS-S scores reported by the SADHART trial (effect size, 0.14; -0.06 to 0.35), the citralopram group of the CREATE trial (effect size, 0.29; 0.05-0.52), the psychotherapy-based ENRICH trial (0.22; 0.11-0.33), and the counseling group of CREATE (-0.22; -0.46 to 0.01). Moreover, neither those trials nor any other trial investigating the effect of treating depression in patients with cardiovascular disease was linked to primary care, delivered primarily via telephone, and/or required patients to obtain their own pharmacotherapy and mental health specialist care at cost. Our findings and mode of intervention delivery thus have major public health implications for medically frail individuals, those living in rural settings, and other individuals with physical challenges impeding face-to-face depression treatment.

The generalizability of our study findings is limited because recruitment occurred in just one US region. Nevertheless, the sociodemographic and clinical characteristics of participants resembled those enrolled in other CABG studies. Additionally, nurse recruiters were required to obtain patients’ prior consent through a hospital staff member before they could initially approach to obtain consent to administer the PHQ-2. This potentially introduced a selection bias if patients with severe depression were less likely to participate in our screening procedures.

Since a substantial minority of patients did not benefit from our depression intervention, it is vital to identify post-CABG patients most likely to become treatment resistant so as to develop more effective treatments for them. Identifying the intervention components that maximally contribute to our outcomes is also of great interest. However, collaborative care is a complex intervention involving a number of separate mechanisms that have proven difficult to disentangle from the nonspecific effects of increased attention by the care manager.

CONCLUSIONS

Compared with usual care, telephone-delivered collaborative care for post-CABG depression can improve HRQL, physical functioning, and mood symptoms at 8-month follow-up. Additional research is necessary to develop improved treatments for women and patients with resistant depression, and to examine the economic effect of this intervention.

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Statistical analysis: Mazumdar.

Obtained funding: Rollman, Reynolds.

Administrative, technical, or material support: Rollman, Herbeck Belnap, LeManager, Counihan, Kapoor, Schulberg, Reynolds.

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Financial Disclosures: Dr Reynolds reports receiving pharmaceutical supplies for his National Institutes of Health (NIH)-sponsored work from Forest Laboratories, Pfizer, Bristol-Myers Squibb, Wyeth, and Eli Lilly. Dr Mazumdar reports stock ownership in Forest Laboratories.

The authors report no disclosures.

Funding/Sponsor: This work was supported by NIH grants R01 HL70000 (Dr Rollman) and P30 MH71944 (Dr Reynolds), and by the LMPAC Endowed Chair in Geriatric Psychiatry (Dr Reynolds). The Role of the Sponsor: The National Heart, Lung, and Blood Institute (NIH) and National Institute of Mental Health (NIMH) had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Bypassing the Blues Study Team: We wish to thank the members of our dedicated study team for their efforts: Erin August, RN,* Amy Boyles, MSW,* Lori Freund,* Lillian Giles, RN,* Kyle Holleran, BS,* Elizabeth Hunt, BS,* Cynthia Kravetz, BS,* Sabrina LeBoys,* Jessica Minzydzak,* Carol Mitchell, RN, BSN,* Eleanor Shirley, MA,* Susan Spillane, RN,* and Sharon Stover, RN,* and Fang Zhu, PhD* (University of Pittsburgh, Pittsburgh, Pennsylvania).

Consultants: We thank our study consultants Nancy Frasure-Smith, PhD (McGill University, Montreal, Canada); Kenneth E. Freedland, PhD* (Washington University, St Louis, Missouri); and Mark Hatley, MD* (Stanford University, Palo Alto, California) for their critical input particularly during the planning and implementation stages of our study.

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*Individuals who received compensation for their work in association with this article.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Heart, Lung, and Blood Institute.

Previous Presentations: Parts of this article were presented at the annual national meetings of the American Psychosomatic Society, Champaign, Illinois, March 5, 2009; Society for Behavioral Medicine, Montreal, Quebec, Canada, April 25, 2009; and Society for General Internal Medicine, Miami, Florida, May 14, 2009.

Additional Information: eTables 1 and 2 and eFigures 1, 2, and 3 are available at http://www.jama.com; other additional information is available at http://www.bypassingtheblues.pitt.edu.

Additional Contribution: We gratefully thank our NHLBI project officer, Susan Czajkowski, PhD, for her long-term support of our efforts.

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