Centralized, Stepped, Patient Preference–Based Treatment for Patients With Post–Acute Coronary Syndrome Depression

CODIACS Vanguard Randomized Controlled Trial

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Importance: Controversy remains about whether depression can be successfully managed after acute coronary syndrome (ACS) and the costs and benefits of doing so.

Objective: To determine the effects of providing post-ACS depression care on depressive symptoms and health care costs.

Design: Multicenter randomized controlled trial.

Setting: Patients were recruited from 2 private and 5 academic ambulatory centers across the United States.

Participants: A total of 150 patients with elevated depressive symptoms (Beck Depression Inventory [BDI] score ≥10) 2 to 6 months after an ACS, recruited between March 18, 2010, and January 9, 2012.

Interventions: Patients were randomized to 6 months of centralized depression care (patient preference for problem-solving treatment given via telephone or the Internet, pharmacotherapy, both, or neither), stepped every 6 to 8 weeks (active treatment group; n=73), or to locally determined depression care after physician notification about the patient’s depressive symptoms (usual care group; n=77).

Main Outcome Measures: Change in depressive symptoms during 6 months and total health care costs.

Results: Depressive symptoms decreased significantly more in the active treatment group than in the usual care group (difference between groups, -3.5 BDI points; 95% CI, -6.1 to -0.7; P=.01). Although mental health care estimated costs were higher for active treatment than for usual care, overall health care estimated costs were not significantly different (difference adjusting for confounding, $-325; 95% CI, $-2639 to $1989; P=.78).

Conclusions: For patients with post-ACS depression, active treatment had a substantial beneficial effect on depressive symptoms. This kind of depression care is feasible, effective, and may be cost-neutral within 6 months; therefore, it should be tested in a large phase 3 pragmatic trial.

Trial Registration: clinicaltrials.gov Identifier: NCT01032018


Depression will soon be the leading cause of years lived with disability worldwide and contributes even more to disability when comorbid with a chronic medical disorder. Every year, approximately 1.2 million Americans survive an acute coronary syndrome (ACS) event, and many have clinically significant and persistent depression. Patients with post-ACS depression have significantly more ambulatory medical appointments, emergency department visits, and higher health care costs than similar patients without depression. Post-ACS depression is also associated with a 150% increased risk of ACS recurrence and a 100% increase in the relative risk of all-cause mortality and persistent depression after an ACS event.
is associated with an even higher morbidity and mortality risk.\textsuperscript{3,12} Reducing persistent post-ACS depression is therefore an important public health objective.

Despite its importance, routine management of post-ACS depression remains poor\textsuperscript{2-13} because of inefficiencies in depression screening,\textsuperscript{12} lack of effective administration of depression treatment,\textsuperscript{12} weak depression treatment effects, and limited treatment options if initial efforts fail.\textsuperscript{14} Published trials have yet to demonstrate clinically significant depressive symptom reduction, have not tested strategies that would be feasible in clinical practice, are not cost-effective, and do not incorporate the preferences of patients after an ACS event for either psychotherapy or psychotropic medications into their treatment algorithms.\textsuperscript{15}

The Comparison of Depression Interventions after Acute Coronary Syndrome (CODIACS) Vanguard trial was designed to determine the feasibility, efficacy, and costs of a centralized, stepped, patient preference–based depression care system for individuals after an ACS event. This system provides depression treatment several months after an ACS, when most transient depressive reactions to ACS have spontaneously remitted but prognostic risk of ongoing depression symptoms is still high. It follows a treatment strategy that incorporates patient preference, adjusts treatment in a stepped manner as symptoms require, and centralizes the provision of care by highly trained depression specialists. We hypothesized that this approach would be cost-effective and produce larger reductions in depression than ad libitum or usual care provided in the patient’s community.

METHODS

SETTING AND STUDY PARTICIPANTS

Briefly, this study was a feasibility, parallel-group, comparative effectiveness randomized controlled trial (RCT), with masked outcome assessments, in patients with persistent depressive symptoms following an ACS event. The study tested whether centralized, patient preference–based depression care is cost-effective and results in larger depressive symptom reductions compared with locally administered, ad libitum depression care. Participants were recruited from sites connected with 5 field centers (Columbia University, New York, New York; Washington University, St Louis, Missouri; University of Pennsylvania, Philadelphia; Emory University, Atlanta, Georgia; and Yale University, New Haven, Connecticut) from March 18, 2010, to January 9, 2012. To be eligible, participants had to demonstrate elevated depressive symptoms on the Beck Depression Inventory I (BDI)\textsuperscript{16} (BDI score $\geq 10$ on 2 screening occasions or $\geq 13$ on 1 occasion) 2 to 6 months after hospitalization for an ACS (ie, unstable angina or myocardial infarction) defined by standard criteria.\textsuperscript{17,18} Participants had to be at least 35 years old, and be fluent in English or Spanish. Exclusion criteria were set for safety, retention, or intervention futility reasons (see Whang et al\textsuperscript{19} for details). The CODIACS Vanguard evaluated different recruitment strategies at different sites; details about each site's recruitment strategy and our conclusions about the most efficient recruiting strategy can be found elsewhere.\textsuperscript{19} Briefly, automated searches of electronic medical records were conducted at most sites to identify patients who met the trial’s ACS and other medical criteria. Potential participants were then approached by a research coordinator or physician for further screening. Institutional review board–approved, written informed consent for participation was obtained before the screening interview and before randomization.

RANDOMIZATION

Participants were randomized in a 1:1 ratio according to a computer-generated, permuted-block randomization scheme, stratified by site and current antidepressant use, that local research assistants accessed by telephone. Patients were randomized to receive 6 months of centralized, stepped, patient preference–based treatment (active treatment group) or locally administered, ad libitum depression care (usual care group). If randomized to the active treatment group, an unmasked research assistant met with the participant to discuss the relative benefits and risks of psychotherapy and medication use, and the participant’s initial choice was then provided.

OUTCOME MEASURES AND MASKING

Research assistants who were masked to randomization administered the BDI and ascertained adverse events, mental health and hospitalization information, and medication use at baseline and 6 months during in-person interviews and at 2 and 4 months by telephone. Patients and clinicians were not masked to group status.

TREATMENT GROUPS

The active treatment was provided by a team of professionals, including a centralized problem-solving treatment (PST) therapists (E.D. and V.M.), centralized psychiatry and clinical psychology supervisors (M.M.B. and P.A.S.), and a local study physician or advanced practice registered nurse responsible for prescribing and managing antidepressant medications. The team met weekly to discuss clinical issues, treatment quality reviews, and stepped care decisions for the active treatment participants.\textsuperscript{20} The Patient Health Questionnaire 9 (PHQ-9)\textsuperscript{21} was administered to participants at each study treatment session to monitor depressive symptoms and determine symptom improvement relative to baseline. If the minimum prespecified improvement criterion (see Whang et al\textsuperscript{19} for details) had not been achieved during the step period (6-8 weeks), the team offered suggestions for subsequent treatment to the clinician, and additional or alternative treatments were subsequently initiated with patient agreement. Additional treatment steps were made every 6 to 8 weeks with the aim of achieving the criterion of depression treatment success (PHQ-9 score $\leq 3$ for 2 consecutive weeks) by the end of the intervention. Depression symptom monitoring and maintenance therapy continued on a pre-specified schedule (weekly, then monthly) for the 6-month duration of the trial for those in the active treatment group who met the depression treatment success criteria.

In the intervention arm, participants chose PST, medication, both, or neither. Problem-solving treatment is an easily disseminated, manualized, problem-focused form of cognitive behavior therapy that teaches patients how to systematically solve self-identified psychosocial problems that can trigger and perpetuate depression.\textsuperscript{22} Initially, PST was administered over the Internet via interactive video calls between the recruiting site and the coordinating center, with subsequent sessions provided by video calls or telephone, either at the clinic or at the home, depending on patient preference.\textsuperscript{23} Participants who chose pharmacotherapy were interviewed by the local study physician or nurse practitioner, and the participant and local health care provider agreed on the appropriate medication (sertraline hydrochloride, citalopram hydrobromide, or bupropion hydrochloride) and dosage based
on the participant’s medication history and current symptoms. Medication dosing followed standard clinical practice. Participants were initially seen in person by the study physician or nurse at 1- to 2-week intervals for dose titration and every 3 to 5 weeks thereafter as needed. For participants who chose pharmacotherapy but who had already been prescribed a nonstudy antidepressant, subsequent treatment was coordinated with their initial prescribing practitioner.

In the usual care condition, the participant’s primary care physician and/or cardiologist was informed by letter about the participant’s participation in the trial and his or her depressive symptom level. The participant was free to obtain any depression care from that physician or another health care provider.

OUTCOMES

The primary outcomes were change in BDI scores over 6 months and health care costs. To estimate costs, we searched the National Death Index, actively surveyed hospital records for ACS events, and proactively queried participants about all hospitalizations, all ambulatory care visits, cardiac procedures, and total number of hospitalization days. Participants also completed the Medical Outcomes Study 12-Item Short Form Health Survey (SF-12) and the National Institutes of Health Patient Reported Outcomes Measurement Information System (PROMIS) anxiety short form at baseline and 6 months.19,23

STATISTICAL ANALYSIS

The trial was powered to detect a between-group difference in the 6-month change in depression symptoms. Assuming a 5% attrition rate, we estimated that a sample of 150 patients would be needed to have 80% power to detect a clinically meaningful differential change in depression scores between groups of 0.46 SD.20

Baseline differences between the active treatment and usual care groups were evaluated using the t test for continuous variables and the χ² test for categorical variables. Latent growth curve modeling procedures were used to generate full-information maximum-likelihood estimates of treatment effects for the entire cohort of trial participants and by subgroups. Primary analyses were conducted according to the intention-to-treat principle. Wald χ² statistics were used to test the significance of the differential change in depression symptoms between groups (group × time interaction). Because the distribution of BDI scores was positively skewed, all analyses were conducted using square-root transformed BDI scores, which were then back-transformed for ease of interpretation.

Logistic regression was used to determine whether exposure to active treatment was associated with increased risk of (1) depression remission (defined in the trial as a BDI score <10 at 6 months), (2) improvement in depressive symptoms (defined herein as ≥0.5-SD decrease on the BDI), (3) 30 or more total depression-free days during the 6-month intervention, (4) improvement in anxiety symptoms (≥0.5 SD on the PROMIS anxiety scale), and (5) improvements in mental and physical functional status (≥0.5 SD on the SF-12 mental and physical health scales). We calculated the number needed to treat (NNT) as the inverse of the absolute risk reduction associated with active treatment vs usual care for each outcome, and for depressive symptoms we calculated a Hedges’ g effect size. The effect size allows comparisons of the effect of an intervention across trials when different depression measures are used.

Ambulatory care costs were based on Current Procedural Terminology codes and Medicare’s Physician Fee Schedule for non–facility-based care, mental health costs on appointment duration, hospitalization costs on Medicare diagnosis-related–group hospital payments with an adjustment for physicians’ professional fees based on length of stay,26 and antidepressant and anxiolytic medication costs on the 2010 Red Book midrange average wholesale price for generic medications.27 All costs are presented in 2011 US dollars and adjusted to the US Consumer Price Index. To determine whether group assignment predicted cost outcomes, we conducted linear regression models, adjusted for age, sex, race/ethnicity, marital status, education, baseline BDI score, type of ACS, and left ventricular ejection fraction (see Ladapo et al28 for details). Cost data were positively skewed but we analyzed them with parametric models without a log transformation to facilitate a more natural interpretation, and because our inferences did not significantly change when a log-linear multivariate regression model was used.

RESULTS

STUDY PARTICIPANTS

Potential participants with ACS (n=724) were asked to participate in an eligibility interview; 177 patients (24.4%) were found to be eligible, and 150 were enrolled and randomly allocated (Figure 1): 73 to active treatment and 77 to usual care. Two participants in each group were lost to follow-up at 6 months, and 4 from each group (5.3% total) had missing 6-month depression data. Table 1 provides baseline demographic and clinical characteristics by group.
Table 1. Characteristics of 150 Patients With Acute Coronary Syndrome and Depression Symptoms

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Active Treatment (n = 73)</th>
<th>Usual Care (n = 77)</th>
<th>P Valueb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>59.2 (9.7)</td>
<td>60.0 (11.1)</td>
<td>.65</td>
</tr>
<tr>
<td>Female</td>
<td>30 (41.1)</td>
<td>33 (42.9)</td>
<td>.83</td>
</tr>
<tr>
<td>Hispanic</td>
<td>16 (21.9)</td>
<td>13 (16.9)</td>
<td>.42</td>
</tr>
<tr>
<td>African American</td>
<td>23 (31.5)</td>
<td>27 (35.1)</td>
<td>.64</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school degree</td>
<td>39 (60.9)</td>
<td>46 (67.6)</td>
<td>.61</td>
</tr>
<tr>
<td>College degree</td>
<td>21 (32.8)</td>
<td>17 (25.0)</td>
<td></td>
</tr>
<tr>
<td>Type of presenting acute coronary syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unstable angina</td>
<td>35 (47.9)</td>
<td>35 (45.5)</td>
<td></td>
</tr>
<tr>
<td>Non-ST-segment elevated myocardial infarction</td>
<td>18 (24.7)</td>
<td>19 (24.7)</td>
<td></td>
</tr>
<tr>
<td>ST-segment elevated myocardial infarction</td>
<td>19 (26.0)</td>
<td>21 (27.3)</td>
<td>.95</td>
</tr>
<tr>
<td>Bundle branch block/un certain type of myocardial infarction</td>
<td>1 (1.4)</td>
<td>2 (2.6)</td>
<td></td>
</tr>
<tr>
<td>Left ventricular ejection fraction ≤0.45c</td>
<td>18 (31.6)</td>
<td>13 (23.2)</td>
<td>.32</td>
</tr>
<tr>
<td>Beck Depression Inventory score ≥16 at baseline</td>
<td>52 (71.2)</td>
<td>50 (64.9)</td>
<td>.41</td>
</tr>
<tr>
<td>Ever prescribed antidepressant or antianxiety medicationd</td>
<td>43 (58.9)</td>
<td>42 (55.3)</td>
<td>.65</td>
</tr>
<tr>
<td>Use of antidepressants at time of enrollmentd</td>
<td>27 (37.0)</td>
<td>26 (33.8)</td>
<td>.68</td>
</tr>
</tbody>
</table>

aData are given as number (percentage) of study participants unless otherwise indicated.

bP values are based on the χ² test for categorical measures and independent sample t test for continuous measures.

cData on left ventricular ejection fraction at index hospitalization were available for only 113 patients (left ventricular ejection fraction not assessed, 36 patients; medical history form not received, 1 patient).

dFindings are based on self-reported data.

Figure 2. Comparison of the Comparison of Depression Interventions after Acute Coronary Syndrome (CODIACS) Vanguard trial with other trials of depression treatments in coronary heart disease and primary care patients.22,23,28,29 *This trial included participants with elevated depressive symptoms; other trials included only patients with major depressive disorder. It is also important to note that some of these trials had more active control conditions, leading possibly to smaller depression differences between groups. Full-information maximum-likelihood estimates were used to determine intention-to-treat treatment effects; other trials may have used other estimating methods. IPT indicates interpersonal psychotherapy; RCT, randomized controlled trial. A larger Hedges’ g indicates a stronger positive effect of the tested intervention. Vertical dashed lines indicate the 95% confidence intervals (CIs) for the Hedges’ g estimates from the 3 meta-analyses. Horizontal solid line indicates the 95% CI for each individual study.

STUDY TREATMENT

Of the 73 active treatment patients, 41 (56.2%) initially chose PST, 9 (12.3%) chose antidepressant medication, 17 (23.3%) chose both, and 6 (8.2%) chose neither. The mean number of PST sessions for those who initially chose PST was 7.7 (range, 1-25). Of the 77 patients randomized to usual care, 9 (11.7%) received psychotherapy, and another 9 (11.7%) received antidepressants new to their treatment regimen.

ANTIDEPRESSANT AND PSYCHOTHERAPY USE BEFORE AND AFTER THE TRIAL

Of the 150 trial participants, 27 of the active treatment and 26 of the usual care participants reported that they were already receiving antidepressants at randomization; at the end of the trial, 37 of the 73 active treatment participants (50.7%) and 28 of the 77 usual care participants (36.4%) were still using antidepressants (χ² = 3.4; P = .06). Before randomization, 6 patients (8.2%) and 7 patients (9.1%) in the active treatment and usual care groups, respectively, were participating in psychotherapy; at the end of the trial, these numbers had increased to 48 (63.8%) and 14 (18.2%), respectively (χ² = 38.8; P < .001).

DEPRESSION OUTCOMES

The active treatment group experienced a greater reduction in BDI scores (−10.1; 95% CI, −12.0 to −8.1) than the usual care group (−6.6; 95% CI, −8.5 to −4.8), resulting in a significant differential change between groups of −3.5 BDI points (95% CI, −6.1 to −0.7; P = .01; Hedges g = 0.59) (Figure 2). Remission of depression (BDI score <10 at 6 months) occurred in 24 active treatment participants (47.1%) and 16 usual care participants (27.6%) (P = .04; NNT = 5). No significant differences were found between groups in the proportion of participants who achieved a 0.5-SD reduction of depressive symptoms or 30 or more depression-free days (Table 2).

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There was also a significant effect of diabetes status on depressive symptom scores. In the active treatment group, the depressive symptom scores of patients with diabetes mellitus decreased more (−6.4; 95% CI, −10.1 to −2.6) than did those of patients without diabetes mellitus in the active treatment group (−6.2; 95% CI, −10.0 to −2.3). No other subgroup differences were found, including the comparison of those with probable mild (BDI, 10-15) vs major (BDI ≥16) depression.

**HEALTH CARE COSTS**

Mental health costs were significantly higher for the active treatment group than for the usual care group (adjusted change, $687; 95% CI, $466-$909; P < .001), while average hospital costs were lower in the active treatment group (adjusted change, −$1010; 95% CI, −$3294 to $1274; P = .39). As a result of this offset, total health care costs in the study intervention group were not higher than in the comparison group (adjusted change, −$325; 95% CI, −$2639 to $1989; P = .78) (Figure 3 and eTable 2).

The CODIACS Vanguard provides a basis for future studies to determine whether treating depression reduces mortality and cardiac event recurrence in patients after an ACS event. It demonstrates that this approach yields a substantial reduction in depressive symptoms, replicating our earlier trial finding. The size of the study intervention’s effect on depressive symptoms (Hedges g = 0.59) compares favorably with the results of interventions tested in other recent depression trials in patients after an ACS event.29-33 and meta-analyses of both psychotherapy and antidepressant medication trials.34

**Post hoc subgroup analyses** revealed a significant sex × group × time interaction (P = .03); women’s depressive symptom scores decreased more (−6.4; 95% CI, −10.1 to −2.6) than did men’s (−1.6; 95% CI, −6.7 to 3.6) in the active treatment group (eTable 1; http://www.jamainternalmed.com). There was also a significant effect of diabetes status × group × time interaction (P = .049); the depressive symptom scores of patients with diabetes mellitus decreased more (−6.2; 95% CI, −10.0 to −2.3) than did those of patients without diabetes mellitus in the active treatment group (−0.9; 95% CI, −4.6 to 2.7). No other subgroup differences were found, including the comparison of those with probable mild (BDI, 10-15) vs major (BDI ≥16) depression.

**Table 2. Six-Month Improvements in Mental Health, Functional Status, Health Utilities, and Clinical End Points**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (%)</th>
<th>Active Treatment</th>
<th>Usual Care</th>
<th>RR (95% CI)</th>
<th>P Value</th>
<th>NNT</th>
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<tbody>
<tr>
<td>Depressive symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>BDI score &lt;10 at 6 mo</td>
<td>24 of 51 (47.1)</td>
<td>16 of 58 (27.6)</td>
<td>1.70 (1.04-2.40)</td>
<td>.04</td>
<td>5</td>
<td></td>
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<tr>
<td>0.5-SD improvement in BDI score</td>
<td>38 of 51 (74.5)</td>
<td>39 of 58 (67.2)</td>
<td>1.11 (0.83-1.30)</td>
<td>.41</td>
<td>14</td>
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<tr>
<td>≥30 Depression-free days</td>
<td>38 of 73 (52.1)</td>
<td>37 of 77 (48.1)</td>
<td>1.08 (0.76-1.40)</td>
<td>.62</td>
<td>25</td>
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<tr>
<td>Anxiety symptoms</td>
<td></td>
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<tr>
<td>0.5-SD improvement in PROMIS anxiety scale</td>
<td>36 of 62 (58.1)</td>
<td>27 of 62 (43.5)</td>
<td>1.34 (0.93-1.70)</td>
<td>.11</td>
<td>7</td>
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<td>0.5-SD improvement in SF-12 Mental composite score</td>
<td>33 of 65 (50.8)</td>
<td>33 of 70 (47.1)</td>
<td>1.08 (0.73-1.42)</td>
<td>.67</td>
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<td>0.5-SD improvement in SF-12 Physical composite score</td>
<td>14 of 65 (21.5)</td>
<td>20 of 70 (28.6)</td>
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Abbreviations: BDI, Beck Depression Inventory; NA, not applicable (because the observed effect did not favor the intervention conditions); NNT, number needed to treat; PROMIS, Reported Outcomes Measurement Information System; SF-12, Medical Outcomes Study 12-Item Short Form Health Survey.

*To calculate the NNT, we used only observed data; thus, sample sizes vary and are presented for each grouping.*

**Figure 3.** Comparison of health care use costs during the 6 months between treatment groups.

Exploratory post hoc subgroup analyses revealed a significant sex × group × time interaction (P = .03); women’s depressive symptom scores decreased more (−6.4; 95% CI, −10.1 to −2.6) than did men’s (−1.6; 95% CI, −6.7 to 3.6) in the active treatment group (eTable 1; http://www.jamainternalmed.com). There was also a significant diabetic status × group × time interaction (P = .049); the depressive symptom scores of patients with diabetes mellitus decreased more (−6.2; 95% CI, −10.0 to −2.3) than did those of patients without diabetes mellitus in the active treatment group (−0.9; 95% CI, −4.6 to 2.7). No other subgroup differences were found, including the comparison of those with probable mild (BDI, 10-15) vs major (BDI ≥16) depression.

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**Figure 3.** Comparison of health care use costs during the 6 months between treatment groups.

The CODIACS Vanguard provides a basis for future studies to determine whether treating depression reduces mortality and cardiac event recurrence in patients after an ACS event. It demonstrates that this approach yields a substantial reduction in depressive symptoms, replicating our earlier trial finding. The size of the study intervention’s effect on depressive symptoms (Hedges g = 0.59) compares favorably with the results of interventions tested in other trials. Figure 3 compares these findings with those of a prior trial that tested a patient preference–based intervention, and other recent depression trials in patients after an ACS event.29-33 and meta-analyses of both psychotherapy and antidepressant medication trials.34

Post hoc testing of 10 subgroup differences identified 2 apparent subgroup effects: the study intervention had stronger effects on depression reduction in women than in men, and in patients with diabetes mellitus than in patients without diabetes mellitus. Some previous depression trials in cardiac populations found weaker treatment effects for women than for men.35,36 Additional studies would be required to confirm whether the study intervention employed here has sex-specific benefits or specific benefit for depressed patients with comorbid diabetes mellitus after an ACS event.

This trial has several limitations. It enrolled patients with elevated depressive symptoms who did not necessarily meet the criteria for a major depressive disorder. Some institutional review board committees consider any delay in treating diagnosed depression as unethical, and the gold standard for diagnosis of major depressive disorder requires a lengthy psychiatric interview conducted by a trained expert. Both these considerations impede the conduct of a pragmatic RCT for post-ACS depression. In addition, even patients with subsyndromal depressive symptoms are at elevated risk for adverse medical outcomes and experience impaired quality of life, suggesting that such patients may benefit from treatment. The usual care condition did not control for the amount of clinical attention participants received. Evidence about the usefulness of any management ap-
approach is cumulative; other control conditions should be considered for future trials. Our estimate of costs must be viewed as very preliminary; although our point estimate indicated a possible cost saving associated with the study intervention, the effect was not significant and the 95% confidence interval was quite wide. In addition, we likely underestimated intervention costs because we did not account for some aspects of care coordination. Finally, central coordination of phone and internet interventions may be the treatment of the future, but may be difficult to implement currently, given the structure of health care treatment of patients with ACS.

The intriguing hypothesis that depression is causally implicated in ACS recurrence and death has never been adequately tested despite decades of observational prospective research reporting that elevated depressive symptoms are strongly associated with these outcomes. Skepticism concerning this causal hypothesis has persisted and contributes to uncertainty among clinicians about whether to treat post-ACS depression. To our knowledge, no RCTs of depression treatment have definitively demonstrated a reduction in cardiovascular disease recurrence or death. Most widely used treatments have limited efficacy for depression reduction in patients after an ACS event, impeding a proper test of the causal hypothesis. Depressive symptoms remain on par with other established coronary heart disease risk factors for strength of association with ACS recurrence and mortality risk. Cardiologists, primary care physicians, and family physicians are being urged to screen for depression, without sufficient trial data to guide subsequent treatment. Advisories and guidelines from the American Heart Association, American Academy of Family Practitioners, European professional cardiology societies, and the British health care system recommend depression screening in patients after an ACS event and referral for treatment if depression is found. However, no cost-effectiveness RCT data are available to inform this large, potentially expensive guideline recommendation. There has been only 1 sufficiently powered RCT on which to base treatment decisions, which is clearly an inadequate basis for empirically supported practice.

We now have new signals of a substantial and possibly cost-neutral depression treatment benefit from this and other RCTs on which to base a definitive ACS depression trial. A large phase 3 trial would inform evidence-based depression treatment guidelines for patients with an ACS, and even has the tantalizing possibility of answering the important question of whether treating depression in patients with ACS lowers mortality and recurrence rates.

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Benefits and Costs of Improving Depression Treatment in People With Heart Disease

In this issue of JAMA Internal Medicine, Davidson et al describe the benefits of an organized depression care program for outpatients experiencing significant symptoms of depression after acute coronary syndrome (ACS). Patients were screened 2 to 6 months after hospitalization for ACS, and those with significant depressive symptoms were randomly assigned to either a systematic depression treatment program or continued usual care (which might include depression treatment from local medical or mental health providers). The Comparison of Depression Interventions after Acute Coronary Syndrome (CODIACS) treatment program included the essential elements proven effective in previous collaborative care or depression care management programs: availability of antidepressant pharmacotherapy and structured psychotherapy, systematic assessment of outcomes, a stepped care algorithm for treatment adjustment or intensification, and organized supervision by consulting mental health specialists. Those offered the organized depression treatment program experienced significantly greater improvement (both statistically and clinically) over 6 months. This finding adds to the substantial evidence for the clinical benefit of depression screening and systematic treatment among people with varying stages of heart disease ranging from outpatients with poorly controlled cardiovascular risk factors to patients discharged after revascularization.

As the CODIACS investigators point out, the observed clinical benefits of the program are on the high end of those reported for various depression care improvement programs. We should be careful not to overinterpret this above-average effect. It is a truism of clinical trials involving new treatments that larger effects are usually observed in the smaller studies. But we could point to 2 aspects of this trial as reasons for a robust clinical benefit. First, rates of treatment in the usual care comparison group were disappointingly low, showing no meaningful increase from baseline to 6 months. In previous trials of depression care improvement programs, the greatest benefits occurred when the usual care showed the greatest “room for improvement.” Second, the depression treatment program was delivered by a centralized team—including delivery of problem-solving psychotherapy by telephone or videoconference. This finding suggests that the benefits of greater standardization and quality control may outweigh any benefits of local knowledge and face-to-face contact. If supported by additional evidence, such a conclusion would have important implications for the wide dissemination of effective depression care programs, especially in rural areas or settings with limited access to local mental health resources. Previous efforts to disseminate effective depression programs have focused on developing local resources and adapting to local conditions. Delivering standardized services from a central location may be a viable (or even preferable) alternative.

While the CODIACS investigators conclude that the depression care program was “cost neutral,” I would be more cautious in interpreting the finding of no significant difference in cost. As expected, mental health treatment costs over 6 months were approximately $700 higher for those assigned to the depression care program. Total health services costs for both groups were approximately $4,500 over 6 months, with inpatient costs accounting for approximately two-thirds of this total. While total costs for the 2 groups did not differ more than ex-