Reducing Readmission of Hospitalized Patients With Depressive Symptoms: A Randomized Trial

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Conflicts of interest: authors report none.

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ABSTRACT

PURPOSE To determine if hospitalized patients with depressive symptoms will benefit from post-discharge depression treatment with care transition support.

METHODS This is a randomized controlled trial of hospitalized patients with patient health questionnaire-9 score of 10 or more. We delivered the Re-Engineered Discharge (RED) and randomized participants to groups receiving RED-only or RED for Depression (RED-D), a 12-week post-discharge telehealth intervention including cognitive behavioral therapy, self-management support, and patient navigation. Primary outcomes were hospital readmission and reutilization rates at 30 and 90 days post discharge.

RESULTS We randomized 709 participants (353 RED-D, 356 RED-only). At 90 days, 265 (75%) intervention participants had received at least 1 RED-D session (median 4). At 30 days, the intention-to-treat analysis showed no differences between RED-D vs RED-only in hospital readmission (9% vs 10%, incidence rate ratio [IRR] 0.92 [95% CI, 0.56-1.52]) or reutilization (27% vs 24%, IRR 1.14 [95% CI, 0.85-1.54]). The intention-to-treat analysis also showed no differences at 90 days in readmission (28% vs 21%, IRR 1.30 [95% CI, 0.95-1.78]) or reutilization (70% vs 57%, IRR 1.22 [95% CI, 1.01-1.49]). In the as-treated analysis, each additional RED-D session was associated with a decrease in 30- and 90-day readmissions. At 30 days, among 104 participants receiving 3 or more sessions, there were fewer readmissions (3% vs 10%, IRR 0.30 [95% CI, 0.07-0.84]) compared with the control group. At 90 days, among 109 participants receiving 6 or more sessions, there were fewer readmissions (11% vs 21%, IRR 0.52 [95% CI, 0.27-0.92]). Intention-to-treat analysis showed no differences between study groups on secondary outcomes.

CONCLUSIONS Care transition support and post-discharge depression treatment can reduce unplanned hospital use with sufficient uptake of the RED-D intervention.

Ann Fam Med 2022;20:246-254. https://doi.org/10.1370/afm.2801

INTRODUCTION

Depression is an important risk factor for poor outcomes among patients with acute and chronic conditions.¹⁻⁵ Among patients hospitalized for acute conditions, comorbid depressive symptoms jeopardize a safe transition from hospital to home. Among patients with chronic illness, depression is linked to increased symptom burden, functional decline, and reduced quality of life. Patients with comorbid depressive symptoms often lack essential coping skills to manage their symptoms and are at risk for medication misuse and missing post-discharge appointments.⁶⁻⁸ Treating comorbid depression can improve physical and psychosocial function,⁹ and additional care transition support is needed to avoid unplanned readmission and emergency department use.

Our team developed and studied the Re-Engineered Discharge (RED), a nationally disseminated readmission reduction program. Our research showed that a systematic approach to hospital discharge can reduce 30-day readmissions and emergency department visits.^{10,11} Despite the use of RED, however, 30-day readmissions and emergency department visits were 1.5 to 2.0 times higher among RED study participants with comorbid depressive symptoms.¹² Other research also showed that increased risk for hospitalization persists among patients with comorbid depressive symptoms for as much as 4 years following an index hospitalization.¹³

To address the increased risk of readmission for hospital patients with depressive symptoms, we studied whether an adapted version of the RED protocol (RED for Depression [RED-D]) with post-discharge and mental health support reduces

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unplanned hospital encounters in patients with depressive symptoms compared with use of the RED protocol alone.¹⁴

METHODS

Overview

In this randomized control trial, we compared the effectiveness of RED and RED-D to reduce readmission rates and emergency department visits among patients with moderate to severe depressive symptoms. The intervention group received the RED-D protocol that included a 12-week post-discharge telehealth intervention, including brief cognitive behavioral therapy, patient navigation, and self-management education. The control group received the RED protocol alone.

The study was conducted according to the Consolidated Standards of Reporting Trials (CONSORT) and the published protocol.^{14,15} The Boston University Medical Campus Institutional Review Board approved study activities. Participants provided written informed consent and an external data monitoring committee reviewed unblinded safety data.

Settings

This study was initially conducted at Boston Medical Center in Boston, Massachusetts. After trial commencement, because of low accrual, a protocol amendment added Mount Auburn Hospital in Cambridge, Massachusetts as second recruitment site. Enrollment occurred from February 6, 2013 through October 25, 2016.

Consent and Eligibility

During recruitment, study staff reviewed a daily list of hospitalized patients admitted within 24 hours and assessed eligibility using medical records. Patients admitted for altered mental status, end-of-life care, sickle cell crisis, or substance use were excluded immediately. A random-number sequence determined the order to approach potentially eligible patients. Inclusion criteria were individuals aged 18 years and older that were able to provide informed consent in English, and had a telephone, a primary care clinician (PCC), and planned to stay in the local area for the study period. From this group, patients that had suicide precautions in place, were incarcerated, were pregnant, undergoing cancer treatment, had been admitted to a surgical trauma unit, or were to be discharged to other institutional settings were excluded.

Post-Consent Final Eligibility

Final eligibility was determined after consent due to the sensitivity of the information collected. The 9-item Patient Health Questionnaire (PHQ-9) was used to screen for depressive symptoms.¹⁶ Participants with PHQ-9 scores of 10 or greater were eligible. We excluded participants reporting a suicide attempt in the last 6 months or current suicidal ideation. Study staff then used the Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders, 4th edition* Axis I Disorders¹⁷ to exclude patients with symptoms of psychosis and bipolar disorder, the 4-item Screening for Alcohol Use¹⁸ questionnaire to exclude those with problem alcohol use (scores >2), and the 10-item Drug Abuse Screening Test¹⁹ to exclude those with problem drug use (scores >5).

Baseline Data Collection

Baseline sociodemographic data, Rapid Estimate of Adult Literacy in Medicine,²⁰ Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form (Q-LES-Q-SF),²¹ Patient Activation Measure (PAM-13),²² and Generalized Anxiety Disorder (GAD-7)²³ were collected. A licensed mental health specialist evaluated participants and determined if criteria for major depression were met at enrollment.

Randomization

Block randomization (block size = 8) randomly assigned participants (50:50) to either RED-only or RED-D groups.²⁴ Randomization assignments were placed in sequentially numbered envelopes that were unsealed after baseline data collection.

Control Condition

A discharge educator delivered the 12-component RED protocol to all study participants. The RED protocol includes a post-discharge telephone call to support medication adherence, confirm the PCC follow-up appointment, and provide education on symptoms and care plan management. Additional details of the RED protocol are described elsewhere.¹¹

Intervention

In addition to the RED protocol, the intervention group participants received the RED-D protocol for up to 12 weeks post discharge. This consisted of telephone sessions facilitated by a licensed Master's-level counselor and supervised by a study psychiatrist. Session structure was tailored to participants' needs and symptom burden, as determined by the counselor.

The components of the RED-D protocol were brief cognitive behavioral therapy, self-management education, and patient navigation. Brief cognitive behavioral therapy²⁵ included orientation to the thought-feeling connection, transforming negative thoughts, and physical symptoms and stress management. Selfmanagement education focused on diet, exercise, medication management, and coping with symptoms. Patient navigation included support for scheduling appointments, coordinating transportation, and adhering to the discharge plan; and sharing information back to primary care clinicians.¹⁴

Using elements of the Collaborative Care Model,²⁶ the counselor discussed all cases with the study psychiatrist and communicated depression symptom ratings to the participant's primary care or psychiatric clinician weekly. We used an evidence-based algorithm to determine recommendations to share with PCCs for depressive symptom management.²⁷

Outcomes

Primary outcomes were 30- and 90-day rate of hospital readmission and reutilization (hospital readmissions, emergency



CAGE = 4-item screening for alcohol use: cutting down, annoyance by criticism, guilty feeling, and eye-openers; DAST = 10-item drug abuse screening test; PHQ-9 = patient health question-naire-9; PHQ-2 = patient health questionnaire-2; RED = re-engineered discharge; RED-D = re-engineered discharge for depression.

^a Medical exclusion occurred in phases. Patients admitted for altered mental status, end-of-life care, sickle cell crisis, or substance use were excluded from the pool immediately. Then, potentially eligible patients were excluded if they were going to be discharged to another inpatient facility, pregnant, under suicide precautions, undergoing cancer treatment; admitted to a surgical trauma unit.

^b Other reasons for exclusion included: incarceration; no access to telephone; no primary care clinician; not staying in the area during the study; aged <18 years; enrolled in another discharge planning program.

c Medical exclusions after consent were for having a serious mental illness diagnosis, self-reported suicidal ideation, and self-reported alcohol or drug abuse (CAGE score >2, DAST score >5).

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department visits, and observations) after index discharge and were collected from electronic health records.

Blinded research assistants collected Q-LES-Q-SF, PHQ-9, PAM-13, and GAD-7 scores at 30 and 90 days after discharge as secondary outcomes.

Sample Size

Based on prior research,¹⁰ we expected 32% of participants to be readmitted or seen at an emergency department within 30 days, and that RED-D would reduce reutilization to 22%, requiring a sample size of 678 to attain 80% power at a significance level of 0.025. Assuming 2% missing observations, we required 692 patients for randomization.

Statistical Analysis

Intention-to-treat analyses of primary outcomes included all randomized participants and computed incidence rate ratios (IRR) and 95% CIs from Poisson models that regressed 30and 90-day outcome counts on each study arm.

As-treated analyses for 30- and 90-day primary outcomes were performed by regressing outcome counts on the number of sessions completed by that time point, using Poisson models.

We checked for confounding due to self-selection into number of sessions by regressing the number of sessions on baseline PHQ-9, GAD-7, and PAM-13 score, major depressive disorder, education, income, sex, recruitment site, and age. Characteristics associated with number of sessions were controlled for in the as-treated regressions.

Secondary outcomes were assessed with an intention-totreat analysis using independent *t*-tests and χ^2 tests, as appropriate, and with an as-treated analysis by regressing 30- and 90-day PHQ- 9, GAD-7, PAM-13, and Q-LES-Q-SF scores on the number of intervention sessions received, using ordinary least squares and controlling for characteristics associated with number of sessions.

Dose-response effects of the self-management, patient navigation, and brief cognitive behavioral therapy components of RED-D were assessed using Poisson models that regressed readmission rate on the time spent receiving each component by 30 and 90 days.

To check sensitivity to missingness, all analyses of primary outcomes were replicated using data imputed by chained equations and predictive mean matching, with results pooled from 50 imputations (Supplemental Table 1).

All statistical tests were run at alpha level 0.05, and parametric tests were checked at 0.025 after applying a Bonferroni correction for multiple testing. R programming language, version 3.4.3 (the R Foundation) was used for all analyses.²⁸

RESULTS

Study Sample

A total of 34,181 hospitalized patients were screened. Of these, 26,996 (79%) were ineligible, 5,154 (14%) declined participation, and 2,031 (6%) consented to participation. After determining final eligibility, 709 participants were randomized (353 RED-D, 356 RED-only) (Figure 1).

The mean ages of RED-D and RED-only groups, respectively, were 50.3 and 50.9 years, 60% and 62% were women, 45% and 41% were non-Hispanic Black people, and 51% and 49% were disabled or unemployed persons. The mean baseline PHQ-9 score was 15 in both groups, indicating moderately severe depressive symptoms. A total of 27% and 31% met clinical criteria for major depressive disorder (Table 1).

Delivery of RED-D Protocol

By 30 days after hospital discharge, 264 (75%) patients in the RED-D group had participated in 1 or more counseling session (median = 2, interquartile range [IQR] 2). One more patient had participated by 90 days (265 [75%], median = 4, IQR 6). By 30 days, 104 (30%) participants had attended 3 or more sessions; by 90 days, 87 (25%) had attended 6 or more sessions. Mean session duration was 62.4 minutes (SD 59.8).

At 90 days, 130 participants received on average 25 minutes of self-management education (SD 27), 121 participants averaged 12 minutes of patient navigation (SD 10), and 126 participated in brief cognitive behavioral therapy sessions.

Primary Outcomes

Intention-to-treat analysis (RED-only vs RED-D) did not show reductions in readmissions at 30 days (10% vs 9%, P = .758, IRR 0.92 [95% CI, 0.56-1.52]) or 90 days (21% vs 28%, P = .106, IRR 1.30 [95% CI, 0.95-1.78]). There were similar findings for hospital reutilization at 30 days (24% vs 27%, P = .386, IRR 1.14 [95% CI, 0.85-1.54]) and 90 days (57% vs 70%, P = .041, IRR 1.22 [95% CI, 1.01-1.49]) (Table 2).

At 30 days, among the 104 intervention patients who received 3 or more sessions, there were fewer readmissions compared with controls (0% vs 10%, IRR 0.30 [95% CI, 0.07-0.84], P = .012). By 90 days, among the 109 patients who received 6 or more sessions, there were fewer readmissions compared with controls (11% vs 21%, IRR 0.52 [95% CI, 0.27-0.92], P = .030). There were similar results for reutilizations (Table 2).

At 30 days, each additional counseling session was associated with a 23% decrease in the per-participant rate of readmissions (P = .077), and an 8% decrease in the rate of reutilizations (P = .276). At 90 days, each additional session was associated with a 10% decrease in the rate of readmissions (P = .003), and a 7% decrease in the rate of reutilizations (P = .002). At 90 days, there was a progressively decreasing readmission rate per session from 27% with 1 session to 8% with 10 sessions. Similarly, reutilization decreased from 72% with 1 session to 27% with 10 sessions (Figure 2).

At 30 and 90 days, the number of RED-D sessions received was not correlated with baseline measurements of PHQ-9, depression diagnosis, GAD-7 score, PAM-13, education, income, and recruitment site (<u>Supplemental Table 2</u>). Differences were detected between participants that received fewer than 3 vs 3 or more sessions at 30 days in age (mean age

| Table 1. Demographic and Clinical Characteristics at Enrollment ^a | | | | | | | |
|--|----------------------|---------------------------|---|----------------------|---------------------------|--|--|
| Characteristic | Control (n = 356) | Intervention (n = 353) | Characteristic | Control (n = 356) | Intervention (n = 353) | | |
| Women, No. (%) | 221 (62.1) | 210 (59.5) | Current employment status, No. (%) | | | | |
| Age, mean (SD) | 51 (13.7) | 50 (13.4) | Full-time | 60 (16.9) | 76 (21.5) | | |
| Race, No. (%) | | | Part-time | 36 (10.1) | 29 (8.2) | | |
| White non-Hispanic | 129 (36.2) | 112 (31.7) | Homemaker | 3 (0.8) | 7 (2.0) | | |
| Black non-Hispanic | 147 (41.3) | 160 (45.3) | Student | 4 (1.1) | 3 (0.8) | | |
| Hispanic | 59 (16.6) | 67 (19.0) | Retired | 63 (17.7) | 51 (14.4) | | |
| Other race | 52 (14.6) | 42 (11.9) | Disabled | 120 (33.7) | 119 (33.7) | | |
| Annual personal income, \$, No. (%) | | | Unemployed | 56 (15.7) | 62 (17.6) | | |
| <10,000 | 48 (13.5) | 40 (11.3) | Other ^c | 14 (3.9) | 5 (1.4) | | |
| 10,000-19,999 | 65 (18.3) | 66 (18.7) | Recruitment site, No. (%) | | | | |
| 20,000-49,999 | 49 (13.8) | 58 (16.4) | Boston Medical Center | 328 (92.1) | 325 (92.1) | | |
| ≥50,000 | 43 (12.1) | 34 (9.6) | Mt Auburn Hospital | 28 (7.9) | 28 (7.9) | | |
| No personal income | 25 (7.0) | 24 (6.8) | Homeless in past 6 months, No. (%) | 28 (7.9) | 24 (6.8) | | |
| Refused | 51 (14.3) | 53 (15.0) | Major depressive disorder, No. (%) ^c | 110 (30.9) | 96 (27.2) | | |
| Did not know | 74 (20.8) | 77 (21.8) | Mean PHQ-9, (SD) ^d | 15 (4.2) | 15 (4.2) | | |
| Education level, No. (%) | | | Q-LES-Q-SF, mean (SD) ^e | 45 (15.9) | 45 (16.0) | | |
| Less than high school | 14 (3.9) | 16 (4.5) | GAD-7, mean (SD) ^f | 11 (5.5) | 10 (5.8) | | |
| Some high school | 47 (13.2) | 40 (11.3) | PAM-13, mean (SD) ^g | 42 (5.6) | 42 (5.5) | | |
| High school graduate or GED | 134 (37.6) | 124 (35.1) | Medication for depression, No. (%) ^h | 140 (39.3) | 123 (34.8) | | |
| Some college | 104 (29.2) | 111 (31.4) | | | | | |
| 4-year college graduate or higher | 57 (16.0) | 61 (17.3) | | | | | |
| Health literacy level, grade level, No. (| %) ^b | | | | | | |
| ≤3 | 0 (0.0) | 3 (0.8) | | | | | |
| 4-6 | 9 (2.5) | 11 (3.1) | | | | | |
| 7-8 | 49 (13.8) | 53 (15.0) | | | | | |
| ≥9 | 232 (65.2) | 196 (55.5) | | | | | |
| Did not report | 66 (18.5) | 90 (25.6) | | | | | |

GAD = generalized anxiety disorder; GED = general equivalency diploma; PAM = patient activation measure; PHQ-9 = patient health questionnaire-9; Q-LES-Q-SF = quality of life enjoyment and satisfaction questionnaire – short form.

^a Not all column percentages sum to 100% due to missing values.

^b REALM (Rapid Estimate of Adult Literacy in Medicine). Health literacy categories correspond to scores of grade 3 or below (REALM score, 0-18), grade 4 to 6 (REALM score, 19-44), grade

7 to 8 (REALM score, 45-60), and grade 9 or above (REALM score, 61-66).²⁰

 $^{\rm c}$ Determined by clinical interview by licensed mental health counselor after enrollment.

^d Patient Health Questionnaire-9 is a 9-item scale. A score of \geq 10 indicates moderate depressive symptoms.¹⁶

^e Quality of Life Enjoyment and Satisfaction Questionnaire Short Form is a 16-item scale indicating the degree of enjoyment and satisfaction experienced by participants in various areas of daily functioning. The reported score is the sum of the question responses rescaled to 100. Higher scores indicate higher enjoyment and satisfaction.²¹

^f Generalized Anxiety Disorder 7 is a 7-item scale. A score of 10-14 indicates possible clinically significant generalized anxiety and \geq 15 indicates that treatment is probably warranted.²³ ⁹ Patient Activation Measure 13 is a 13-item scale indicating the degree of patients' willingness and ability to take independent actions to manage their health and care. Raw scores converted to range from 0-100 with \leq 47.0 not believing activation important; 47.1-55.1 indicating a lack of knowledge and confidence to take action; 55.2-67.0 beginning to take action; and \geq 67.1 taking action.²²

^h Self-reported answer to the question "Are you currently taking medication for depression?"

49 years vs 53 years, P = .006) and sex (62% vs 73% female, P = .047), and between participants that received fewer than 6 vs 6 or more sessions at 90 days in age (mean age 48 years vs 54 years, P < .001) (<u>Supplemental Table 2</u>). Results were not sensitive to controlling for these variables.

Secondary Outcomes

Intention-to-treat analysis showed no differences in 30-day PHQ-9 (10.0 vs 10.6), GAD- 7 (8.7 vs 8.6), PAM-13 (37.6 vs 36.3), Q-LES-Q-SF (52.4 vs 51.9), having a PCC (97% vs 96%), seeing a PCC within 30 days (61% vs 64%), discussing

depression with a PCC (44% vs 52%), or seeing other doctors (58% vs 53%) (<u>Supplemental Table 3</u>). There were similar findings at 90 days.

In the as-treated analyses, each additional session was associated with a PHQ-9 score that was, on average, 1 point lower at 30 days (than if that session had not occurred; 95% CI, -1.8 to 0.3; P = .009) and 0.3 points lower at 90 days (95% CI, -0.6 to 0.1; P = .111), and with a GAD-7 score that was 0.6 points lower at 30-days (95% CI, -1.5 to 0.2; P = .146), and 0.1 point lower at 90 days (95% CI, -0.5 to 0.3; P = .737). Each additional session was also associated with participants

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| | | Intention-to As-Treat | o-Treat Analysis ted Analysis | As-Treated | l Analysis | | | |
|------------------------------------|--------------------------------|---|----------------------------------|--|--|--|--|--|
| | 30-Day Outcomes | | | | | | | |
| Type of Primary Outcome | Controlª (n = 356), No. (%) | Intervention ^b (n = 353), No. (%) | P Value, IRR (95% CI) | ≥3 Sessions ^c (n = 104), No. (%) | P Value, IRR (95% CI) | | | |
| Hospital utilizations ^d | 82 (0.24) | 89 (0.27) | .386, 1.14 (0.85-1.54) | 20 (0.17) | .377, 0.80 (0.48-1.28) | | | |
| ED visits | 32 (0.09) | 32 (0.10) | .839, 1.05 (0.64-1.72) | 9 (0.09) | .653, 0.93 (0.42-1.86) | | | |
| Readmissions ^e | 33 (0.10) | 29 (0.09) | .758, 0.92 (0.56-1.52) | 3 (0.03) | .012, 0.30 (0.07-0.84) ^f | | | |
| Observations | 17 (0.05) | 28 (0.09) | .215, 1.73 (0.96-3.23) | 8 (0.08) | 0.343, 1.55 (0.63-3.49) | | | |
| | 90-Day Outcomes | | | | | | | |
| | Controlª (n = 356), No. (%) | Intervention ^b (n = 353), No. (%) | P Value, IRR (95% CI) | ≥6 Sessions ^g (n = 109), No. (%) | P Value, IRR (95% CI) | | | |
| Hospital utilizations ^d | 189 (0.57) | 219 (0.70) | .041, 1.22 (1.01-1.49) | 48 (0.44) | .162, 0.78 (0.56-1.06) | | | |
| ED visits | 82 (0.25) | 86 (0.27) | 0.504, 1.11 (0.82-1.50) | 23 (0.21) | .544, 0.86 (0.53-1.34) | | | |
| Readmissions ^e | 71 (0.21) | 87 (0.28) | .106, 1.30 (0.95-1.78) | 12 (0.11) | .030, 0.52 (0.27-0.92) ^f | | | |
| Observations | 36 (0.11) | 46 (0.15) | .177, 1.35 (0.88-2.10) | 13 (0.12) | .797, 1.1 (0.56-2.03) | | | |

ED = emergency department; IRR = incidence rate ratios; RED = re-engineered discharge; RED-D = re-engineered discharge for depression.

^a Control group received the components of the re-engineered discharge (RED).¹⁰

^b Intervention group received the components of the re-engineered discharge, and were offered up to 12 weekly counselling sessions that included brief cognitive behavioral therapy, patient navigation, and self-management (RED-D).

 $\epsilon \ge 3$ sessions includes those patients in the intervention group receiving 3 sessions of the intervention by 30 days.

^d Hospital reutilizations are defined as the sum of hospital readmission plus emergency department visits and observations after index discharge.

e Readmissions are defined as 30 and 90 day all cause hospital readmissions after index discharge.

^f Results are statistically significant.

 $g \ge 6$ sessions includes those patients in the intervention group receiving 6 sessions of the intervention by 90 days.

having a Q-LES-Q-SF score that was 2.1 points higher at 30 days (95% CI, -0.2 to 4.4; P = .070) and 0.9 points higher at 90 days (95% CI, -0.1 to 2.0; P = .087), and with no difference in PAM-13 score at 30 days (95% CI, -0.7 to 0.7; P = .995), but a PAM-13 score that was 0.3 points higher at 90 days (95% CI, 0.0-0.1; P = .051) (Supplemental Figure 1 and Supplemental Figure 2).

Figure 3 shows the predicted readmission rate at 90 days by the number of minutes per RED-D component. There was a decrease in readmission rates associated with time spent receiving each component. Patient navigation was associated with the largest and most rapid decline in readmissions.

Adverse Events

Adverse events were reviewed by study clinicians, the Boston University Medical Campus Institutional Review Board, and the Data and Safety Monitoring Board. Adverse events (n = 26) recorded included 13 reports of suicidal ideation, 2 hospitalizations due to suicide attempt or ideation, and 11 all-cause deaths during study participation. Adverse events were not significantly different between groups and determined to be expected and unlikely related to the intervention.

DISCUSSION

This study adds to the literature showing the importance of post-discharge counseling and care transition support to reduce hospital readmissions among those with chronic illness and a high burden of cognitive and somatic symptoms of depression. An intention-to-treat analysis detected no difference in all-cause hospital readmission or reutilization at 30 or 90 days after index hospital discharge among hospitalized patients with depressive symptoms (PHQ-9 score ≥ 10) offered the RED-D intervention compared with RED alone. In the as-treated analysis, however, readmissions decreased 70% at 30 days and 48% at 90 days—showing that, with sufficient uptake, the intervention reduced re-hospitalizations. Furthermore, the RED-D intervention can be delivered by Figure 2. Readmission and reutilization rates for intervention patients by the number of counselling sessions completed at 90 days.

| Outcome measured | Control | 1-3 Sessions | 4-6 Sessions | 7-9 Sessions | 10-12 Sessions |
|--------------------|---------|---------------------|---------------------|---------------------|---------------------|
| No. of patients | 333 | 94 | 84 | 61 | 26 |
| Readmission rate | | 0.36 | 0.35 | 0.11 | 0.08 |
| IRR (95% CI) | 0.21 | 1.51 (0.97-2.31) | 1.38 (0.87-2.13) | 0.36 (0.15-0.73) | 0.26 (0.04-0.83) |
| Reutilization rate | | 0.93 | 0.83 | 0.43 | 0.27 |
| IRR (95% CI) | 0.57 | 1.55 (1.18-2.03) | 1.29 (0.97-1.71) | 0.56 (0.36-0.83) | 0.37 (0.16-0.72) |

Predicted 90-day readmission & reutilization rates by dosage



Note: Labeled points indicate predicted values from Poisson regression of 90-day readmission and reutilization rates on cumulative dosage of the intervention. Each value represents the readmission or reutilization rate we would expect at that associated dosage, based on regression models.

primary care teams after discharge to reduce readmissions among patients with depressive symptoms.²⁹⁻³²

Research has linked higher PHQ-9 scores in hospitalized patients with increased functional impairment, number of disability days, health care use, mortality rate, and hospital readmission.³³⁻³⁵ The high burden of physical symptoms during hospitalization could exacerbate depressive symptoms in chronically ill patients. Our prior work showed that hospitalized individuals with PHQ-9 scores of 10 or more have nearly 2 times the rate of readmissions compared with those who score in the non-depressive range (PHQ-9 score <5). Yet, while all RED-D participants had PHQ-9 scores of 10 or more, only one-third had confirmed depression based on clinical psychiatric interview.^{12,36} Interestingly, those with confirmed

clinical depression were not more likely to engage with the intervention, or to benefit from it, compared with those who did not have confirmed depression. This suggests that depressive symptoms measured by the PHQ-9 identify patients with a high symptom burden and increased risk for readmission who could benefit from post-discharge support and counseling, as delivered by RED-D.

This study identifies the relative contributions of the brief cognitive behavioral therapy, self-management, and patient navigation components of RED-D. Each component contributes to the decrease in readmission rates with patient navigation being most effective in the first 30 days. These data support that early post-discharge navigational assistance, including support with appointment tracking and adherence to new medication, can benefit patients during a time where transition of care challenges emerge.10 Later, counseling focused on chronic disease self-management may become important.

Several features of the trial design should be considered. First, the 2-step application of eligibility criteria excluded participants with a high likelihood of substance abuse. This resulted in a group of participants with depressive symptoms but without alcohol and substance use co-morbidities, a group that is likely to respond differently to a post-discharge counseling intervention, allowing the results to be better generalized to patients with depressive symptoms. Second, both study groups had the evidence-based re-engineered discharge program initiated before discharge. RED

was shown to reduce readmissions and emergency department use in the 30 days after discharge.¹⁰ Our data show that, while assigning RED-D by itself does not out-perform RED, fully administering the RED-D intervention for at least 3 sessions would reduce 30-day readmissions by 1 more than if those participants had received RED alone. This finding provides an example of tailoring transition of care interventions based on clinical characteristics, an approach with great potential.

This study also has several limitations. Because we observed an effect of the RED-D intervention in the as-treated analysis but not the intention-to-treat analysis, we strongly suspect that low study adherence was responsible for the null findings. Given that the uptake of counseling services is low among patients in community settings,³⁷ it is not surprising



Figure 3. Predicted readmission rate at 90 days by type of post-discharge support for intervention participants

Note: Predicted values were generated using Poisson regression.

* Self-management was counselling focused on chronic disease self-management, including diet/nutrition, exercise, managing medications, talking to your doctor, and coping with exacerbations

^b Patient navigation includes guidance in navigating difficult aspects of the health care system, such as overcoming financial barriers, scheduling appointments, and coordinating transportation services, as well as adherence to the discharge plan and follow-up care.

^c Brief cognitive behavior therapy includes orientation to the thought-feeling connection, transforming negative thoughts, behavior activation, physical symptoms, and stress management and navigating relationships, and homework.25

that acceptance of a 12-week counseling intervention was low among recently discharged patients, particularly when the reason for recommending counseling services was unrelated to the admission primary diagnosis. For this reason, the as-treated findings are likely to be more predictive of implementation in clinical practice, even while this study design cannot rule out confounding from unobserved covariates.38

Other factors limiting gerneralizability include high levels of unemployment and disability, low educational attainment, and lower incomes of our study population. Also, primary outcome data were collected from electronic health records and therefore missed reutilization at other hospitals, estimated to be 10% from prior studies.¹⁰ However, a preferential impact on study groups is unlikely. Sensitivity analyses controlling for hospital site did not impact our results (Supplemental Table 4).

CONCLUSION

Assignment to the RED-D intervention by itself does not produce a detectable effect. Sufficient uptake of RED-D by hospitalized patients with depressive symptoms, however, has an important positive impact on readmission rates.



Key words: depression; hospitalization; patient discharge; telemedicine

Submitted August 11,2021; submitted, revised, November 22, 2021; accepted December 2, 2021.

Funding support: Supported by the Agency for Health Research and Quality (RO1HS019700) and the Blue Cross Blue Shield Foundation of Massachusetts (MHCA-2269).

Trial registration: ClinicalTrials.gov NCT01840826

Acknowledgments: Dr Bruce Rollman and Ekaterina Sadikova

Supplemental materials



References

- Büla CJ, Wietlisbach V, Burnand B, Yersin B. Depressive symptoms as a predictor of 6-month outcomes and services utilization in elderly medical inpatients. Arch Intern Med. 2001;161(21):2609-2615. <u>10.1001/archinte.161.21</u>. <u>2609</u>
- Reese RL, Freedland KE, Steinmeyer BC, Rich MW, Rackley JW, Carney RM. Depression and rehospitalization following acute myocardial infarction. Circ Cardiovasc Qual Outcomes. 2011;4(6):626-633. <u>10.1161/CIRCOUTCOMES.111</u>. <u>961896</u>
- Hasin DS, Goodwin RD, Stinson FS, Grant BF. Epidemiology of major depressive disorder: results from the National Epidemiologic Survey on Alcoholism and Related Conditions. Arch Gen Psychiatry. 2005;62(10):1097-1106. <u>10.1001/archpsyc.62.10.1097</u>
- Almagro P, Barreiro B, Ochoa de Echagüen A, et al. Risk factors for hospital readmission in patients with chronic obstructive pulmonary disease. *Respiration.* 2006;73(3):311-317. 10.1159/000088092
- Jiang W, Alexander J, Christopher E, et al. Relationship of depression to increased risk of mortality and rehospitalization in patients with congestive heart failure. Arch Intern Med. 2001;161(15):1849-1856. <u>10.1001/archinte.161</u>. <u>15.1849</u>
- DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med.* 2000;160(14):2101-2107. 10.1001/archinte.160.14.2101
- Dowson CA, Town GI, Frampton C, Mulder RT. Psychopathology and illness beliefs influence COPD self-management. J Psychosom Res. 2004;56(3):333-340. 10.1016/S0022-3999(03)00040-0
- Katon WJ. Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. *Biol Psychiatry*. 2003;54(3):216-226. 10.1016/S0006-3223(03)00273-7
- Katon W, Lin E, Kroenke K. The association of depression and anxiety with medical symptom burden in patients with chronic medical illness. Gen Hosp Psychiatry. 29(2):147-155. 10.1016/j.genhosppsych.2006.11.005
- Jack BW, Chetty VK, Anthony D, et al. A reengineered hospital discharge program to decrease rehospitalization: a randomized trial. Ann Intern Med. 2009;150(3):178-187. 10.7326/0003-4819-150-3-200902030-00007
- Jack BW, Paasche-Orlow M, Mitchell S, Forsythe S, Martin J. An Overview of the Re-Engineered Discharge (RED) Toolkit. Published 2012. https://www.ahrq. gov/patient- safety/settings/hospital/red/toolkit/index.html
- Cancino RS, Culpepper L, Sadikova E, Martin J, Jack BW, Mitchell SE. Doseresponse relationship between depressive symptoms and hospital readmission. J Hosp Med. 2014;9(6):358-364. 10.1002/jhm.2180
- Saravay SM, Pollack S, Steinberg MD, Weinschel B, Habert M. Four-year follow-up of the influence of psychological comorbidity on medical rehospitalization. Am J Psychiatry. 1996;153(3):397-403. 10.1176/ajp.153.3.397
- Mitchell SE, Martin JM, Krizman K, et al. Design and rationale for a randomized controlled trial to reduce readmissions among patients with depressive symptoms. Contemp Clin Trials. 2015;45(Pt B):151-156. <u>10.1016/j.cct.2015.08</u>. <u>016</u>
- Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMC Med. 2010;8(1):18. <u>10.1186/1741-7015-8-18</u>
- Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16(9):606-613. <u>10.1046/j.1525-1497.2001.016009606.x</u>
- Kübler U. Structured Clinical Interview for DSM-IV (SCID). In: Encyclopedia of Behavioral Medicine. Springer New York; 2013:1919-1920. 10.1007/ 978-1-4419-1005-9_66
- Ewing JA. Detecting alcoholism: the CAGE questionnaire. JAMA. 1984; 252(14):1905-1907. 10.1001/jama.1984.03350140051025
- 19. Skinner HA. The drug abuse screening test. Addict Behav. 1982;7(4):363-371. 10.1016/0306-4603(82)90005-3

- Davis TC, Long SW, Jackson RH, et al. Rapid estimate of adult literacy in medicine: a shortened screening instrument. *Fam Med.* 1993;25(6):391-395. https://www.ncbi.nlm.nih.gov/pubmed/8349060
- Endicott J, Nee J, Harrison W, Blumenthal R. Quality of life enjoyment and satisfaction questionnaire: a new measure. *Psychopharmacol Bull*. 1993;29(2): 321-326. https://www.ncbi.nlm.nih.gov/pubmed/8290681
- Hibbard JH, Mahoney ER, Stockard J, Tusler M. Development and testing of a short form of the patient activation measure. *Health Serv Res.* 2005;40(6 Pt 1):1918-1930. 10.1111/j.1475-6773.2005.00438.x
- Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006;166(10): 1092-1097. 10.1001/archinte.166.10.1092
- Efird J. Blocked randomization with randomly selected block sizes. Int J Environ Res Public Health. 2011;8(1):15-20. 10.3390/ijerph8010015
- Cully JA, Stanley MA, Petersen NJ, et al. Delivery of brief cognitive behavioral therapy for medically ill patients in primary care: a pragmatic randomized clinical trial. J Gen Intern Med. 2017;32(9):1014-1024. <u>10.1007/</u> s11606-017-4101-3
- Katon WJ, Lin EHB, Von Korff M, et al. Collaborative care for patients with depression and chronic illnesses. N Engl J Med. 2010;363(27):2611-2620. 10.1056/NEJMoa1003955
- Trivedi MH, Rush AJ, Wisniewski SR, et al; STAR*D Study Team. Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: implications for clinical practice. *Am J Psychiatry*. 2006;163(1): 28-40. 10.1176/appi.ajp.163.1.28
- R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. https://www.R-project.org/
- Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. N Engl J Med. 2009;360(14):1418-1428. 10.1056/NEJMsa0803563
- Dajczman E, Robitaille C, Ernst P, et al. Integrated interdisciplinary care for patients with chronic obstructive pulmonary disease reduces emergency department visits, admissions and costs: a quality assurance study. Can Respir J. 2013;20(5):351-356. 10.1155/2013/187059
- 31. Roberge J, McWilliams A, Zhao J, et al. Effect of a virtual patient navigation program on behavioral health admissions in the emergency department: a randomized clinical trial. JAMA Netw Open. 2020;3(1):e1919954. <u>10.1001/</u>jamanetworkopen.2019.19954
- Balaban RB, Galbraith AA, Burns ME, Vialle-Valentin CE, Larochelle MR, Ross-Degnan D. A patient navigator intervention to reduce hospital readmissions among high-risk safety-net patients: a randomized controlled trial. J Gen Intern Med. 2015;30(7):907-915. <u>10.1007/s11606-015-3185-x</u>
- Beach SR, Januzzi JL, Mastromauro CA, et al. Patient health questionnaire-9 score and adverse cardiac outcomes in patients hospitalized for acute cardiac disease. J Psychosom Res. 2013;75(5):409-413. <u>10.1016/j.jpsychores.2013.08.</u> <u>001</u>
- Pederson JL, Majumdar SR, Forhan M, Johnson JA, McAlister FA. Current depressive symptoms but not history of depression predict hospital readmission or death after discharge from medical wards: a multisite prospective cohort study. *Gen Hosp Psychiatry*. 2016;39:80-85. <u>10.1016/j.genhosp</u> psych.2015.12.001
- 35. Piepenburg SM, Faller H, Gelbrich G, et al. Comparative Potential of the 2-Item Versus the 9-Item Patient Health Questionnaire to Predict Death or Rehospitalization in Heart Failure. Circ Hear Fail. 2015;8(3):464-472. 10.1161/CIRC HEARTFAILURE.114.001488
- Mitchell SE, Paasche-Orlow MK, Forsythe SR, et al. Post-discharge hospital utilization among adult medical inpatients with depressive symptoms. J Hosp Med. 2010;5(7):378-384. 10.1002/jhm.673
- 37. Lake J, Turner MS. Urgent need for improved mental health care and a more collaborative model of care. Perm J. 2017;21:17-024. <u>10.7812/TPP/17-024</u>
- Adler AI, Latimer NR. Adjusting for nonadherence or stopping treatments in randomized clinical trials. JAMA. 2021;325(20):2110. <u>10.1001/jama.2021</u>. <u>2433</u>

