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Mobile App-Based Mindfulness Intervention for Addressing Psychological Distress Among Survivors of Hospitalization for COVID-19 Infection

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Abstract

BACKGROUND: Psychological distress symptoms are present and persistent among many patients who survive a critical illness like COVID-19.

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RESEARCH QUESTION: Could a self-directed mobile app-delivered mindfulness intervention be feasibly and rapidly implemented within a clinical trials network to reduce distress symptoms?

STUDY DESIGN AND METHODS: A randomized clinical trial was conducted between January 2021 and May 2022 at 29 US sites and included survivors of hospitalization due to COVID-19-related illness with elevated symptoms of depression at discharge. Participants were randomized to intervention or usual care control. The intervention consisted of four themed weeks of daily audio, video, and text content. All study procedures were virtual. The primary outcome was depression symptoms assessed with the Patient Health Questionnaire 9 at 3 months. Secondary outcomes included anxiety (Generalized Anxiety Disorder 7-item scale), quality of life (EQ-5D), and adherence. We used general linear models to estimate treatment arm differences in outcomes over time.

RESULTS: Among 56 randomized participants (mean age ± SD, 51.0 ± 13.2 years; 38 female [67.9%]; 14 Black participants [25%]), 45 (intervention: n = 23 [79%]; control: n = 22 [81%]) were retained at 6 months. There was no difference in mean improvement between intervention and control participants at 3 months in Patient Health Questionnaire 9 (−0.5 vs 0.1), Generalized Anxiety Disorder 7-item scale (−0.3 vs 0.1), or EQ-5D (−0.03 vs 0.02) scores, respectively; 6-month results were similar. Only 15 participants (51.7%) initiated the intervention, whereas the mean number ± SD of the 56 prescribed intervention activities completed was 12.0 ± 15.2. Regulatory approvals delayed trial initiation by nearly a year.

INTERPRETATION: Among survivors of COVID-19 hospitalization with elevated psychological distress symptoms, a self-directed mobile app-based mindfulness intervention had poor adherence. Future psychological distress interventions mobilized at broad scale should focus efforts on patient engagement and regulatory simplification to enhance success.

TRIAL REGISTRATION: ClinicalTrials.gov; No.: NCT04581200; URL: www.clinicaltrials.gov

Keywords

COVID-19; critical illness; mobile app; post-intensive care unit syndrome; psychological distress

Over 2 million patients are treated in ICUs annually in the US for cardiorespiratory failure caused by pneumonia, sepsis, and congestive heart failure, among others.[1] After discharge, patients experience clinically important symptoms of psychological distress—depression, anxiety, and posttraumatic stress disorder (PTSD)—symptoms that are both common (50%-70%) and persistent.[2–4] Pneumonia, the second-most common cause of hospitalization, places its survivors at high risk for persistently worsened health status. Acute infection with SARS-CoV-2 which leads to COVID-19 caused the largest pandemic of pneumonia in > 100 years. Survivors of COVID-19 respiratory failure commonly experience not only physical symptoms, but persistent symptoms of psychological distress, including depression, anxiety, and PTSD.[5]

However, a key challenge during a pandemic (eg, COVID-19) is the difficulty of identifying serious psychological symptoms and delivering therapy at a population scale—when face-to-face interaction is impossible and both health care and personal resources may be limited.[6-8] A further problem is the mental health equity gap driven by access to care

barriers including physician shortages, economic adversity, and geographic inconsistency of available interventions.

The Lift mobile mindfulness intervention is ideally positioned to overcome care access barriers during a pandemic like COVID-19. Its tested mindfulness content promotes a practice of nonjudgmental awareness that can alleviate distress by uncoupling emotional reactions and habitual behavior from unpleasant symptoms, thoughts, and emotions—content that improves symptoms of depression, anxiety, and PTSD.[9-11] Its self-directed delivery through any digital device allows direct access by nearly anyone in the country. However, few behavioral interventions have been tested during a global pandemic.

The primary aim of this trial was to determine the feasibility and clinical effect of a completely self-directed mobile app-based mindfulness intervention on symptoms of psychological distress assessed over 6 months posthospital discharge.

Study Design and Methods

Study Design

This was a parallel-arm prospective randomized controlled trial with 6-month follow-up conducted among participants from 29 clinical sites across the US participating in the National Heart, Lung, and Blood Institute-funded Prevention and Early Treatment of Acute Lung Injury (PETAL) Network's Biology and Longitudinal Epidemiology: COVID-19 Observational Study (BLUE CORAL) observation cohort study, which assessed several patient-reported and clinical outcomes with telephone interviews at 1, 3, and 6 months after discharge for a hospitalization caused by COVID-19.[12,13] Enrollment occurred between January 25, 2021, and January 30, 2022, with follow-up completed on May 30, 2022. In this trial, the Lift intervention was compared with usual care control. This trial is registered at ClinicalTrials.gov (No. NCT04581200) and was approved by the Duke University Central institutional review board (Protocol No. 00106306).

Participants

All participants were recruited through their enrollment in the BLUE CORAL study. Inclusion criteria were adults hospitalized within 14 days of a positive polymerase chain reaction test for COVID-19 and evidence of acute COVID-19 (fever or respiratory manifestations [eg, cough, dyspnea, tachypnea, hypoxemia, infiltrates on chest imaging]). Exclusions were < 72 h of continuous hospitalization prior to enrollment, comfort care orders in place at the time of enrollment and/or unexpected by physician to survive for 24 h, imprisoned people, and previous enrollment in BLUE CORAL.

For this clinical trial, additional inclusion criteria were survival to hospital discharge; English-speaking; domiciled with access to a working telephone and smartphone, tablet, or computer with Wi-Fi or internet connection; and absence of severe dementia or severe functional disability before hospitalization or at time of 1-month postdischarge interview. Exclusions were Patient Health Questionnaire 9 (PHQ-9) score < 5 (less than mild symptoms) or suicidal ideation at time of the baseline (1-month postdischarge) BLUE

CORAL interview. Our formal distress management protocol for handling serious distress throughout the trial is described in e-Appendix 1 and e-Appendix 2. Study participants were allowed to seek other forms of mental health services during the trial.

Screening, Informed Consent, and Randomization

Screening was performed for one-half of the trial by the BLUE CORAL outcomes center staff (University of Michigan) and subsequently by the three core Lift sites' staff (Duke University, Oregon Health & Science University, and University of Colorado) (e-Fig 1). At the time of the baseline 1-month postdischarge BLUE CORAL-prescribed telephone interview, study staff would determine the respondent's PHQ-9 score. For those with a PHQ-9 score ≥ 5, the research staff then conducted an informed consent discussion with the respondent at the conclusion of the interview if possible or prepped the respondent for a follow-up call by the core Lift study team at a more convenient time over the next few days. All telephone consent procedures followed a formal Duke University Central Institutional Review Board-approved telephone script. For those who preferred an electronic informed consent, we sent an email containing a unique URL linked to a study-specific REDCap e-consent form. Study staff augmented the consent process by sending potential participants a link to the trial website and a short animated information video that described the trial (e-Appendix 1). The mobile app platform performed randomization in a 1:1 ratio using a minimization algorithm aiming to balance two baseline characteristics: age (≥ 50 vs < 50 years) and PHQ-9 score (≥ 10 vs < 10).[14] Randomization occurred immediately after the research staff entered the name and baseline characteristics of a consented participant. An email was generated to study staff with each randomization. For those randomized to intervention, the study team would monitor the platform for initiation of the Lift intervention. If no activity was logged within the first few days, a team member called the participant to assist them.

Intervention

The Lift mobile mindfulness program has been described in detail elsewhere; further details and screenshots are included in e-Appendix 2.[9,15] In contrast to prior trials involving Lift, there was no formal study staff onboarding process for participants with the app nor involvement of a therapist.[9,15-17] Furthermore, all participants were enrolled from ICUs rather than hospital wards and generally received mechanical ventilation support. In contrast, the version of the Lift in this study was completed self-directed and focused on those hospitalized in either ICUs or ward settings. The app guides users through different daily activities across four thematically unique weeks of 60 different elements of content using text and visual prompts including rationale and awareness of breathing (week 1), body scan and mindful movement (week 2), awareness of thoughts and feelings to acknowledge difficult emotions and cultivate feelings of kindness and compassion (week 3), and mindfulness in everyday life using awareness of daily activities (week 4). Each week begins with an animated video presentation describing the weekly theme's rationale (3-5 min), and each day includes an audio-guided mindfulness meditation that emphasizes core principles of nonjudgmental self-awareness (10 min). Other video and text content is spread throughout each week. At the end of each week, the app prompts completion of the PHQ-9. Based on the dominance of either emotional or somatic depression symptoms, the platform

displays additional video and text content to those whose PHQ-9 scores increased in relation to the prior week or whose PHQ-9 scores were ≥ 20. Any endorsement of suicidal ideation on the PHQ-9's relevant item prompted a phone call from study staff as part of the Distress Management Protocol (e-Appendix 1).

Usual Care Control

Control participants completed all BLUE CORAL study outcome measures per protocol, but did not receive additional attention from the study team nor access to the Lift app.

Outcomes

Trained study staff at the University of Michigan BLUE CORAL outcomes center collected data by telephone from participants 1, 3, and 6 months after hospital discharge. The primary trial outcome was the PHQ-9 (range, 0-27) at 3 months postdischarge (ie, 2 months postrandomization).[18] In addition to PHQ-9 scores at 6 months, secondary outcomes at 3- and 6-month measures included the Generalized Anxiety Disorder 7-item scale (GAD-7) (range, 0-21),[19] the EQ-5D-5L quality of life scale,[20] and cardiopulmonary symptom frequency. Finally, we used direct interrogation of app platform analytics at the individual participant level to assess intervention adherence by quantification of the number of app uses over time and completion of prescribed intervention content elements (eg, videos, audio).[9,17,21]

Sample Size and Power Calculations

The trial was originally intended to include 300 participants. This sample size would provide a power of 80% to detect a differential between-group PHQ-9 improvement at 3 months as small as 2.5 units, substantially less than the minimal clinically important difference of 5.0 units, even with a 40% dropout rate at 3 months and conservative assumptions (SD = 6.0, $\rho = 0.5$, two-sided test, type I error of 5%; calculations based on mixed-models tests for a difference in slopes using PASS 16 Software [v16.0.5; NCSS Statistical Software]). However, due to regulatory delays, we recruited 56 participants. With 44 participants (22 in each arm) at 3 months, we have 80% power to detect a 5.1-unit difference on the PHQ-9 using the same assumptions and procedures previously described.

Statistical Analyses

We compared mean differences, and analyzed all clinical continuous outcomes, using a general linear model with unstructured covariance matrix specified to account for the correlation between longitudinal repeated measures. This statistical model allowed us to estimate the intervention effect at both 3 and 6 months. We used constrained longitudinal analysis, which is the most powerful analysis under a randomized design.[22] All analyses were adjusted for the minimization variables. Binary and categorical secondary and exploratory outcomes (eg, cardiopulmonary symptoms) were compared descriptively using counts and percentages. Adherence metrics were derived from the mobile app platform for intervention recipients and summarized using means and SDs for continuous variables and counts and percentages for categorical variables.

Results

Enrollment and Participant Characteristics

From a total of 164 respondents screened and 106 approached for consent, 56 (53%) provided informed consent and were randomized to the intervention (n = 29) or control (n = 27) group (Fig 1). Participants had a mean age ± SD of 51 ± 13.2 years, and 38 (67.9%) were female (Table 1). Race was most commonly White (n = 31, 55.4%) or Black (n = 14, 25.0%), and 11 (19.6%) reported Hispanic ethnicity. Patients had a median Charlson Comorbidity Index score of 2.0 units (interquartile range [IQR], 0.5-3.0) at baseline. At the time of randomization, a total of 14 patients (25%) self-reported the presence of depression and 16 (28.6%) reported anxiety. All participants previously lived at home.

Clinical Characteristics and Hospital Outcomes

Participants had moderate illness severity at admission with a median Acute Physiology and Chronic Health Evaluation II score of 11.0 (IQR, 6.5-15.0) (Table 2). A total of 18 (32.1%) and five (8.9%) received care in an ICU or step-down unit, respectively, during hospitalization. Ten participants (17.9%) received mechanical ventilation. Most participants' maximal World Health Organization Ordinal Scale score was 4 (n = 26, 46.4%), representing hospitalization with nasal cannula or facemask oxygen. At discharge, 38 (67.9%) believed that their ability to self-care at the time of discharge was the same as or better than before their illness.

Primary and Secondary Outcome Analysis

At baseline, participants had a mean PHQ-9 score ± SD of 9.7 ± 4.3 representing moderately high depression symptoms and a mean GAD-7 score ± SD of 6.5 ± 5.1 representing mild anxiety symptoms (Table 1).

Mean PHQ-9 and GAD-7 scores at 3 and 6 months remained similar to scores at the time of randomization. There was no clinically or statistically significant difference between the intervention and control groups in mean estimated change from baseline in PHQ-9 score at 3 months (0.64; 95% CI, −1.66 to 2.95) and 6 months (0.21; 95% CI, −2.71 to 3.13) (Table 3). Similar results were seen for the GAD-7 at 3 months (0.01; 95% CI, −2.63 to 2.65) and 6 months (−0.49; 95% CI, −2.95 to 2.09) (e-Tables 1, 2; Table 3).

Adherence: Adherence with the intervention was generally poor (e-Table 3, e-Table 5). Among the 29 intervention recipients, only 15 (51.7%) initiated the program. Of these, five were active for 1 week only and 10 remained active through the fourth week. Participants completed a median of 3.0 (IQR, 0-28.0) and a mean ± SD of 12 ± 15.2 of the 56 mobile app assigned tasks and a median of 1.0 (quartile 1-3, 0-11.0) and a mean of 6.6 ± 8.9 of 30 possible audio-guided meditations.

Quality of Life and Cardiopulmonary Symptoms:

Similarly, no group-based differences were observed in the mean estimated Euro-QOL 5 dimension quality of life visual analog scale change scores at 3 months (0.02; 95% CI, −0.11 to 0.15) and 6 months (−0.02; 95% CI, −0.15 to 0.11) (Table 3). Cardiopulmonary

symptoms were similar between treatment groups at both time points (e-Tables 4, 5; e-Tables 3, 4; Fig 2). There was a higher rehospitalization rate in the intervention arm than the control arm at both 3 and 6 months (Table 4).

Discussion

In the face of growing numbers of COVID-19 survivors and concerning reports of significant persisting distress, we attempted to quickly mobilize a scalable mobile mindfulness intervention designed to improve patients' psychological symptoms. Unfortunately, adherence with the self-directed intervention deployed entirely without direct participant contact was poor, and intention to treat analyses demonstrated no effect of the intervention at 3 and 6 months postdischarge. Despite these findings, we were able to mobilize an entirely self-directed psychological distress intervention during a rapidly evolving pandemic within a large national research network.

Currently, there are significant clinical and evidence gaps in psychological distress management for those with serious cardiorespiratory conditions. Screening is uncommon,[23] access to mental health care is challenging and geographically inconsistent (particularly for racially and ethnically minoritized populations),[24,25] and therapy generally includes medications or in-person therapist visits.[26] This contrasts with patients' need for therapy that is easily accessible from home because of physical disability, distance from medical centers, financial hardship, and worries about exposure to COVID-19[6,7,27-29]; content that reflects their unique experiences[30]; and avoidance of greater polypharmacy.[31,32] Systematic reviews and trials have shown no effect on depression or anxiety symptoms of either hospital-based interventions (eg, music therapy,[33] ICU-based psychologist consultation,[34] ICU diaries[35,36]) or postdischarge interventions (eg, follow-up clinics,[37,38] management programs,[39] self-guided or nurse-led rehabilitation programs[40,41]).

However, pandemics and large-scale public health crises demand rapid and broad mobilization of interventions because these events dramatically increase psychological distress symptoms in the general population, whereas hospitalization for serious illness further worsens it.[5,42] Distress symptoms also worsen quality of life and limit the pace of recovery. A mobile app-based strategy (eg, Lift) is an ideal approach because it requires no direct patient contact, is easily disseminatable, and is self-directed.

However, despite the promise of this highly scalable intervention with past successes in prepandemic trials conducted among ICU survivors,[9] the current trial showed no greater improvement in distress symptoms among Lift recipients. There are likely several explanations that are directly relevant to future public health emergencies and the conduct of nested trials within active research networks worth considering.

Most importantly, the intervention dose was minimal and participant engagement was weak. App analytics revealed that only one-half initiated the intervention and that these participants viewed just 20% of the prescribed content. Such adherence is dramatically different from past mobile app-based trials our group has conducted in which complete 4-week adherence was observed for > 80% of participants.[9,21]

A key difference with the current trial compared with past work is the lack of a human touch in the introduction, onboarding, and support of the mobile app—a conscious choice designed to maximize scalability given the clinical research network setting and pandemic-related limitations on study staff entry into hospitals.[15] In essence, every element of the trial relied on the participant to do all tasks—the most minimalistic approach possible. Although the app prompted use daily, there was no other study team contact in person, by phone, or email/text as in our recent Lift trials. Although we included several extremely detailed video and text supports for users, there was much less user engagement observed than expected. Because there was no formal onboarding, were there to be a problem, it would be easiest for a participant to simply quit rather than try to figure out how to get help. In a past trial, we found that an intervention group who received a brief kickoff call from a trained therapist had greater retention and intervention effect than an intervention group who received no therapist contact.[21] In contrast, a recently completed multicenter trial testing eight different versions of Lift that compared approaches favoring user engagement (ie, therapist introduction and response to symptom changes) vs simplicity (ie, app-based introduction and response to symptom changes) found no differential effect on adherence or retention—both of which were very high.[43] That said, this trial included a robust study team presence at the time of hospital enrollment and phone check-ins from these same people to ensure app functionality. Given the stark contrast between this recent work and the current trial, it seems that a human presence is most valuable early in the engagement period—although there does not appear to be a need for specialized training (eg, therapist) to provide it effectively. These observations may help improve the success of future trials within research networks.

It is also possible that our protocol itself limited enthusiasm, and thus consent rates (53%) and engagement. First, BLUE CORAL participants had to complete a comprehensive multisurvey battery by telephone before they were approached for this trial and were often too tired to do another task. Of note, nearly all participants reported symptoms consistent with long COVID, including fatigue, shortness of breath, and so forth, further challenging their stamina. Second, participants frequently required a callback for consent from another unfamiliar phone number that likely included an area code that differed from the patient's own, likely increasing failure to contact rates. Third, the BLUE CORAL staff were much less expert than our core group in discussing the intervention; however, we thought that we were more likely to lose an opportunity to consent a patient with a second call from an unfamiliar phone number. Fourth, although this is speculative, patients may have suffered research fatigue after likely being approached for several trials during their hospitalization, which may have limited the likelihood of taking on yet another research project. Finally, the fact that all interactions were impersonal (ie, phone) and anonymized likely contributed to the lower than anticipated consent rate.

This trial also demonstrated some of the challenges of trying to rapidly integrate external protocols within an existing research network appropriately focused on its own projects, including regulatory delays associated with the complexity of navigating several institutional review boards, a clinical coordinating center, a data coordinating center, multiple data use agreements, and other factors. Although funding agencies prioritize the use of networks as research platforms to maximize shared resources and leverage costly infrastructure, there

may be differences in shared vision, capacity constraints, and complex multisite regulatory barriers that may be problematic for the timely conduct of such trials such as ours. Unfortunately, these delays greatly diminished the time window within which participants could be enrolled leading to a much smaller sample size than targeted. It may be valuable for funding agencies to review processes to enhance the success of future collaborative work on a large scale (eg, national research networks).

Limitations

The most notable limitation is the smaller than planned sample size, which we have previously described. The low dose of the intervention resulting from poor adherence is also problematic. Additionally, the primary outcome was assessed 2 months after randomization and 1 month after the intervention was completed in contrast to our past work that assessed intervention effect immediately after its completion. It is possible these factors could have minimized the measured intervention effect. Also, the lower-than-expected sample size and consent rate raise questions about generalizability. Finally, it is important for the reader to interpret the results while considering that this project was planned as a well-powered efficacy-focused trial, but ended up essentially being a feasibility study.

Interpretation

This completely self-directed mobile app-based mindfulness intervention deployed by distance during the COVID-19 pandemic had poor adherence overall. Future psychological distress interventions mobilized at broad scale should focus efforts on patient engagement and simplification of clinical trial network navigation to enhance success.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS:

BLUE CORAL	Biology and Longitudinal Epidemiology: COVID-19 Observational Study
GAD-7	Generalized Anxiety Disorder 7-item scale
IQR	interquartile range
PHQ-9	Patient Health Questionnaire 9

PTSD	posttraumatic stress disorder

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Take-home Points

Study Question:

Can a self-directed mobile app-delivered mindfulness intervention work when deployed without direct contact from a study team within a clinical trials network during a pandemic?

Results:

The intervention did not reduce psychological distress symptoms compared to control, however the adherence was very poor.

Interpretation:

This trial suggests that a focus on optimizing patient engagement with self-directed interventions is key to success.

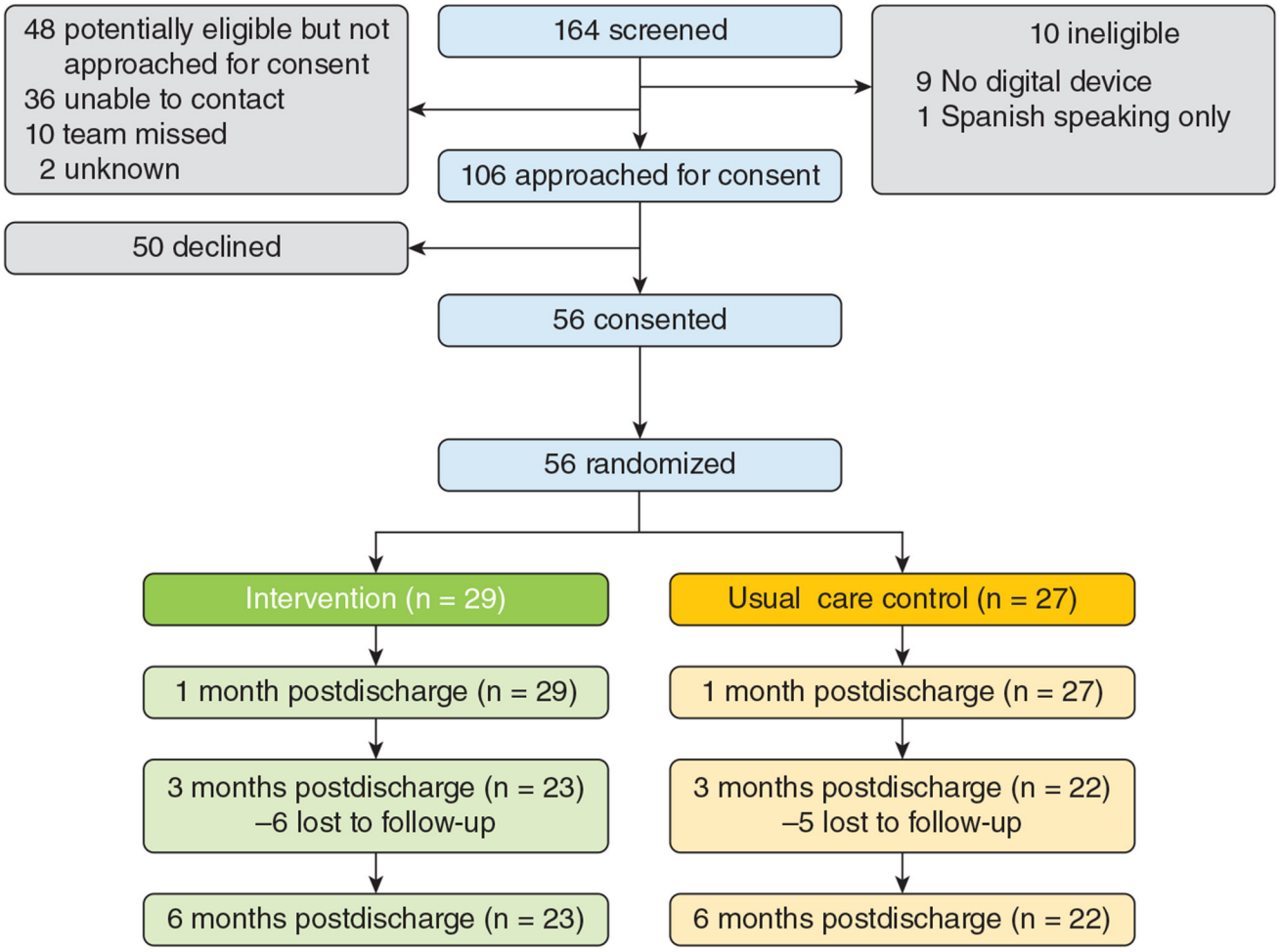

Figure 1 –.
Consolidated Standards of Reporting Trials diagram.

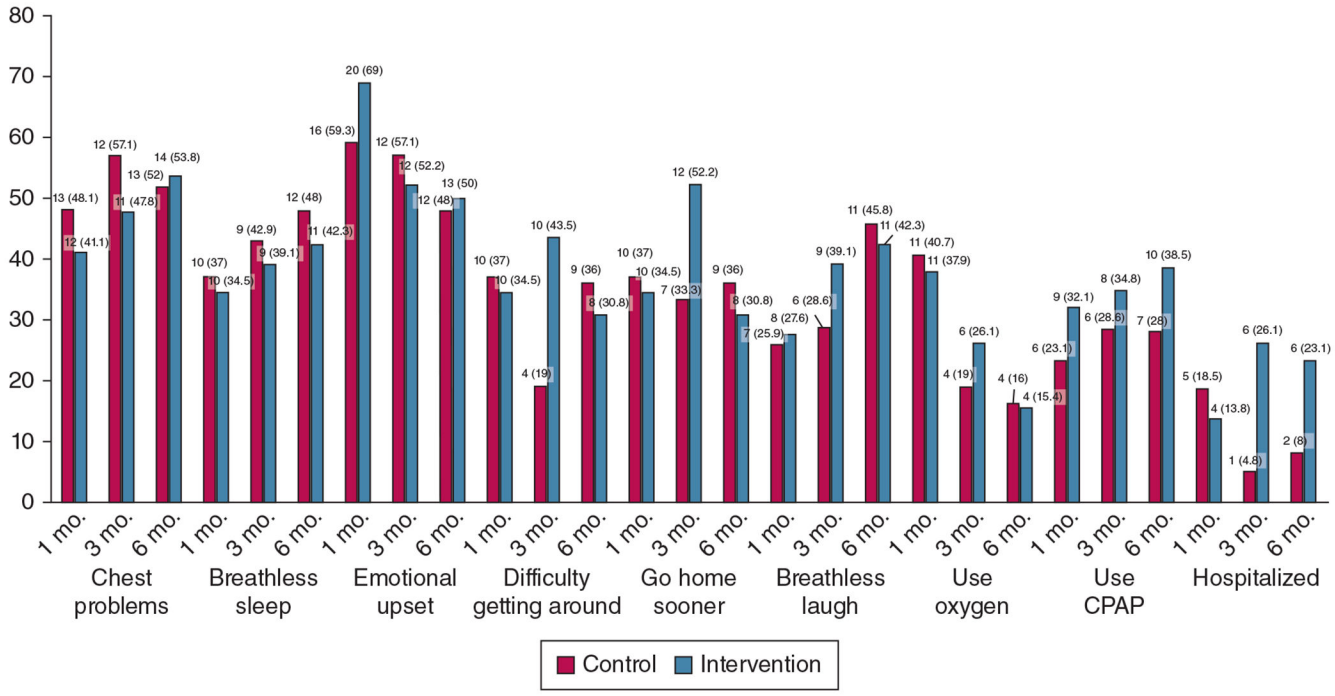

Figure 2 –.

Binary outcome summaries. Cardiopulmonary symptom frequency at 3 and 6 mo postdischarge for intervention (blue) and control (red) participants is shown.

TABLE 1]

Baseline Characteristics

Characteristic	Intervention Group (n = 29)	Control Group (n = 27)	Total (N = 56)
Age, y			
Mean ± SD	49.0 ± 14.2	53.1 ± 11.9	51.0 ± 13.2
Median (quartile 1-3)	52.3 (37.5-60.7)	53.9 (43.3-64.0)	52.4 (40.5-62.9)
Minimum, maximum	24.7, 70.6	33.9, 69.6	24.7, 70.6
Sex			
Male	9 (31.0)	9 (33.3)	18 (32.1)
Female	20 (69.0)	18 (66.7)	38 (67.9)
Race			
American Indian/Alaska Native	0 (0.0)	2 (7.4)	2 (3.6)
Black/African American	8 (27.6)	6 (22.2)	14 (25.0)
White	14 (48.3)	17 (63.0)	31 (55.4)
Other/declined[a]	5 (17.2)	2 (7.4)	7 (12.5)
Unknown/unavailable	2 (6.9)	0 (0.0)	2 (3.6)
Ethnicity			
Not Hispanic or Latino	19 (65.5)	23 (85.2)	42 (75.0)
Hispanic or Latino	8 (27.6)	3 (11.1)	11 (19.6)
Unknown	2 (6.9)	1 (3.7)	3 (5.4)
Recent living status			
Home independently	27 (93.1)	24 (88.9)	51 (91.1)
Home with help	2 (6.9)	3 (11.1)	5 (8.9)
Charlson Comorbidity Index score, without age points			
Mean ± SD	1.2 ± 1.7	1.3 ± 1.6	1.2 ± 1.7
Median (quartile 1-3)	0.0 (0.0-2.0)	1.0 (0.0-2.0)	1.0 (0.0-2.0)
Minimum, maximum	0.0, 6.0	0.0, 7.0	0.0, 7.0
Charlson Comorbidity Index score, with age points			

Characteristic	Intervention Group (n = 29)	Control Group (n = 27)	Total (N = 56)
Mean ± SD	1.9 ± 2.0	2.2 ± 1.9	2.0 ± 2.0
Median (quartile 1-3)	1.0 (0.0-3.0)	2.0 (1.0-3.0)	2.0 (0.5-3.0)
Minimum, maximum	0.0, 8.0	0.0, 8.0	0.0, 8.0
Comorbidity: alcohol abuse			
No	29 (100.0)	27 (100.0)	56 (100.0)
Comorbidity: drugs			
No	28 (96.6)	27 (100.0)	55 (98.2)
Yes	1 (3.4)	0 (0.0)	1 (1.8)
Comorbidity: psychosis			
No	29 (100.0)	26 (96.3)	55 (98.2)
Yes	0 (0.0)	1 (3.7)	1 (1.8)
Comorbidity: depression			
No	22 (75.9)	20 (74.1)	42 (75.0)
Yes	7 (24.1)	7 (25.9)	14 (25.0)
Comorbidity: PTSD			
No	29 (100.0)	26 (96.3)	55 (98.2)
Yes	0 (0.0)	1 (3.7)	1 (1.8)
Comorbidity: anxiety			
No	22 (75.9)	18 (66.7)	40 (71.4)
Yes	7 (24.1)	9 (33.3)	16 (28.6)
What is the patient's preferred language?			
English	29 (100.0)	27 (100.0)	56 (100.0)
Enrolled in Medicare?			
Missing	2 (6.9)	2 (7.4)	4 (7.1)
Yes	7 (24.1)	7 (25.9)	14 (25.0)
No	20 (69.0)	18 (66.7)	38 (67.9)
PHQ-9 score, baseline			
Mean ± SD	9.4 ± 3.6	10.0 ± 5.0	9.7 ± 4.3

Characteristic	Intervention Group (n = 29)	Control Group (n = 27)	Total (N = 56)
Median (quartile 1-3)	9.0 (7.0-11.0)	9.0 (6.0-13.0)	9.0 (6.0-11.5)
Minimum, maximum	5.0, 18.0	5.0, 24.0	5.0, 24.0
GAD-7 score, baseline			
Mean ± SD	6.5 ± 4.9	6.5 ± 5.4	6.5 ± 5.1
Median (quartile 1-3)	5.0 (3.0-9.0)	6.0 (1.0-11.0)	5.5 (2.5-10.5)
Minimum, maximum	0.0, 21.0	0.0, 16.0	0.0, 21.0

[a]Other indicates a self-response from participants who did not select one of the races provided. Values are No. (%) or as otherwise indicated. GAD-7 = Generalized Anxiety Disorder 7-item scale; PHQ-9 = Patient Health Questionnaire 9; PTSD = posttraumatic stress disorder.

TABLE 2]

Clinical Characteristics and Hospital Outcomes

Characteristic	Intervention Group (n = 29)	Control Group (n = 27)	Total (N = 56)
APACHE II acute physiology score			
Mean ± SD	7.5 ± 5.8	6.1 ± 4.7	6.8 ± 5.3
Median (quartile 1-3)	6.0 (4.0-9.0)	5.0 (3.0-7.0)	6.0 (3.5-8.0)
Minimum, maximum	2.0, 27.0	0.0, 24.0	0.0, 27.0
APACHE II total score			
Mean ± SD	11.8 ± 6.4)	10.5 ± 5.4	11.2 ± 6.0
Median (quartile 1-3)	11.0 (7.0-15.0)	10.0 (6.0-14.0)	11.0 (6.5-15.0)
Minimum, maximum	3.0, 27.0	3.0, 26.0	3.0, 27.0
ICU or step-down unit within 24 h of hospital admission?			
No	16 (55.1)	14 (51.9)	30 (53.6)
ICU	3 (10.3)	7 (25.9)	10 (17.9)
Step-down unit	7 (24.1)	2 (7.4)	9 (16.1)
Missing	3 (10.3)	4 (14.8)	7 (12.5)
ICU or step-down unit at any point during hospital admission			
No	17 (58.6)	16 (59.3)	33 (58.9)
ICU	8 (27.6)	10 (37.0)	18 (32.1)
Step-down unit	4 (13.8)	1 (3.7)	5 (8.9)
Invasive ventilation within 24 h of hospital arrival			
No	23 (79.3)	21 (77.8)	44 (78.6)
Yes	3 (10.3)	2 (7.4)	5 (8.9)
Missing	3 (10.3)	4 (14.8)	7 (13.5)
Invasive ventilation at any point during hospital admission			
No	23 (79.3)	23 (85.2)	46 (82.1)
Yes	6 (20.7)	4 (14.8)	10 (17.9)
No. of episodes of mechanical ventilation during encounter			
1	4 (13.8)	3 (11.1)	7 (12.5)

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Characteristic	Intervention Group (n = 29)	Control Group (n = 27)	Total (N = 56)
2	2 (6.9)	1 (3.7)	3 (5.4)
Missing	23 (79.3)	23 (85.2)	46 (82.1)
Noninvasive ventilation at any point during hospital admission			
No	25 (86.2)	21 (77.8)	46 (82.1)
Yes	1 (3.5)	2 (7.4)	3 (5.4)
Missing	3 (10.3)	4 (14.8)	7 (12.5)
Maximum respiratory state			
High flow nasal cannula	3 (10.3)	5 (18.5)	8 (14.3)
Noninvasive ventilation	0 (0.0)	1 (3.7)	1 (1.8)
None	5 (17.2)	6 (22.2)	11 (19.6)
Oxygen therapy	15 (51.7)	11 (40.7)	26 (46.4)
Mechanical ventilation	6 (20.7)	4 (14.8)	10 (17.9)
WHO COVID-19 maximum ordinal outcomes state summative outcome and summa			
3 (Hospitalized, not on oxygen)	5 (17.2)	6 (22.2)	11 (19.6)
4 (Hospitalized, on nasal cannula or face mask oxygen)	15 (51.7)	11 (40.7)	26 (46.4)
5 (Hospitalized, on noninvasive ventilation or high flow oxygen)	3 (10.3)	6 (22.2)	9 (16.1)
6 (Hospitalized, on mechanical ventilation)	1 (3.4)	1 (3.7)	2 (3.6)
7 (Hospitalized, on mechanical ventilation plus other organ support)	5 (17.2)	3 (11.1)	8 (14.3)
Hospital length of stay, d			
Mean ± SD	9.6 ± 9.8	8.8 ± 9.5	9.2 ± 9.5
Median (quartile 1-3)	7.0 (4.0-10.0)	6.0 (4.0-10.0)	6.0 (4.0-10.0)
Minimum, maximum	2.0, 42.0	3.0, 43.0	2.0, 43.0
At discharge, patient able to walk independently (> 50 ft, use of gait aid permitted)?			
No	5 (17.2)	3 (11.1)	8 (14.3)
Yes	22 (75.9)	21 (77.8)	43 (76.8)
Unknown	2 (6.9)	3 (11.1)	5 (8.9)
At discharge, patient able to perform ADLs independently?			
No	4 (13.8)	5 (19.2)	9 (16.4)

Characteristic	Intervention Group (n = 29)	Control Group (n = 27)	Total (N = 56)
Yes	23 (79.3)	18 (69.2)	41 (74.5)
Unknown	2 (6.9)	3 (11.5)	5 (9.1)
Hospital disposition at discharge			
Home	24 (82.8)	23 (85.2)	47 (83.9)
Home with home services	2 (6.9)	3 (11.1)	5 (8.9)
Inpatient rehabilitation facility	2 (6.9)	0 (0.0)	2 (3.6)
Nursing facility	1 (3.4)	0 (0.0)	1 (1.8)
Long-term acute care facility	0 (0.0)	1 (3.7)	1 (1.8)
How does ability to self-care at discharge compare vs before illness?			
Same as before illness	18 (62.1)	17 (63.0)	35 (62.5)
Worse than before illness	7 (24.1)	7 (25.9)	14 (25.0)
Better than before illness	2 (6.9)	1 (3.7)	3 (5.4)
Unknown	2 (6.9)	2 (7.4)	4 (7.1)

Values are No. (%) or as otherwise indicated. ADLs = activities of daily living; APACHE = Acute Physiology and Chronic Health Evaluation; WHO = World Health Organization.

TABLE 3]

Primary and Secondary Outcomes

Outcome	Time Point	Control Group	Intervention Group	Estimate, Intervention Group-Control Group (95% CI)
PHQ-9 score	Month 1	10.0 ± 5.0	9.4 ± 3.6	…
	Month 3	9.3 ± 6.5	9.5 ± 4.9	…
	Month 6	9.2 ± 6.9	8.6 ± 6.5	…
	Change, month 3 – month 1	−0.5 ± 4.3	0.1 ± 3.2	0.64 (−1.66 to 2.95)
	Change, month 6 – month 1	−0.8 ± 4.7	−0.6 ± 5.8	0.21 (−2.71 to 3.13)
GAD-7 score	Month 1	6.5 ± 5.4	6.4 ± 4.9	…
	Month 3	6.6 ± 6.9	6.6 ± 4.5	…
	Month 6	7.0 ± 6.5	6.4 ± 5.7	…
	Change, month 3 – month 1	−0.3 ± 5.3	0.1 ± 4.8	0.01 (−2.63 to 2.65)
	Change, month 6 – month 1	0.7 ± 4.6	0.3 ± 4.8	−0.43 (−2.95 to 2.09)
EQ-5D-5L index	Month 1	0.6 ± 0.3	0.6 ± 0.3	…
	Month 3	0.6 ± 0.3	0.6 ± 0.3	…
	Month 6	0.7 ± 0.3	0.6 ± 0.4	…
	Change, month 3 – month 1	−0.03 ± 0.25)	0.02 ± 0.19	0.02 (−0.11 to 0.15)
	Change, month 6 – month 1	0.03 ± 0.17	0.03 ± 0.29	−0.02 (−0.15 to 0.11)
ADLs score	Month 1	1.3 ± 1.6	1.6 ± 1.7	…
	Month 3	1.2 ± 1.6	1.9 ± 1.8	…
	Month 6	1.0 ± 1.5	1.5 ± 1.8	…
	Change, month 3 – month 1	−0.1 ± 1.8	0.1 ± 1.2	0.53 (−0.22 to 1.27)
	Change, month 6 – month 1	−0.2 ± 1.1	−0.1 ± 1.3	0.21 (−0.43 to 0.84)
IADLs score	Month 1	2.4 ± 1.9	2.3 ± 1.6	…
	Month 3	2.4 ± 1.9	2.4 ± 1.5	…
	Month 6	2.3 ± 2.1	2.3 ± 1.8	…
	Change, month 3 – month 1	< 0.001 ± 2.07	< 0.001 ± 0.95	0.002 (−0.84 to 0.85)
	Change, month 6 – month 1	0.04 ± 1.90	0.04 ± 1.76	0.03 (−0.90 to 0.96)
MOCA score	Month 1	16.5 ± 2.4	16.1 ± 3.2	…
	Month 3	16.9 ± 2.8	16.7 ± 3.9	…

Outcome	Time Point	Control Group	Intervention Group	Estimate, Intervention Group-Control Group (95% CI)
	Month 6	17.4 ± 2.8	16.8 ± 4.4	…
	Change, month 3 – month 1	0.8 ± 2.4	1.2 ± 2.2	0.67 (−0.72 to 2.06)
	Change, month 6 – month 1	1.0 ± 2.6	1.5 ± 1.9	−0.01 (−1.45 to 1.44)

Values are mean ± SD or as otherwise indicated. ADLs = activities of daily living; EQ-5DL = Euro-QOL 5 dimensional quality of life scale; GAD-7 = Generalized Anxiety Disorder 7-item scale; IADLs = instrumental activities of daily living; MOCA = Montreal Cognitive Assessment; PHQ-9 = Patient Health Questionnaire 9.

TABLE 4]

Binary Outcome Summaries

Outcome	Time Point	Control Group	Intervention Group
Chest problems	Month 1	13 (48.1)	12 (41.4)
	Month 3	12 (57.1)	11 (47.8)
	Month 6	13 (52.0)	14 (53.8)
Breathless sleep	Month 1	10 (37.0)	10 (34.5)
	Month 3	9 (42.9)	9 (39.1)
	Month 6	12 (48.0)	11 (42.3)
Emotional upset	Month 1	16 (59.3)	20 (69.0)
	Month 3	12 (57.1)	12 (52.2)
	Month 6	12 (48.0)	13 (50.0)
Difficulty getting around	Month 1	10 (37.0)	10 (34.5)
	Month 3	4 (19.0)	10 (43.5)
	Month 6	9 (36.0)	8 (30.8)
Go home sooner	Month 1	10 (37.0)	10 (34.5)
	Month 3	7 (33.3)	12 (52.2)
	Month 6	9 (36.0)	8 (30.8)
Breathless laugh	Month 1	7 (25.9)	8 (27.6)
	Month 3	6 (28.6)	9 (39.1)
	Month 6	11 (45.8)	11 (42.3)
Use oxygen	Month 1	11 (40.7)	11 (37.9)
	Month 3	4 (19.0)	6 (26.1)
	Month 6	4 (16.0)	4 (15.4)
Use CPAP	Month 1	6 (23.1)	9 (32.1)
	Month 3	6 (28.6)	8 (34.8)
	Month 6	7 (28.0)	10 (38.5)
Hospitalized since last visit	Month 1	5 (18.5)	4 (13.8)
	Month 3	1 (4.8)	6 (26.1)
	Month 6	2 (8.0)	6 (23.1)

Values are No. (%).