Comparing the effectiveness of existing anxiety treatment options among patients evaluated for chest pain and anxiety in the emergency department setting: study protocol for the PACER pragmatic randomized comparative effectiveness trial

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Abstract

Background: Anxiety disorders are a common underlying cause of symptoms among low-risk chest pain patients evaluated in the emergency department setting. However, anxiety is often undiagnosed and undertreated in any setting, and causes considerable functional impairment to work, family, and social life.

Objectives: The **P**atient-Centered Treatment of **A**nxiety after Low-Risk **C**hest Pain in the **E**mergency **R**oom (PACER) study is a pragmatic randomized trial to test the comparative effectiveness of existing anxiety treatments of graduated intensities and determine what options work best for patient subgroups based on anxiety severity and other comorbidities.

Methods: The PACER trial will enroll 375 emergency department patients with low-risk chest pain and anxiety (GAD-7 score ≥ 8) and randomize them to either: 1) referral to primary care with enhanced care coordination, 2) online self-administered cognitive behavioral therapy with guided peer support, or 3) therapist-administered cognitive behavior therapy. Outcomes include anxiety symptoms (primary) as well as physical symptom burden, depression symptoms, functional impairment, ED recidivism, and occurrence of major adverse cardiac events. Statistical analyses will be conducted primarily using linear mixed models to perform a repeated measures analysis of patient-reported outcomes, assessed at 3, 6, 9, and 12-month follow-ups.

Discussion: PACER is an innovative and pragmatic clinical trial that will compare the effectiveness of several evidence-based telecare-delivered treatments for anxiety. Results have the potential to inform clinical guidelines for evaluation and management of low-risk chest pain patients and promote adoption of findings in ED departments across the country.

Trial Registration: clinicaltrials.gov **Identifier:** NCT04811521.

Keywords: Chest pain, Emergency medicine, Anxiety, Panic, Patient-centered outcomes research, Telehealth

1. Introduction

Chest pain is the second most common reason for visits to US Emergency Departments (ED), accounting for more than 8 million ED visits in 2019.[1] Most resources, research and clinical efforts focus on detection and treatment of acute coronary syndrome; however, about 80% of all patients presenting to the ED with complaints of chest pain do not have cardiac disease or any other cardiopulmonary emergency by conventional testing at the time of evaluation.[2-4] People rarely seek medical care specifically for anxiety but are commonly seen in EDs with physical symptoms (chest pain, palpitations, shortness of breath) that can mimic a heart attack but are the result of autonomic arousal, better known as the 'fight or flight' response. In fact, anxiety disorders have been established as a major cause of symptoms in low-risk (non-cardiac) chest pain (LRCP) patients evaluated in the ED setting.[2,3,5-10]

Although cognitive behavioral therapy (CBT) is among the most evidence-based of treatments for anxiety disorders,[11] patients with anxiety who present with chest pain and related symptoms, often do not receive a clear explanation for their symptoms or recommendations for further care after discharge. Patients often remain confused about the cause of their ongoing symptoms and what to do about them and end up returning to the same or different ED for repeat diagnostic testing at great expense and of little benefit to the patient. Fear of a missed diagnosis, unclear pathways to access mental health services, shortages of mental health professionals, and separation of physical and mental health needs are all treatment barriers that can be overcome. While psychological therapies such as CBT have been tested in the LRCP population, and effects are at least moderate, the benefits of CBT are not fully understood in this population.[12] In addition to methodological challenges of the existing research, two main limitations to these studies exist. The first is clinical heterogeneity in terms of variation in interventions and characteristics of patients.

Second, receptivity to psychological therapies among LRCP patients has been identified as a major contributor to low participation in research and adherence to treatment protocols.

2. Methods

2.1 Overview of Study Design, Research Aims & Hypothesis

The **P**atient-Centered Treatment of **A**nxiety after Low-Risk **C**hest Pain in the **E**mergency **R**oom (PACER) study is a pragmatic randomized comparative effectiveness trial with two intervention arms and an active comparator arm. The study population is comprised of patients who are evaluated for chest pain in the Emergency Department, deemed low risk for a major adverse cardiac event, and screen positively for moderate to high anxiety. Enrolled patients are randomly assigned to one of the three arms that are graduated in the level of resource intensity and have demonstrated efficacy for real world adoption: 1) referral to primary care with enhanced care coordination; 2) online cognitive behavioral therapy (CBT) with guided peer support; or 3) therapist-led CBT. The specific aims are:

Aim 1: Compare the effectiveness of three treatment options on anxiety symptoms (primary outcome) as well as physical symptom burden, depression symptoms, and functional impairment at 3, 6, 9, and 12 months.

Hypothesis 1: *All three interventions will demonstrate a significant within-group treatment effect immediately post-treatment (3 months) that will be maintained through 12 months.* Hypothesis 2: *Online and therapist-led CBT will demonstrate greater improvement than primary care coordination, at 3, 6, 9, and 12 months*.

Aim 2: Compare the effect of treatment options on return trips to the ED and occurrence of major adverse cardiac events at 12 months.

Hypothesis 3: Over the 12-month period, all three treatment options will show a reduction in return ED visits compared with the known 36% rate of 1- year ED recidivism[13] and none of the three treatment options will show an increased rate of major adverse cardiac events compared to the known population prevalence of 2%.[14]

Aim 3: Determine the heterogeneity of treatment effects for all three arms among participants with more severe anxiety or psychiatric comorbidities (e.g., depression, substance use disorders, and post-traumatic stress disorder). Hypothesis 4: *Participants with psychiatric comorbidities and more severe anxiety symptoms will demonstrate greater treatment response than other participants, especially to more resource intense interventions (therapist-led CBT > online CBT > primary/coordinated care) at 3, 6, 9, and 12 months.*

The study was initially approved under full board review by the academic Institutional Review Board in March 2021. A four-member Data and Safety Monitoring Board meet bi-annually to review study progress.

2.2 Conceptual Model

All three arms receive one-time Screening, Brief Intervention, and Referral to Treatment (SBIRT) which uses motivational interviewing during the brief intervention (BI) component to enhance motivation to participate in treatment and maximize therapeutic engagement. A diagram shows our conceptual framework that explains how CBT and emotional support result in improved outcomes through causal mechanisms (**Figure 1**). Changes in self-efficacy have been shown to temporally precede and predict changes in anxiety symptoms following CBT.[15] Emotional and social support is provided by the therapist (in the high-intensity arm) or peer (in the medium intensity arm) to facilitate active participation in CBT activities and optimize outcomes. There may be multiple pathways by which emotional support may be directly beneficial in combination with traditional

healthcare delivery models, including enhanced social integration, improved self-efficacy, normalization of healthy behavior, and informal preventative health care.[16]

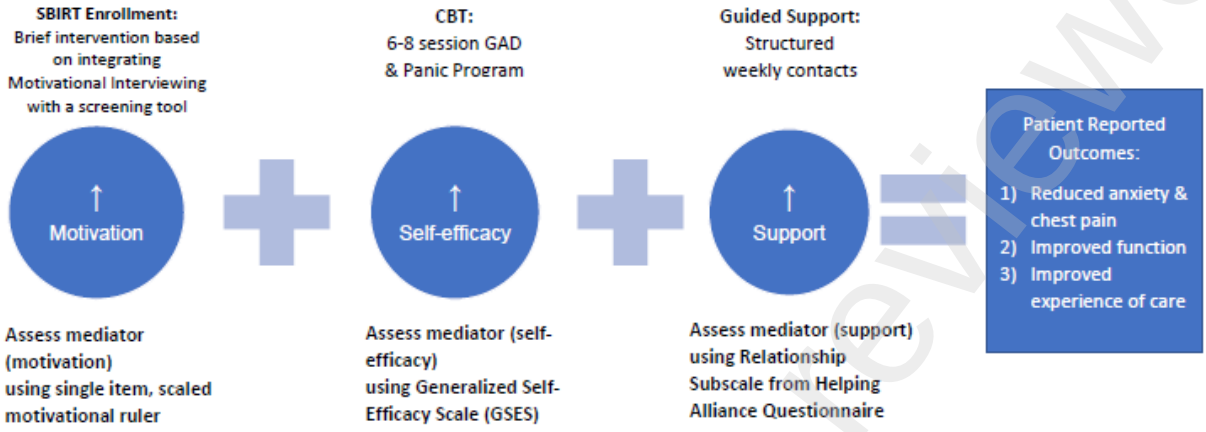

Figure 1. Hypothesized Causal Pathway of Cognitive Behavioral Therapy Interventions

2.3 Eligibility

Potential participants are patients ≥18 years old presenting to the ED with chest pain leading to a standard of care diagnostic protocol to rule out possible acute coronary syndrome. Discharge from the ED or observation unit within 24 hours are also pre-requisites for enrollment. In addition, screening results must reach a threshold of moderate to severe anxiety as defined by a GAD-7 score ≥ 8[17-19] or a PHQ panic screener score ≥ 2.[20,21] Low-risk chest pain is operationalized using an institution specific accelerated diagnostic protocol incorporating the Beckman-Coulter high sensitivity troponin I and the HEART score[14] (the acronym standing for history, EKG, age, risk, and troponin) as shown in **Figure 2**. Exclusion criteria include a HEART score ≥ 7; a new diagnosis of coronary artery disease adjudicated by the physician investigator to be high risk; traumatic chest pain; admission to the hospital; hemodynamic instability; active psychosis, schizophrenia, or suicidal ideation; and barriers to the telecare interventions (e.g., incarceration, homelessness and non-English speaking).

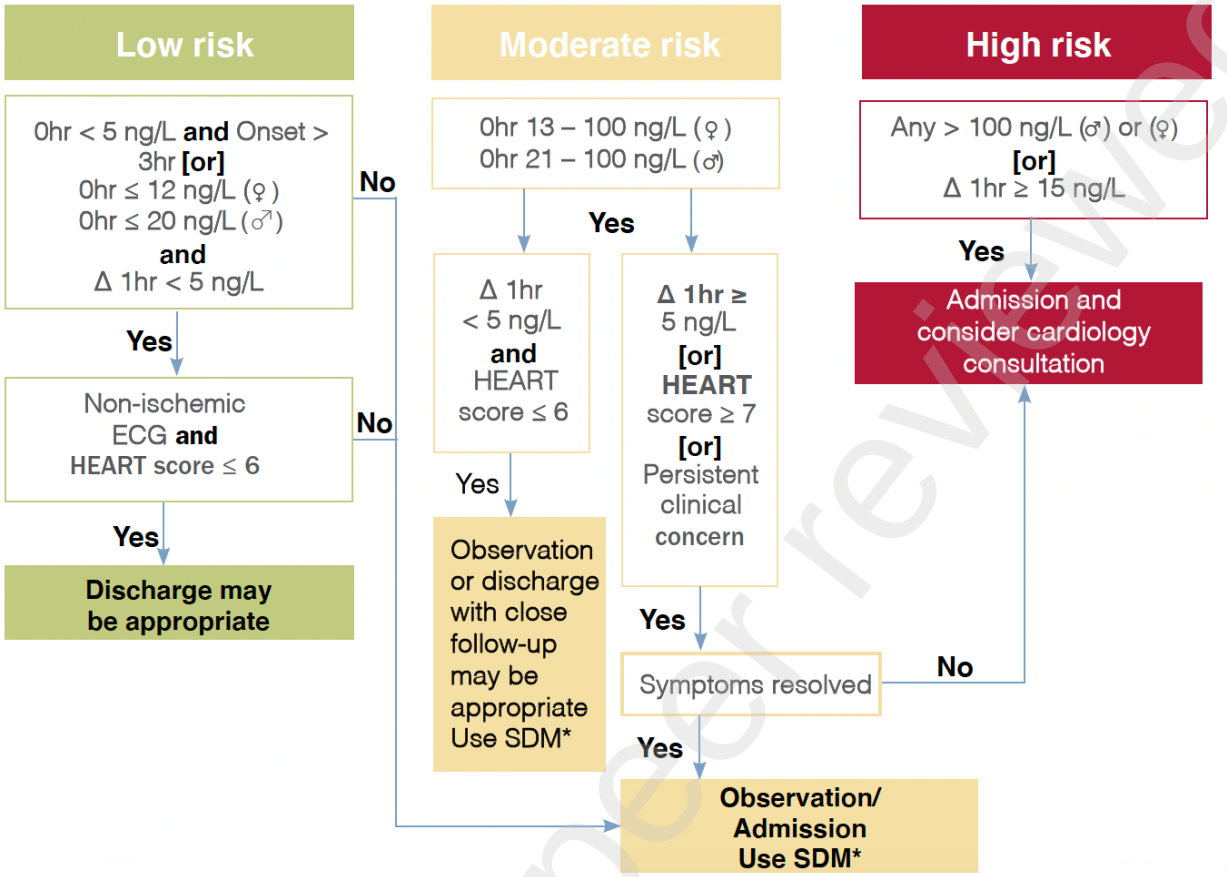

Figure 2. High-sensitivity troponin I accelerated diagnostic protocol for ACS in evaluation using the Beckman Coulter Access hsTnI. Protocol does not apply to STEMI or dynamic ST depression with chest pain. All lab values (ng/L) shown in figure refer to troponin. Figure adapted from the May 2021 IU Health high-sensitivity troponin ADP.

2.4 Recruitment

All patients eligible for study inclusion receive a brief intervention delivered by trained study personnel. A guide was developed for the screening and enrollment conversation based on the SBIRT model which often includes MI integration. This guided conversation to gauge and motivate interest in the study includes: 1) an initial discussion about anxiety as a common cause of symptoms among low-risk chest pain patients; 2) review of anxiety/panic screening results; 3) brief education about anxiety, symptoms, and treatments; 4) connection between patient symptoms and anxiety; 5) assessment of receptivity to psychological therapies; and 6) exploration of any ambivalence

between symptom burden and receptivity to treatment. The brief intervention is followed by solicitation to participate in the study. Participants who agree to participate complete the informed consent process.

2.5 Randomization

Enrolled participants are randomized to one of the three study arms in a permuted block design, using randomly varying block sizes of 6 or 12 to ensure allocation concealment. In addition, randomization is stratified on anxiety severity by using separate randomization lists generated by a SAS macro using a random number generator for two baseline strata: GAD-7 ≥ 15 (severe anxiety) and GAD-7 score of 8-14 (moderate anxiety).

2.6 Intervention

Table 1 provides an overview of the form of the interventions for all three arms: 1) coordinated primary care follow-up (low intensity); 2) 6 to 8 sessions of online cognitive behavioral therapy (CBT) with peer support guidance (medium intensity); and 3) 8-week course of therapist-led CBT via telehealth (high intensity). Our goal will be to complete both arm 2 and arm 3 interventions within a 12-week period whenever possible.

Table 1. Form and Dose of Interventions

Intervention arm	Mode of delivery	Providers involved	Materials required	Dose	Frequency/ Intensity
ARM 1: Enhanced primary care coordination	In-person or Telephonic	Research Personnel	Handout	Single	15 minutes
ARM 2: Online self-administered CBT with guided peer support	On-line + Telephonic	Peer	On-line CBT program	6 online lessons + 6-8 peer calls over 12 weeks	45-60 minutes
ARM 3: Therapist-Administered CBT	Telephonic	Mental health specialist	Manualized CBT plus homework	8 sessions over 12 weeks	60 minutes

2.6.1 Arm 1: Enhanced Primary Care Coordination

Enhanced primary care coordination includes referral back to an outpatient (primary or mental health) provider for further evaluation and treatment of mental health symptoms. The referral has 3 components: (1) assistance in identifying a primary care provider for participants who do not have one, (2) sharing results of diagnostic testing (including anxiety screening) with the primary care provider (results sent via electronic medical record note, mailed letter, or delivered by participant at appointment); and (3) an educational brochure on anxiety and treatment.

2.6.2 Arm 2: Online Self-Administered CBT with Guided Peer Support

This treatment arm couples online CBT with guided support provided by a mental health peer who is state certified as a Certified Recovery Specialist. The computerized portion consists of free access to six evidence-based CBT modules in the This Way Up Generalized Anxiety Program to be completed weekly or bi-monthly.[22,23] Individuals who screen positive for panic will complete two additional peer calls with supplementary handouts on exposure therapy from the This Way Up Panic Program.

The peer component includes individual, virtual contacts between completion of online lessons. The primary purpose of the peer visits is to guide discovery, self-awareness, and application of CBT knowledge and skills to develop self-efficacy for managing GAD symptoms. In addition, peers provide emotional support, share lived experience, and encourage independent completion of This Way Up online lessons and action plans. The role of the peer is not to teach the online portion or provide medical advice, but rather to facilitate a conversation guided by the participant's interest in lesson content that is most relevant or applicable to their own experience. Peers also receive enhanced training in motivational interviewing as a supportive communication strategy.

The structure for peer support contacts is based on a widely used model of peer support, adapted to integrate the lesson summary and action plan available at the end of each This Way Up session. This structure includes: 1) a brief check-in of participant's current experience of anxiety symptoms, 2) transition to a discussion about what information resonated most from the lesson and how it may be applied to the individual's anxiety experience, and 3) a closing portion focused on choosing at least one strategy or skill from the action plan to practice during the upcoming week.

2.6.3 Arm 3: Therapist-Administered CBT

Individuals randomized to Arm 3 receive therapist-led CBT delivered via telehealth. Participation includes 8 one-hour sessions over the course of 8 to 10 weeks delivered by therapists who are master's-degreed clinicians trained in CBT. Therapists will follow a manualized protocol for delivering CBT for anxiety based on the manual published by Dugas & Robichaud (2007),[24] a widely used and disseminated protocol that specifically targets generalized anxiety disorder (GAD), with a special focus on worry management. Individuals who screen positive on the PHQ panic measure will additionally receive training in exposure therapy. For participants whose predominant symptoms are related to panic disorder, the therapist can tailor CBT accordingly. Although many CBT trials have a standard length of 12 sessions, brief CBT lasting 4-8 sessions is equally efficacious.[25]

2.7 Intervention Fidelity

Approaches to promote and monitor intervention fidelity are aligned with strategies related to study design, provider training, and treatment delivery as recommended by the NIH Treatment Fidelity Workgroup recommendations.[26,27] In terms of study design, the form and treatment dose for the two intervention arms and active comparator is described **Table 1**. The dose across the two telehealth interventions (Arms 2 and 3) is approximately equivalent. For both these arms, the goal for participation is to attend all or most of the sessions (but at a minimum at least 4 sessions) over a

12-week period. In addition to using standardized intervention curriculums for CBT as described above, loosely structured scripts (e.g., facilitator guides) and visit checklists aid the standardization of delivery for the guided peer support component. Standardized training procedures are also used to train staff. For both arms, MI is integrated with CBT and Guided Peer Support conversations to enhance engagement and participation to support changes in managing anxiety.

The intervention fidelity monitoring plan is shown in **Table 2**. Interventionists in both arms will document completion of telehealth visits between the participant and peer or therapist in a REDCap database. Documentation includes mode (audio only or video), duration of visit, and the CBT lesson/module focused on for each visit. In Arm 2, initiation of online lessons is provided via a dashboard generated by the proprietor, and peers document whether the online lesson (or hardcopy) was completed prior to the peer call. In addition, Arm 2 documentation includes completion of essential visit components (i.e., check-in, discussion, closing).

Table 2. Intervention Fidelity Monitoring Plan.

Component	Online Self-Administered CBT with Guided Peer Support	Therapist-Administered CBT
Dosage (Participation) Measures	# online lessons initiated Completion of peer support calls: Mode (audio only or video) Duration of call (minutes) # Completed GAD lesson calls # Completed Panic lesson calls	Completion of therapist-client sessions Mode (audio only or video) Duration of call (minutes) # completed telehealth visits # unique CBT modules covered
Fidelity Measures:		
Visit Checklist	Completed each visit by peer and during quarterly audits of recorded visits	Not applicable
Cognitive Therapy Scale	Guided Discovery subscale rating completed by observers during audits of recorded visits	Full scale completed by therapist each visit and sample recording used during monthly group feedback sessions with supervisor
MI Spirit Scale	Completed by observers during audits of recorded visits	Completed by observers during audits of recorded visits
Supervisor visits	# of bi-monthly visits documented by supervisor	# monthly visits documented by supervisor

Quarterly audits are conducted on a sample of audio recorded sessions for each interventionist. Audits include ratings on the visit checklist (Arm 2), a 11-item Cognitive Therapy Scale, and a 6-item Motivational Interviewing (MI) Spirit Scale. The full CTS scale is used in Arm 3 while the guided discovery subscale is used in Arm 2. In Arm 2, observers rate scales and feedback is provided to peers during ongoing quarterly training to improve performance. In Arm 3, self-ratings and monthly group discussions of a randomly selected recording are held during supervisory visits to improve performance.

2.8 Outcome Measures Schedule and Mode of Administration

Table 3 summarizes the study outcome and process measures in addition to the schedule regarding frequency of assessments. The baseline assessment will be conducted by research assistants either in-person in the ED or telephonically (if telephonically, this will optimally within a few days of their ED visit). Follow-up assessments will be collected by a REDCap link sent by email or text. Those not completing the on-line REDCap survey will have the follow-up assessments completed telephonically by a research assessment.

Table 3. Outcome and Process Measures and Schedule of Administration

Domain	Measure	# Items	Schedule (month)				
			0	3	6	9	12
Primary outcome: Anxiety symptoms	GAD-7 total score[28]	7	X	X	X	X	X
Secondary outcomes							
Panic disorder screener	PHQ panic screener[20]	1-4	X	X	X	X	X
Depression symptoms	PHQ-8 total score[29]	8	X	X	X	X	X
Physical symptoms	PHQ-14 total score[30,31]	14	X	X	X	X	X
Work/family/social functioning	Sheehan Disability scale[32,33]	3	X	X	X	X	X
Global change	Patient-rated global change[34]	1		X	X	X	X
Utilization	Return visits to ED	1	X	X	X	X	X
Adverse Events	Major adverse cardiac events	1	X	X	X	X	X
Covariates							
Demographics	Eight sociodemographic variables	8	X				
Substance use	Substance use screener[35-37]	8	X				
Posttraumatic stress disorder (PTSD)	PTSD screener[38,39]	4	X				
Psychotropic medications			X	X			
Process measures							
Acceptability of intervention	Net Promotor Score (NPS)[40]	1		X	X		
Satisfaction with intervention	Telecare intervention satisfaction	6			X		
Self-efficacy	Generalized Self-Efficacy Scale (GSES)[41]	6	X	X	X		
Therapeutic alliance	Helping Alliance Questionnaire (HAQ-I Patient version) Relationship Subscale by peer/therapist[42]	6		X	X		
Intervention fidelity	CBT and peer support (completed sessions; approximate time)	2	Every CBT and peer support session				
Collaborative Capacity	Butterfoss' Coalition Characteristics Scale[43,44] (among partners)	42	Annually				

2.9 Statistical Considerations

2.9.1 Statistical Analysis

The analyses for *Aim 1* will be conducted using linear mixed models to perform a repeated measures analysis of patient-reported outcomes, assessed at 3, 6, 9, and 12-month follow-up, adjusted for the baseline measure of the outcome score. A separate model will be performed for each continuous outcome variable. These models will allow use of data from persons missing some but not all follow-up measures. Intent-to-treat analysis will be conducted by analyzing persons according to their randomized group assignment regardless of their protocol adherence. Theoretically important and potentially confounding baseline demographic characteristics will be adjusted for including age, sex, race, ethnicity, income, education, comorbid conditions (PTSD, SUD, depression), and perceived therapeutic alliance.

Within-arm efficacy will be tested with the model's Time effect. Within-arm effect sizes will be calculated using the standardized response mean (SRM; change in mean score from baseline to each follow-up, divided by SD of change scores). Between-group efficacy will be tested using the model's Group effect (omnibus, and pairwise tests). Pairwise effect sizes will be calculated using Cohen's *d* (difference between adjusted means, divided by group-pooled baseline SD). Interactions between randomized arm and time will be tested to determine whether arms differ significantly in how their outcomes change over time.

Dose-response relationships will be examined by testing the association between participation measures (e.g., CBT modules and peer support sessions completed) and outcomes for each treatment arm separately. The MPLUS software[45] will be used to test the indirect, direct, and total effects of mechanism measures (e.g., general self-efficacy) as mediators of intervention effectiveness on the outcomes. Participant acceptance of interventions will be assessed with the Net Promoter Score (NPS) and brief interviews with participants at completion.

For *Aim 2*, exact binomial tests of single proportions will be used to compare each arm to known populations rates for return trips to the ED and occurrence of major adverse cardiac events, respectively, using a two-sided inequality test of 12-month recidivism rates and a one-sided non-inferiority test of 12-month major cardiac event rates.

For *Aim 3*, heterogeneity of treatment effects will be tested by including interaction terms between arm and potential effect moderators. The latter will include baseline anxiety severity (GAD-7 score) and other psychiatric comorbidities (depression, elevated AUDIT-C score for risky drinking, or screen positive for PTSD or panic). We hypothesize that the between-arm efficacy superiority of the two CBT-based arms vs enhanced-coordinated primary care will be even greater among participants with severe anxiety symptoms (GAD-7 ≥ 15), co-morbid PTSD, and co-morbid SUD, compared to participants with moderate anxiety symptoms (GAD-7 = 8-14), and without co-morbid PTSD and SUD.

2.9.2 Sample Size and Power

Power was calculated with the PASS software (v.19.0.1). Assuming 20% 3-month attrition, an enrolled baseline sample of 125 in each arm will provide 100 in each arm at 3 months, which will achieve 84% power for the 3-arm between-group two-sided omnibus F-test, and 80% power for pairwise two-sided t-tests between primary care and each CBT intervention arm, for continuous patient-reported outcome scales. This calculation assumed a hypothesized Cohen's *d* effect size of 0.40 between each CBT arm and the coordinated primary care arm, and a Cohen *d* of 0.00 (zero; i.e., comparable) effect size between online CBT versus therapist-led CBT. The 3-month assessment is the first follow-up time point and the primary time point used to determine sample size for which power calculations are conservative because repeated measures of patient-reported outcome data (3, 6, 9, 12 months) will be analyzed simultaneously in linear mixed models.

The primary outcome will be the GAD-7 anxiety score which has proven responsive in prior pragmatic trials.[46,47] The GAD-7 has comparable responsiveness to other legacy anxiety measures and an effect size of 0.40 is approximately 2 points.[48] Tests of secondary outcomes will be adjusted for multiple comparisons using the False Discovery Rate approach.[49]

A 3-month sample of 100 per arm will provide (1) 94% power to detect a difference between 12-month ED recidivism rates of 20% for each intervention versus the known 36% population recidivism rate, using a two-sided exact binomial test, and (2) 86% power to detect a 6% absolute difference at 12 months between each intervention and the known 2% population major cardiac event rate (i.e., 2% vs 8%), using a one-sided exact binomial non-inferiority test, and assuming the actual rate difference is 0 (zero).

2.10 Patient and Stakeholder Involvement

Patients, providers, researchers, and health system leaders were involved from the beginning of research planning through an engagement award designed to develop a multi-stakeholder research partnership and capacity for collaborative research. Initial engagement activities including listening sessions, a photovoice project[50], and multi-stakeholder discussions were undertaken to improve understanding of multiple perspectives on anxiety and patient experience of care in the ED.[51] These engagement activities informed several aspects of study design such as: 1) identification of the SBIRT approach to study recruitment and enrollment, 2) selection of study interventions and comparators, and 3) identification of treatment effect moderators.

All stakeholders also provided input into the selection of types of outcomes (e.g., cognitive, physical, and functional) and specific outcome measures. Of primary interest to patients was inclusion of functional outcomes for which they felt the Sheehan Disability Index resonated with their lived experience of anxiety. Interestingly, patients placed high importance on measuring ED recidivism, which we had anticipated would be of most interest to clinical and administrative

stakeholders. However, from the patient perspective, it was important to avoid unnecessary and time-consuming trips to the ED for care that may not be beneficial and wastes money that could be better spent on treatment.

During conduct of the research study, the research partnership grew to include a primary focus of patient and stakeholder engagement activities to review progress toward study recruitment, enrollment, and retention milestones and provide recommendations to improve study performance. Examples of patient involvement during the start-up phase includes reducing jargon and improving clarity of informed consent documents, creating training videos for guided conversations during enrollment, and developing a recruitment brochure. Other key focus areas of patient and stakeholder engagement activities throughout the study include identifying and mitigating barriers to study intervention participation; ensuring equitable participation among social identity groups that are discriminated against, stigmatized, or otherwise underappreciated in society; and return of study results to research participants.

3. Discussion

The PACER trial is the first patient-centered outcomes research study to compare the effectiveness of established anxiety treatment options among patients evaluated for chest pain in the ED who are deemed low-risk for a major adverse cardiac event with presence of moderate to high symptoms of anxiety and panic. This study has potential to inform clinical guidelines for the evaluation and management of patients presenting with recurrent low-risk chest pain. We designed this pragmatic trial to inform and mitigate known barriers to improving care for these patients by: a) not only assessing benefit but also risk of major adverse cardiac events to alleviate fear of a missed diagnosis among physicians, b) creating clear pathways to accessing mental health services among LRCP patients with anxiety and panic symptoms so providers can act on screening results, c) addressing shortages of mental health professionals by delivering interventions via telehealth and

including self-help CBT treatment options coupled with mental health peer support which fall within the rapidly expanding use of community health workers, d) and connecting the dots between common mental health problems and physical symptoms with 'no discernable cause'. We also address primary limitations to prior research by having sufficient power to detect between and within group differences in comparing effectiveness of interventions, using manualized interventions, and assessing heterogeneity of treatment effects (e.g., which treatment option might work better for patients with certain characteristics). Furthermore, based on input from patients, we implemented the brief intervention component of the SBIRT model to improve patient receptivity to participation in psychological therapies.

However, delivering evidence-based treatments in a new setting and population also presents patient-level implementation challenges to the study. As mentioned previously, we implemented SBIRT enrollment principles to ease patients' cognitive transition from thinking they are having a heart attack to contemplating anxiety as a cause of symptoms. Our early experience suggests additional barriers to being confident and ready to initiate participation in mental health intervention exist such as discomfort with virtual technology and an online learning environment, mistrust of health services among communities of color and other social identity groups at risk for discrimination and competing demands due to resource constraints related to social determinants of health. This study poses an opportunity to learn from exploration and mitigation of these additional barriers to participation that also have implications for potential adoption of study findings. In the absence of a hybrid effectiveness-implementation study design, we have undertaken an ancillary study to PACER to explore barriers and facilitators of participation to expedite the dissemination and implementation phase of research.

In conclusion, the PACER trial is an innovative research approach to solving the problem of '*getting the right care to the right patient at the right time*' for low-risk chest pain patients with anxiety and panic evaluated in the emergency department setting.

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Statement of Competing Interests:

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