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Study to promote innovation in rural integrated telepsychiatry (SPIRIT): Rationale and design of a randomized comparative effectiveness trial of managing complex psychiatric disorders in rural primary care clinics

John C. Fortney[a,b,*], Patrick J. Heagerty[c], Amy M. Bauer[a], Joseph M. Cerimele[a], Debra Kaysen[a], Paul N. Pfeiffer[d,e], Melissa J. Zielinski[f], Jeffrey M. Pyne[f,g], Deb Bowen[h], Joan Russo[a], Lori Ferro[a], Danna Moore[i], J.P. Nolan, Florence C. Fee[j], Tammy Heral, Jode Freyholtz-London[k], Bernadette McDonald[a], Jeremey Mullins[a], Erin Hafer[l], Leif Solberg[m], Jürgen Unützer[a]

[a] Department of Psychiatry and Behavioral Sciences, School of Medicine, University of Washington, Seattle, WA, USA
[b] Department of Veterans Affairs, Health Services Research and Development, Center of Innovation for Veteran-Centered and Value-Driven Care, Seattle, WA, USA
[c] Department of Biostatistics, School of Public Health, University of Washington, Seattle, WA, USA
[d] University of Michigan Medical School, Ann Arbor, MI, USA
[e] Department of Veterans Affairs, Health Services Research and Development, Center for Clinical Management Research, VA Ann Arbor Healthcare System, Ann Arbor, MI, USA
[f] Department of Psychiatry, College of Medicine, University of Arkansas for Medical Sciences, Little Rock, AR, USA
[g] Department of Veterans Affairs, Health Services Research and Development, Center for Mental Healthcare and Outcomes Research, Little Rock, AR, USA
[h] Department of Bioethics and Humanities, University of Washington, Seattle, WA, USA
[i] Social and Economic Sciences Research Center at Washington State University, Pullman, WA, USA.
[j] NHMH - No Health without Mental Health, San Francisco, CA, Arlington, VA, USA.
[k] Wellness in the Woods, Eagle Bend, MN, USA
[l] Community Health Plan of Washington, Seattle, WA, USA
[m] Health Partners Institute, Minneapolis, MN, USA

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ABSTRACT

Objective: Managing complex psychiatric disorders like PTSD and bipolar disorder is challenging in Federally Qualified Health Centers (FQHCs) delivering care to U.S residents living in underserved rural areas. This protocol paper describes SPIRIT, a pragmatic comparative effectiveness trial designed to compare two approaches to managing PTSD and bipolar disorder in FQHCs.

Interventions: Treatment comparators are: 1) Telepsychiatry Collaborative Care, which integrates consulting telepsychiatrists into primary care teams, and 2) Telepsychiatry Enhanced Referral, where telepsychiatrists and telepsychologists treat patients directly.

Methods: Because Telepsychiatry Enhanced Referral is an adaptive intervention, a Sequential, Multiple Assignment, Randomized Trial design is used. Twenty-four FQHC clinics without on-site psychiatrists or psychologists are participating in the trial. The sample is patients screening positive for PTSD and/or bipolar disorder who are not already engaged in pharmacotherapy with a mental health specialist. Intervention fidelity is measured but not controlled. Patient treatment engagement is measured but not required, and intent-to-treat analysis will be used. Survey questions measure treatment engagement and effectiveness. The Short-Form 12 Mental Health Component Summary (SF-12 MCS) is the primary outcome.

Results: A third (34%) of those enrolled (n = 1004) are racial/ethnic minorities, 81% are not fully employed, 68% are Medicaid enrollees, 7% are uninsured, and 62% live in poverty. Mental health related quality of life (SF-12 MCS) is 2.5 standard deviations below the national mean.

Discussion: We hypothesize that patients randomized to Telepsychiatry Collaborative Care will have better outcomes than those randomized to Telepsychiatry Enhanced Referral because a higher proportion will engage in evidence-based treatment.

* Corresponding author at: Division of Population Health, Department of Psychiatry, University of Washington, 1959 Pacific Street, Box 356560, Seattle, WA 98195-6560, USA.
E-mail address: fortneyj@uw.edu (J.C. Fortney).

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1. Introduction

Federally Qualified Health Centers (FQHCs) deliver primary care (PC) services in areas with geographical, financial, and/or cultural barriers to care. There are nearly 1400 FQHCs with over 10,000 clinic locations that provide services to 27 million Americans [1]. FQHCs are America's healthcare safety net. Almost half (44%) of FQHC patients live in rural areas [2], 90% live in poverty [3], and 56% are racial/ethnic minorities [3]. Psychiatric disorders are 50% more prevalent among Medicaid enrollees and those living in poverty than the general population [4]. In 2017, over 2 million FQHC patients were diagnosed with a mood disorder, and 2 million were diagnosed with an anxiety disorder or posttraumatic stress disorder (PTSD) [5]. Many more patients with psychiatric disorders likely went undiagnosed.

The percentage of PC patients screening positive for PTSD ranges from 14%–23% [6–12]. Without systematic screening, PTSD usually goes undetected, with only 11%–18% of PC patients meeting clinical criteria for PTSD having a documented diagnosis [12,13]. Of those individuals eventually diagnosed with PTSD, an average of 12 years elapses between onset and diagnosis [14]. Only 34.4% of individuals meeting clinical criteria for PTSD receive specialty mental health care during the course of a year, and only 23% have a psychiatrist visit [15]. In PC, only 13% of patients meeting clinical criteria for PTSD receive adequate care (e.g., two months of an antidepressant or evidence-based psychotherapy) compared to 57% of patients receiving specialty mental health care [15,16].

Among PC patients with depression, the percentage of patients screening positive for lifetime mania ranges from 21%–31% [17]. One study found that none of the 112 PC patients screening positive for bipolar disorder (BD) had a documented diagnosis [18]. Of those individuals eventually diagnosed with BD, an average of 6–8 years elapses between onset and diagnosis [14,19]. Only 34% of individuals meeting clinical criteria for BD receive specialty mental health care during the course of a year and only 23% have a psychiatrist visit [15]. Partially due to lack of recognition, patients with BD in PC are often prescribed antidepressants in the absence of a concomitant mood stabilizer, which clinical guidelines strongly advise against [20]. In PC, only 9% of patients meeting clinical criteria for BD receive adequate care (e.g., mood stabilizer) compared to 54% of patients receiving specialty mental health care [15,16].

Managing complex psychiatric disorders is especially challenging in the FQHC setting. While 87% of FQHCs offer on-site mental health services, only 15% of mental health staff are psychiatrists or licensed clinical psychologists [21]. FQHC providers and patients consistently report problems accessing off-site specialty mental health services [22–24]. The *Study to Promote Innovation in Rural Integrated Telepsychiatry* (SPIRIT) is a pragmatic trial (PCORI PCS-1406-19,295) comparing two telemedicine approaches to managing PTSD and BD in FQHCs serving rural populations. One approach, Telepsychiatry Collaborative Care (TCC), uses consulting psychiatrists embedded in a primary care team while the other approach, Telepsychiatry Enhanced Referral (TER), uses psychiatrists and psychologists to deliver specialty treatment directly to patients. This paper describes the methods used in the trial and the baseline sample.

2. Methods

The study protocol was approved and monitored by the Institutional Review Boards at the University of Arkansas for Medical Sciences, University of Michigan, and the University of Washington. Participating FQHCs obtained a Federalwide Assurance designating their state's medical school's Institutional Review Board as having oversight of human subjects protection, allowing FQHC staff to be fully engaged in research activities. Study progress and patient safety was monitored biannually by an external Data Safety Monitoring Board comprised of a statistician, primary care physician and psychiatrist.

2.1. Stakeholder input on design and conduct of trial

The SPIRIT trial was designed with substantial input from our consumer, advocate, provider and payor stakeholders. The rationale for the trial was informed by prior collaborations between state medical schools, FQHCs, and Medicaid plans [24–27]. Through these prior collaborations we learned that the vast majority of FQHC patients with PTSD (77%) and/or BD (74%) were not receiving specialty mental health care [28]. FQHC patients told us they faced insurmountable barriers to off-site specialty mental health care. FQHC providers told us they felt *obligated*, yet *unprepared*, to treat patients with complex psychiatric disorders.

The methods and materials of the SPIRIT trial were developed in close collaboration with our Consumer Advisory Board and Policy Advisory Board, both before and after receiving research funding. Our Consumer Advisory Board includes FQHC patients, veterans, and representatives from consumer advocacy groups such as the *National Alliance on Mental Illness*, *Depression and Bipolar Support Alliance*, *Wellness in the Woods,* and *NHMH - No Health without Mental Health*. The Consumer Advisory Board focused on recruitment materials, choosing and refining survey questions, creating new scales specifically designed for the trial, qualitative interview guides, suicide risk assessment and safety planning protocols, and acceptability of intervention components. The Consumer Advisory Board also provided feedback on the storyboards and prototypes of the SPIRIT App (described below) [29]. Our Policy Advisory Board includes FQHC Executive Directors, and representatives from the state level FQHC *Primary Care Associations,* the *National Association of Community Health Centers*, and the *National Association of Rural Mental Health*. The Policy Advisory Board focused on provider issues such as credentialing and privileging, access to electronic health records, indemnity, and billing. Both the Consumer Advisory Board and Policy Advisory Board will be involved in interpreting the results of the trial and in disseminating the findings.

2.2. Study design

The SPIRIT trial is designed to examine the potential tradeoff between treatment effectiveness and patient treatment engagement. From a population health perspective, the goal of the two treatments delivered in SPIRIT is to maximize “population-level effectiveness” [30] which is the product of reach (i.e., percent of patients receiving treatment) and effectiveness (percent of reached patients who respond to treatment) [30,31]. Reach depends on both patient treatment engagement and the capacity of the healthcare system. There is no universally agreed upon definition of treatment engagement. We adopt the definition proposed by the Center for Advancing Health - “actions individuals must take to obtain the greatest benefit from the health care services available to them” [32]. Patient treatment engagement depends on access to care, perceived need for treatment, and beliefs about treatment-seeking [33]. Both TCC and TER were designed to increase patient engagement in mental health treatment by increasing geographic access. However, by fully integrating mental health care and physical health care, TCC is hypothesized to further engage patients by normalizing beliefs about treatment-seeking and improving cultural access (e.g., trust in providers). Theoretically, by leveraging scarce psychiatry resources TCC should also have higher capacity than TER, however this trial does not examine capacity. Effectiveness depends on clinical expertise, including the training, experience and skill of providers. TER is hypothesized to have greater effectiveness for those patients reached because the care is being delivered by mental health specialists (psychiatrists and psychologists) rather than by a primary care team. Theoretically, TCC and TER represent clinical equipoise with respect to population-level effectiveness, with the former expected to have greater reach, but lower effectiveness (for those patients reached) and the latter expected to have lower reach, but greater effectiveness (for those patients who are reached). Nevertheless, in our planned

intent-to-treat analysis, we hypothesize that the greater treatment engagement in the TCC arm will result in better outcomes as compared to the TER arm.

SPIRIT is a pragmatic [34] trial with broad inclusion criteria and limited exclusion criteria. Intervention fidelity is measured but not controlled. Patient engagement in treatment is measured but not required, and intent-to-treat analysis will be conducted for primary analysis. Telepsychiatrists and telepsychologists from the state medical schools provide the specialty mental health care, which may seem less than pragmatic [34]. However, because publicly funded academic medical centers are the predominant practice setting for delivering telemedicine services to rural areas [35], our results should generalize to wider routine care.

2.3. Sites and study population

Twenty four clinics from 12 FQHCs from three states (Arkansas, Michigan and Washington) in the U.S. are participating in the trial. FQHC clinics were eligible for participation if they had no psychiatrists or psychologists practicing on site. Most clinics had social workers practicing on-site, but these providers had not previously been trained to deliver evidence-based psychotherapies for PTSD or BD. The characteristics of the participating FQHCs are presented in Table 1, along with FQHC national averages for comparison. Patients were recruited from November 16, 2016 to June 30, 2019.

2.4. Screening for PTSD and BD

FQHCs routinely screen for depression using the PHQ-9 (see Table 1). To participate in the SPIRIT trial, clinics also had to implement systematic screening for PTSD and BD as part of a quality improvement initiative. As a result, patients were not asked to provide informed consent for screening. The screening protocol was developed previously through collaborations with FQHC providers and clinical experts [24]. In order to minimize the rate of false positives and to minimize screening burden on FQHC staff and patients, only patients screening positive for depression (PHQ-9 $\geq$ 10) are screened for PTSD and BD. The PTSD Check List (PCL-6) is being used to screen for current PTSD and the Composite International Diagnostic Interview (CIDI 3.0) is being used to screen for lifetime mania. In VA primary care clinics, the PCL-6 has good sensitivity (0.80) and specificity (0.76) [36]. In the general population, the CIDI has good sensitivity (0.87) and specificity (0.99) [37]. We contracted with the electronic health record vendors used by participating FQHCs to develop electronic screening templates for PTSD and BD.

2.5. Patient inclusion and exclusion criteria

Patients are eligible to participate if they screen positive for PTSD (PCL-6 $\geq$ 14) and/or BD (CIDI $\geq$ 8). Exclusion criteria are minimal. Children (age $<$ 18) are excluded, as are those who could not communicate in English or Spanish, or lacked the capacity to consent. Patients not expected to receive care at the participating FQHC in the future are also excluded. Because collaborative care has been widely adopted by Washington FQHCs [38], we excluded those patients in Washington state already enrolled in a collaborative care program. In addition, because the trial focused on patients who could not be successfully referred off-site for specialty mental health services, we also exclude patients who report currently being prescribed a psychotropic medication by mental health specialist (e.g., psychiatrist, psychiatric nurse practitioner) in the community. This exclusion criterion also minimized the likelihood that study participants would receive multiple psychotropic prescriptions from different mental health specialists. Note that we did not exclude patients who were receiving counseling from an on-site or community therapist at baseline, because we did not anticipate that the evidence-based psychotherapies offered to study participants as part of the trial would be contraindicated to the counseling concurrently being delivered by on-site or community therapists as a part of routine care.

2.6. Recruitment

FQHC staff recruit and consent patients. Following a positive PTSD or BD screen, FQHC staff assess study eligibility prior to recruiting the patient and engaging them in the informed consent process. FQHCs were reimbursed $600 for each patient consented to cover the cost of the research activities of recruiting and consenting. Once a patient gives consent, FQHC staff upload screening results and other personal

Table 1
Characteristics of FQHCs Participating in the SPIRIT Trial.

Characteristic	FQHC 1	FQHC 2	FQHC 3	FQHC 4	FQHC 5	FQHC 6	FQHC 7	FQHC 8	FQHC 9	FQHC 10	FQHC 11	FQHC 12	US Ave
Total number of patients[1]	17,104	28,262	210,894	22,784	16,078	2700	15,767	18,086	24,130	51,367	44,065	68,221	19,792[3]
% Adult[1]	53.2%	58.0%	64.3%	60.9%	72.5%	69.0%	57.9%	75.7%	57.1%	66.1%	61.7%	50.1%	73.4%[3]
% Non-Hispanic White[1]	71.9%	89.4%	51.0%	27.8%	32.5%	16.2%	95.1%	90.0%	95.9%	59.3%	47.5%	37.0%	43.7%[3]
% Hispanic/Latino Ethnicity[1]	42.4%	57.1%	35.84%	67.9%	3.0%	1.8%	6.0%	4.8%	1.0%	11.1%	35.0%	33.9%	27.5%[3]
% African American[1]	0.9%	1.6%	5.7%	1.6%	64.5%	82.5%	0.3%	3.9%	0.8%	28.6%	39.6%	26.1%	22.9%[3]
% Native American[1]	5.6%	0.8%	1.2%	1.4%	0.1%	0.0%	0.5%	1.0%	0.7%	0.4%	0.5%	0.4%	2.8%[3]
% Best served in another language[1]	23.0%	20.8%	30.6%	29.7%	1.0%	1.6%	3.4%	6.1%	1.2%	3.3%	20.8%	22.7%	19.2%[3]
% At or below 200% Poverty[1]	84.7%	90.9%	95.5%	93.7%	97.5%	94.8%	75.7%	94.3%	75.4%	93.7%	94.8%	95.7%	90.0%[3]
% Uninsured[1]	19.7%	18.5%	16.8%	15.8%	24.6%	18.0%	8.6%	8.6%	3.7%	25.9%	27.1%	21.4%	25.2%[3]
% Medicaid[1]	51.8%	52.8	63.1%	65.1%	40.5%	23.9%	40.8%	54.1%	24.5%	46.9%	50.2%	57.8%	44.3%[3]
% Medicare[1]	12.1%	7.9%	6.3%	9.8%	18.7%	19.6%	20.3%	13.7%	23.5%	12.5%	10.2%	6.6%	10.7%[3]
% Private Insurance[1]	16.4%	20.8%	13.9%	9.4%	16.2%	38.5%	30.3%	23.6%	48.4%	14.7%	12.5%	14.3%	17.6%[4]
% Patients receiving mental health services[1]	2.5%	4.2%	6.2%	6.8%	3.1%	0.00%	0.00%	10.2%	2.4%	10.7%	12.7%	8.4%	8.5%[3]
% Patients receiving substance abuse services[1]	0.00%	0.00%	1.5%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	3.0%	0.00%	2.8%	1.2%[3]
% Patients screened for depression and care plan[1]	61.7%	92.1%	96.0%	89.7%	88.3%	73.5%	94.8%	75.7%	57.0%	65.9%	64.5%	85.6%	64.4%[3]
Total cost per patient[1]	$1116	$1005	$866	$1091	$906	$1567	$833	$784	$908	$895	$782	$1031	$1046[3]
Number of clinics[2]	5	3	34	3	7	4	11	5	9	23	7	8	10,400[5]
Number of clinics in trial	2	1	2	1	2	1	2	3	4	2	2	2	NA

[1] Uniform Data System, 2017.
[2] Website of participating FQHC.
[3] Uniform Data System, 2017, average percent/mean across all 1373 FQHC.
[4] Uniform Data System, 2017, average/% across all 27,174,372 FQHC patients.
[5] http://www.nachc.org/wp-content/uploads/2017/11/Americas_Health_Centers_Nov_2017.pdf.

identifying information to a web-based portal designed for the study. A progress note describing study participation and randomization status is entered into the electronic health record in order to notify the PC provider that the patient has been enrolled and randomized. The enrollment target is 1000 patients (400 from Washington, 400 from Michigan and 200 from Arkansas).

2.7. Randomization

The TER model is an adaptive intervention (see below) and therefore, a Sequential, Multiple Assignment, Randomized Trial (SMART) design is used to compare the two treatment arms (See Fig. 1) [39]. Adaptive interventions are used to customize the treatment for patients whose needs are not being met, defined by a *tailoring* variable. The tailoring variable in the SPIRIT trial is whether each study participant did or did not engage in TER care as determined by intermediate clinical evaluation.

First Stage Randomization - The first stage randomization is being conducted at the patient level immediately after being administered the baseline research assessment (described below). Randomization is stratified by FQHCs (i.e., for each clinic, equal numbers of patients will be allocated to TCC and TER) to avoid bias due to site-level variation. In addition, we stratify by disorder to ensure that equal numbers of patients screening positive for PTSD and BD are randomized to each group. Because patients with BD are often at elevated risk for experiencing trauma, many patients with BD also screen positive for PTSD [40]. For patients screening positive for both PTSD and BD, we categorize them as BD for purposes of stratification.

Second Stage Randomization – Patients initially randomized to the TER arm will be randomized a second time if they have not engaged in TER during the first six months of the trial. Specifically, the tailoring variable (non-engagement) is defined as ≤ 2 interactive video encounters in the first 6 months. The number of telepsychiatry and telepsychology encounters as documented by the telepsychiatrist and telepsychologist is used to define the tailoring variable. At six months, those patients not engaging in care are randomized (a second time) to either continued TER or to Phone Enhanced Referral (PER, described below). Randomization is again stratified by clinic and having a positive screen for PTSD or BD. We anticipate that PER will provide better access and greater treatment engagement than TER, but potentially have less clinical effectiveness than TER for those reached because it has lower therapeutic bandwidth (i.e., the ability of providers and patients to communicate, and establish a strong interpersonal relationship) [41]. Lower therapeutic bandwidth during a telephone encounter may reduce the number of communication cues (e.g., verbal content, visual cues, prosody) [41] and compromise clinical effectiveness.

2.8. Study interventions

University telepsychiatrists and telepsychologists had access to the FQHC electronic health record and were credentialed and privileged to practice as FQHC providers [35]. Psychiatrists were given permission to e-prescribe medications and order lab tests

2.9. Telepsychiatry collaborative care (TCC)

TCC is a team-based care model in which a care manager and telepsychiatry consultant provide support to the PC provider, who prescribes all psychotropic medications. In the SPIRIT version of TCC, an *on-site* care manager (typically a registered nurse and licensed clinical social worker) provides psychoeducation to patients about symptoms and treatment options, delivers evidence-based behavioral interventions, promotes adherence to treatment, and monitors symptom severity, side effects, and treatment response. The care manager coordinates care between the patient, PC provider, and a consulting telepsychiatrist, as well as other providers involved in the care of the patient. Care manager encounters (either phone or face-to-face depending on patient preference) are intended to be completed every two weeks to foster proactive communications between an activated informed patient and a coordinated care team. A web-based patient registry, Care

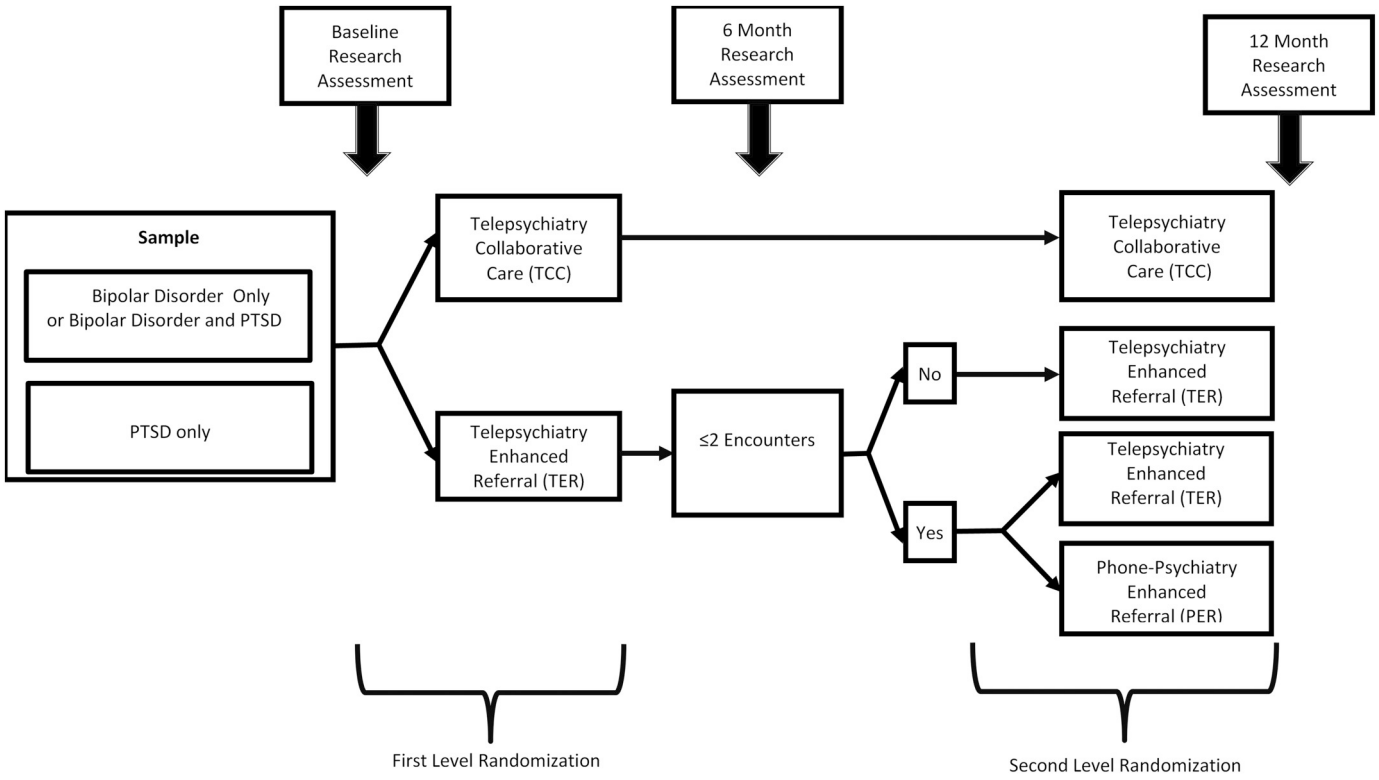

Fig. 1. Smart two stage randomization design used in the SPIRIT trial.

Management Tracking System (CMTS) [42] is used by care managers to track patients and document encounters. Encounters are also documented in each FQHC's electronic health record. A mobile application (SPIRIT App) is available for patients to download onto their Android phones. The SPIRIT App encourages patients to self-manage their conditions, including monitoring their own symptom scores which are automatically imported into CMTS for care managers to view [29,43]. A consulting telepsychiatrist works closely with each care manager to provide psychiatric consultation on all patients in the care manager's caseload. The majority of this consultation occurs indirectly via a weekly meeting referred to as a 'systematic case review' during which the telepsychiatrist and care manager review and adjust treatment plans for patients who are not improving as expected, or are not engaging in care [44]. The consulting telepsychiatrist uses CMTS to sort the caseload by patients' symptom scores and follow-up dates to prioritize patients for review. The consulting telepsychiatrist has access to the FQHC's electronic health record for these reviews. Due to the complexity of the psychiatric disorders experienced by patients in the SPIRIT trial, case reviews are augmented with direct telepsychiatry consultation in which the telepsychiatrist provides an initial diagnostic assessment for all patients and is available to provide 1–4 follow-up visits as needed for patients not responding to treatment. The telepsychiatrist maintains a consultative role, suggesting treatment to the PC provider, who retains responsibility for oversight of the patients' care. The consulting telepsychiatrist enters treatment recommendations for the PC providers in the FQHC's electronic health record. Pharmacotherapy – Medication recommendations for both PTSD and BD follow established treatment guidelines for these conditions and are individualized for each patient based on the current medication, tolerability, and treatment history of the patient. Behavioral Activation (BA) – BA is a brief psychotherapy that has evidence for reducing both PTSD [45–48] and depression [49] symptoms (which often occur with BD) and can be delivered in a flexible, patient-centric format of 6–8 sessions in PC. Moreover, non-mental health specialists (e.g., nurses) can be trained to deliver BA making it feasible for use in FQHC settings with a range of individuals in the care manager role. Care managers follow a BA treatment manual adapted to treat both depression and PTSD symptoms that includes a trauma exposure element focusing on avoidance behaviors [45,46]. Delivery of BA is recorded in CMTS, including which specific elements were discussed during each session.

2.10. Telepsychiatry enhanced referral (TER)

The offsite telepsychiatrist and/or telepsychologist deliver the PTSD and/or BD assessment and treatment via interactive video to patients located at the FQHC. Telepsychiatrists order and review appropriate laboratory tests and on-site PC providers support the telepsychiatrist as needed by monitoring relevant parameters, (e.g., body mass index, blood serum levels, lipids, etc.). The first encounter is usually with the telepsychiatrist to establish diagnosis and develop a treatment plan. All telepsychiatry and telepsychology encounters are documented in CMTS as well as the FQHC's electronic health record. Pharmacotherapy - The telepsychiatrists use treatment guidelines, algorithms and a treatment manual to inform medication treatment decisions. For patients with both PTSD and BD, the telepsychiatrist considers which symptoms are most bothersome to the patient to inform medical treatment decisions. Psychotherapy - Patients are offered either Cognitive Processing Therapy (CPT) for PTSD or Cognitive Behavioral Therapy (CBT) for BD. CPT is predominantly a cognitively based therapy with brief written exposure and is effective for PTSD [50,51]. Psychologists follow Resick's *Cognitive Processing Therapy: Therapist's Manual* [52]. For BD, psychotherapy is recommended as an augmentation to pharmacotherapy in the acute phase of treatment for depression (but not mania) [53]. Psychologists follow a shortened version of Otto's *Managing Bipolar Disorder: A Cognitive Behavior Treatment Program Workbook* [54]. Patients with both PTSD and BD may choose whichever psychotherapy best fits their needs and have the option of completing both forms of psychotherapy. Care Coordination – Clinic staff are responsible for scheduling appointments and reminding patients to attend. The intensity of these efforts varied by clinic according to their standard practices.

Adaptive Engagement Intervention: Phone-Psychiatry Enhanced Referral (PER) - The adaptive engagement intervention involves delivering treatment (either initially or exclusively) by telephone to patients in their home. Clinic staff call the patient to schedule appointments with the telephone psychologist. The telepsychologist initiates the calls to the patient's home and encourages the patient to have interactive video encounters with the telepsychiatrist or telepsychologist using motivational interviewing techniques. The telepsychologist also can deliver the psychotherapy (CPT or CBT) by phone if the patient prefers. Home-based phone encounters further increase patients' geographical and cultural access to mental health specialists beyond PC based interactive video encounters, and thus should increase treatment engagement. However, because the therapeutic bandwidth associated with the phone is lower than interactive video, this approach may reduce clinical effectiveness.

2.11. Measurement-based care

All patients in both treatment arms are monitored with the PHQ-9 for depression symptoms. Patients with PTSD are also monitored using the 20-item Patient Check List version 5 (PCL-5). To assess manic symptoms, patients with BD are also monitored using an instrument (SPIRIT Mania Rating Scale) designed for the study using the same format and scoring as the PHQ-9. Existing psychometrically validated scales assessing patient reported manic symptoms were used as part of the evaluation (see below) and to avoid habituation bias we chose not use the same scales for evaluation and measurement based care. In the TCC arm, the care manager administers the rating scales. In the TER arm, clinic staff administer the rating scales, with backup by the telepsychiatrist/telepsychologist. Symptom severity scores are entered into the CMTS and the FQHC's electronic health record.

2.12. Reimbursement for clinical services

Because collaborative care manager encounters and systematic case reviews with the consulting psychiatrist were not yet billable during the study, research funds are being used to support this clinical activity. Phone encounters with patients randomized to PER are not billable and also are being paid for with research funds. Reimbursement issues for telepsychiatry and telepsychology encounters are discussed in a companion article [35]. Telepsychiatry and telepsychology encounters were not reimbursable in Arkansas or Washington at the beginning of the trial, so research funds are used to pay for those clinical services. In Michigan, where these encounters are reimbursable, the FQHCs contracted with the University of Michigan to purchase a fixed number of telepsychiatry and telepsychology hours per month and the FQHC bills the patient's insurance company for the tele-encounter and the host site fee. Research funds are used to pay for clinical services for patients who do not have insurance or are enrolled in Medicare (which does not permit FQHCs to bill for telepsychiatry or telepsychology encounters). In addition, research funds are used to cover the FQHCs' no-show costs if the no-show rate is $\leq 20\%$. If the no-show rate is $> 20\%$, the FQHC was responsible for paying the University of Michigan the cost of the missed encounters above 20%.

2.13. Primary data collection

Hour-long telephone or web-based surveys are administered to study participants at baseline and at 6- and 12-month follow-ups in English or Spanish (depending on patient preference) using a Computer Assisted Telephone Interviewing system or web system software.

Table 2
Survey items used in the SPIRIT trial.

Scales/Items	Construct(s)	Baseline	Follow-ups
Casemix			
Socio-Economic Characteristics			
Socio-Demographics	Age	X	
	Gender		
	Race		
	Ethnicity		
	Marital Status		
	Education		
	Veteran Status		
	Employment status		
	Household Income		
	Health Insurance		
Sexual Orientation and Transgender	Sexual Orientation		X
	Transgender status		
Endorsed and Anticipated Stigma Inventory (EASI) [55]	Beliefs About Mental Health Treatment	X	X
	Beliefs About Mental Health Treatment-seeking	X	
	Stigma Loved Ones	X	
Health Literacy Screener [58]	Health Literacy	X	
eHealth Literacy Scale (eHEALS) [57]	Use of information technology for health	X	
Pew Survey of Telephone and Internet Access [59].	Use of Mobile Devises	X	
Clinical Characteristics			
Perceived need (NCS-R)	Perceived need for mental health treatment	X	
Treatment history (NCS-R)	Age first used psychotherapy/psychotropic medications	X	
Depression Outcomes Module Comorbidity Checklist [60]	Physical Health Comorbidities	X	
PTSD Trauma Criteria (Brief Trauma Questionnaire) [61]	Trauma Exposure	X	
Borderline Personality (Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II)) [62]	Borderline Personality Disorder	X	
Panic Disorder World Health Organization Composite International Diagnostic Interview [56]	Panic Disorder	X	
Tobacco Use (HSI modified) [74]	Frequency of tobacco use	X	
Drug Use (DAST10) [75].	Problems related to drug use	X	
Outcomes			
Clinical Outcomes			
Short Form (SF12) Mental Health Component Summary and Physical Health Component Summary [63]	Health-related Quality of Life	X	X
	Mental Health		
	Physical Health		
Recovery Assessment Scale (RAS) [64,90]	Recovery outcomes:	X	X
	Confidence and Hope		
	Willingness to Ask for Help		
	Goal and Success Orientation		
	Reliance on Others [1]		
	No Domination by Symptoms		
Hopkins Symptoms Checklist (SCL-20) [67]	Depression Symptom Severity	X	X
Altman Mania Rating Scale [69]	Mania Symptom Severity	X	X
Internal State Scale, V2.0 [70,91]	Bipolar Disorder Symptom Severity	X	X
PTSD Checklist (PCL-5) [92]	PTSD Symptom Severity	X	X
Pittsburg Sleep Quality Index (PSQI) [71]	Sleep Quality	X	X
Generalized Anxiety (GAD-7) [72]	Generalized Anxiety Symptom Severity	X	X
Alcohol Use (AUDIT) [73]	Alcohol consumption	X	X
Side Effects (SPIRIT Side Effects Assessment)	Medication side effects	X	X
Treatment Experience			
SPIRIT Perceived Access Scale (SPAS)	Access to mental health services	X	X
Service Utilization	Use of primary care and mental health outpatient services and inpatient and emergency department care	X	X
Patient Centeredness (Patient Assessment of Care for Chronic Conditions – PACIC) [79]	Patient centeredness domains of ask, advise, agree, assist and arrange		X
Therapeutic Alliance (Kim Alliance Scale) [80,81]	Therapeutic alliance with care team		X
SPIRIT Mental Health Activation Questionnaire (SMHAQ)	Patient Activation for Mental Health		X
Patient Satisfaction (CAHPS-ECHO)	Satisfaction with care for personal and emotional problems		X
Spirit Telehealth Outcomes Scale (STOS)	Experience with interactive video encounters		X
Spirit Smartphone App Questionnaire (SSAP)	Experience using Smartphone app		X
Treatment Engagement			
Medication Adherence SCAP-HQ [83]	Medication adherence	X	X

The item “Even when I don't believe in myself, other people do” was inadvertently dropped from this scale/subscale.

Prefaces to survey questions varied slightly between the phone and web survey formats. Reminder letters, texts and emails about follow-up interviews are mailed out to patients six weeks in advance of the target completion date. Study participants are remunerated $30 for completing each survey and a $5 bill was included in the follow-up reminder letters. All baseline and follow-up interviews are completed within 30 days of the target date, or they were considered lost to follow-up. Our data collection approach is consistent with Thorpe's recommendations for conducting pragmatic trials because it does not require patients to attend clinic visits in order to complete research assessments, and thus minimizes patient burden and attrition bias [34]. This is especially important for assessing outcomes for rural residents

who often face long travel times to the FQHCs. In addition, because surveys are completed independently of treatment engagement, outcomes are measured for all study participants including those not initiating or dropping out of treatment. This is important because we expect different levels of treatment engagement in TCC and TER.

Casemix – At baseline, we obtained self-reported information about socio-demographics using standard items (see Table 2). Items about sexual orientation and transgender status were added midway through the trial and were only included in the 12 month follow-up interview. Beliefs about mental health treatment, beliefs about mental health treatment-seeking and beliefs about stigma were measured using three sub-scales from the Endorsed and Anticipated Stigma Inventory (EASI) [55]. The Consumer Advisory Board made slight modifications to some of the wording on EASI items. For example, the Consumer Advisory Board recommended changing the word "stupid" to "foolish" for the survey question "If I were to seek mental health treatment, I would feel foolish for not being able to fix the problem on my own." to more accurately reflect how people feel about asking for help for mental health problems. The Consumer Advisory Board also recommended adding two questions to the EASI because they thought important issues were not being measured: 1) "If I had a mental health problem, I would get help from family, friends or clergy instead of going to a mental health professional" and 2) "If I had a mental health problem and friends and family knew about it, they would think I deserved it." Treatment history and perceived need for mental health treatment are assessed using items from the National Comorbidity Survey Replication (NCS-R) study [56]. We use the eHealth Literacy Scale (eHEALS) to assess patients' perceived skills at using information technology for health [57]. We use the 3-item health literacy screener to identify patients with low health literacy [58]. To assess the use of mobile devices we use items from the Pew Survey of Telephone and Internet Access [59]. The Depression Outcomes Module Comorbidity Checklist is used to assess the presence of physical health comorbidities [60]. We use the Brief Trauma Questionnaire (version 2) to assess whether patients have been exposed to a traumatic event that meets DSM-5 criteria [61]. Borderline Personality Disorder is screened for using the self-report screener from the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II) [62]. Panic disorder is screened for using the screener for the World Health Organization Composite International Diagnostic Interview used in the NCS-R study [56].

Outcomes – Patient-reported clinical and recovery-oriented outcomes are assessed using psychometrically validated instruments. Health-related quality of life – The primary outcome measure for this study is health-related quality of life at the 12-month follow-up. This construct is measured using the Short-Form (SF) 12 Mental Health Composite summary score which is normed to the population, and thus easily interpretable [63]. This measure is a non-disease specific assessment of vitality, role functioning, social functioning and feeling calm and peaceful, and scores have been shown to be sensitive to change. Recovery - SAMHSA defines recovery as "A process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential." Recovery-oriented outcomes are measured using the Recovery Assessment Scale which covers five domains: confidence and hope, willingness to ask for help, goal and success orientation, reliance on others, and no domination by symptoms [64]. Self-Reported Symptoms - To avoid patient habituation to symptom rating scales used for measurement based care, different scales are used for the evaluation. The exception is that the PCL-5 [65,66] is used for both evaluation and measurement based care because at the time the study began no other self-reported symptom severity scales for PTSD had been updated for the DSM-5 criteria. Depression symptoms are assessed using the SCL-20 [67,68]. Mania symptoms are assessed using the Altman Mania Rating Scale [69], and manic, depressed and mixed states are measured using the Internal State Scale [70]. The Altman Mania Rating scale was modified for phone administration by shortening the response categories to: 1) None of the time, 2) Occasionally, 3) Often, 4) Most of the time, and 5) All of the time. Likewise, the Internal State Scale was modified for phone/web administration by asking participants to give a number from 1 (Not at All) to 100 (Very Much So), rather than choosing a location on a visual analogue scale. Sleep quality is measured with the Pittsburgh Sleep Quality Index (PSQI) [71]. Generalized anxiety is measured with the GAD-7 [72]. Alcohol use is measured with the AUDIT-C [73]. Tobacco use is measured with the Heaviness of Smoking Index, modified to include vaping [74]. Drug use is measured using the DAST10 [75]. Side Effects - We measure the self-reported presence and severity of 20 common side effects of psychotropic medications [76].

Treatment Experience – Process of care is measured in the following domains: 1) Access, 2) Therapeutic Alliance, 3) Patient-Centeredness, 4) Patient Activation, 5) Utilization, and 6) Satisfaction. Access – Perceived access to mental health services is measured using the SPIRIT Perceived Access Scale (SPAS), developed for the trial in close collaboration with the Consumer Advisory Board. The Consumer Advisory Board specifically recommended that the questions be phrased in a neutral manner rather than asking about barriers. For example, the question about trust in providers was phrased as "How much did your trust in providers affect getting the mental health care you needed?" instead of "How much did lack of trust in your providers interfere with getting the mental health care you needed?". Utilization – We ask patients about receipt of treatment (e.g., medications, counseling), number of visits, the location of care (PC, specialty mental health care, hospital) and mode of delivery (face-to-face, interactive video, telephone) [76]. Patient-Centeredness - The National Academy of Medicine defines patient-centered care as: "Providing care that is respectful of and responsive to individual patient preferences, needs, and values, and ensuring that patient values guide all clinical decisions." [77] Patient centeredness is measured using a modified version of the Patient Assessment of Chronic Illness Care (PACIC) originally developed to assess the 5As (ask, advise, agree, assist and arrange) for patients with diabetes [78]. We use a revised version designed for patients with depression [79] and modified it for mental health in general. Therapeutic Alliance - We use the Kim Alliance Scale to measure patients' perception about their therapeutic alliance with their providers [80,81]. We modified the scale to ask about multiple providers rather than a specific psychotherapist so we could compare therapeutic alliance in both study arms for all patients (regardless of whether they initiated psychotherapy). The Kim Alliance Scale includes 4 dimensions of therapeutic alliance including communication, integration, collaboration, and patient empowerment [80]. Activation - Patient activation represents an individual's knowledge, skill, and confidence for managing his/her own health and health care [82]. Because there is no patient activation scale focused on mental health, we developed the SPIRIT Mental Health Activation Questionnaire in close collaboration with the Consumer Advisory Board. Satisfaction – A single item from the Experience of Care Survey is used to measure overall satisfaction with care received for personal or emotional problems. For those having an interactive video encounter, the satisfaction with this experience is assessed using the Spirit Telehealth Outcomes Scale (STOS) which was developed for the study in collaboration with the Consumer Advisory Board. The STOS has four subscales: 1) improved access, 2) clinical quality, 3) technical quality, 4) privacy, and 5) satisfaction. For those patients in the TCC arm who use the SPIRIT app, their experience is assessed with the Spirit Smartphone App Questionnaire (SSAQ) which was designed for the study. All instruments designed for the study are being assessed for internal consistency and test-retest reliability.

Treatment Engagement – We operationalize our conceptualization of engagement using observable patient behaviors that can be measured accurately, reliably, and similarly for both intervention groups. Pharmacotherapy Engagement – Pharmacotherapy engagement is measured using two items that assess whether the patient accepted a prescription for a psychotropic medication and their adherence to the prescribed medication. Specifically, the medication adherence item

from the SCAP-HQ [83] is used which has the following responses: 1) I never missed taking my medicine; 2) I missed only a couple of times, but basically took all the medicine; 3) I missed the medicine several times, but took at least half of it; 4) I took less than half of what was prescribed; and 5) I stopped taking the medicine altogether. Those responding that they never missed or missed only a couple times are considered adherent [84]. Psychotherapy engagement - Psychotherapy engagement is measured by the number of CBT, CPT, or BA counseling sessions that were attended as documented in CMTS.

Fidelity – Fidelity to the TCC and TER protocols will be measured retrospectively from data extracted from CMTS and aggregated to the FQHC level. For TCC fidelity, we will measure: 1) percentage of patients with an initial care manager assessment, 2) percentage of patients with an initial assessment with a follow-up assessment within 2–4 weeks, 3) percent of follow-up care management encounters in which a PHQ-9, PCL-5, or SPIRIT Mania Rating Scale was administered, 4) percent of follow-up care manager encounters in which core elements of BA were delivered, 5) average time in care (days between first and last care manager encounter), 6) percentage of patients with a telepsychiatry consultation, 7) average number of systematic case reviews, and 8) average number of changes to the treatment plan for patients not responding to treatment (e.g., medication change or initiation of BA). For TER fidelity, we will measure: 1) percentage of patients with an initial telepsychiatry or telepsychology encounter, 2) average time until initial telepsychiatry or telepsychology encounter (days between randomization date and first encounter), 3) percent of telepsychiatry encounters in which a PHQ-9, PCL-5, or SPIRIT Mania Rating Scale was administered, 4) percent of telepsychology encounters delivered per protocol (e.g., CPT session 1 included an impact statement), 5) average time in care (days between first telepsychiatry/telepsychology encounter and last telepsychiatry/telepsychology encounter), and 6) average number of changes to the treatment plan for patients not responding to treatment (e.g., medication change or initiation of CPT or CBT). Descriptive statistics will be used to describe variation in fidelity to TCC and TER across FQHCs.

2.14. Suicide risk assessment and safety planning protocol

Because the survey includes three questions about suicide (two from the SCL-20 and one from the Borderline Personality Disorder screener), a suicide risk assessment and safety planning protocol was developed in close collaboration with the Consumer Advisory Board. This protocol (see Fig. 2) begins by assessing current intent on self-harm. Those endorsing current thoughts of self-harm or giving non-committal responses are immediately randomized to a treatment arm and given options for a safety plan including a warm handoff to the National Suicide Prevention Lifeline (primary option), contacting a local Crisis Center, going to their FQHC, or going to the nearest hospital emergency room. Study participants are able to complete the survey at a later date/time after following through with their chosen safety plan. We contact emergency responders and request a safety check for those participating in a telephone survey who refuse to pick a safety plan. Tailored emails are automatically generated and immediately sent to designated FQHC staff and research staff indicating their patient's responses to the suicide ideation and intent questions, and the chosen safety plan. FQHC staff are responsible for reaching out to patients to ensure the chosen safety plan was followed. Research staff communicate directly with designated FQHC staff to confirm receipt of the email and safety of the patient. On-site FQHC staff use existing protocols to evaluate and manage patients reporting suicidal thoughts, and assist in handling mental health emergencies. Prior to trial commencement, safety protocols were reviewed by the TER and TCC lead psychiatrists and modified to account for treatment delivery via interactive video and for patients not in the clinic. The TER telepsychiatrist or TCC consulting telepsychiatrist are available to help with suicide safety planning, but not immediate crisis management.

2.15. Pre-planned statistical analysis

Missing Data – To account for non-response to 6- and 12-month follow-up surveys, as well as missing responses to individual survey items, we will use multiple imputation methods [85] using all available baseline and follow-up data. Use of multiple imputation will maximize the generalizability of the follow-up data to the baseline sample.

Hypothesis 1. Patients randomized to TCC will have better treatment experiences (access, therapeutic alliance, patient-centeredness, activation, beliefs about mental health treatment, and satisfaction) and treatment engagement (medication adherence, psychotherapy appointments attended) than patients randomized to TER.

Hypothesis 2. Patients randomized to TCC will have better self-reported clinical outcomes (e.g., symptoms, side effects), recovery-oriented outcomes (e.g., health-related quality of life, progress towards life goals) and other outcomes (alcohol use, sleep, and generalized anxiety), than patients randomized to TER.

For Hypotheses 1 and 2, the explanatory variable of interest will be group randomization status (i.e., TCC versus TER). No covariates will be included in the regression beyond those required to account for stratification. Regression models will be specified with the appropriate distribution and link functions to match the dependent variable (e.g., linear for the PHQ-9 score, binomial/logistic for medication initiation, negative binomial/log for visits, ordinal for satisfaction level). The primary outcome is the SF12 Mental Health Composite summary score, which is tested in Hypothesis 2. Other dependent variables are secondary outcomes. We will conduct a comprehensive longitudinal analysis using available data for baseline, 6 months, and 12 months. The regression analyses will take into account stratification by clinic and probable disorder (BD or PTSD). For disorder-specific samples, the regression analyses will take into account stratification by clinic.

Hypothesis 3. Patient treatment engagement will completely mediate any observed differences in self-reported and recovery-oriented outcomes between patients randomized to TCC and TER.

For Hypothesis 3, we will analyze only those outcomes found to be significant when testing Hypothesis 2. We will conduct longitudinal analyses using available data for baseline, 6 months, and 12 months.

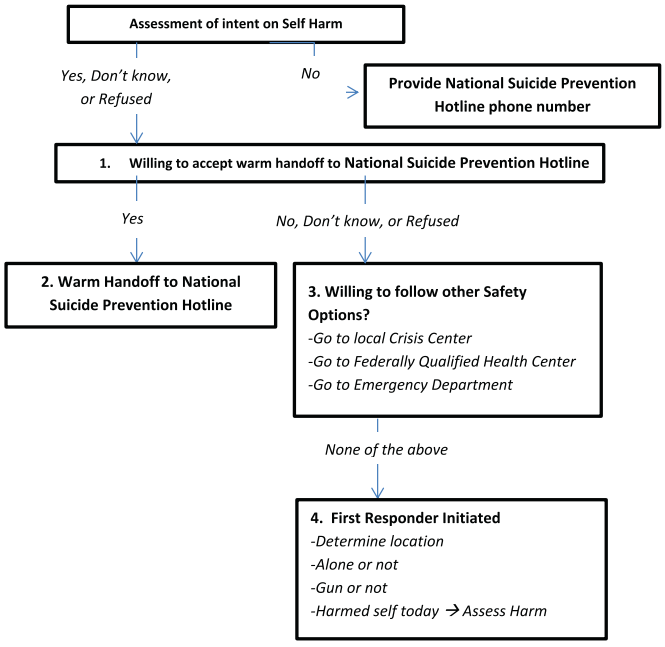

Fig. 2. SPIRIT suicide risk assessment and safety planning protocol.

The mediator variables will represent the time period from baseline to follow-up, whereas the dependent variables will represent the brief time period (e.g., two weeks) immediately prior to the follow-up. Thus, all mediators represent the time period after baseline, but before the measurement of the dependent variable. The first phase of the analysis will be to examine whether there are differences in the hypothesized mediator variables across the TCC and TER groups. Separate regression analyses will be estimated for each hypothesized mediator with group randomization status specified as the explanatory variable of interest. This analysis will already have been completed for the treatment engagement mediators (Hypothesis 1). The second phase of the analysis will use the same regression specifications that are used to test Hypothesis 2 in order to assess the degree of mediation.

Hypothesis 4. Patients randomized to PER will have a better treatment experience and engagement in care during the second 6-month period

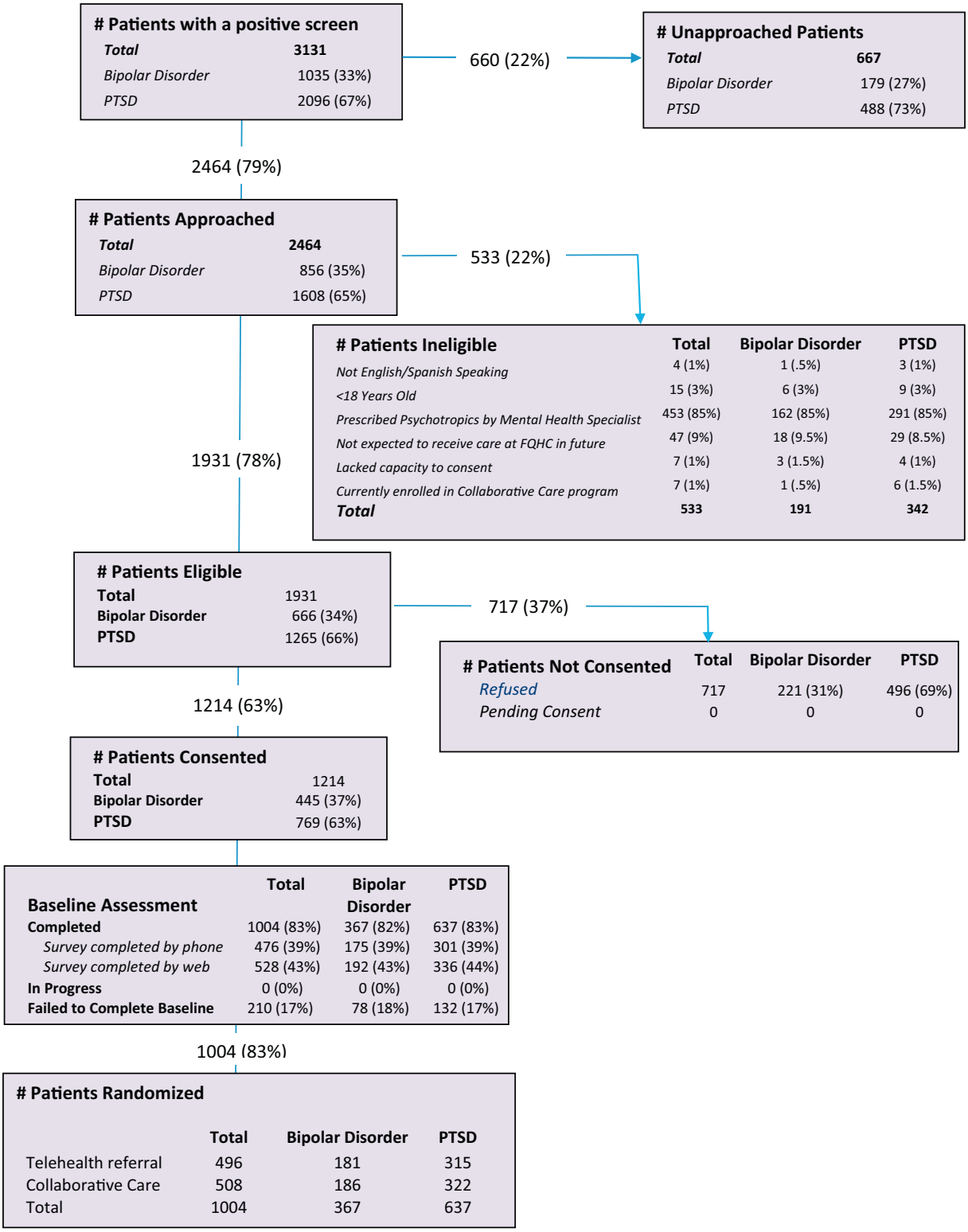

Fig. 3. SPIRIT CONSORT diagram.

than patients randomized to continued-TER.

Hypothesis 5. Patients randomized to PER will have better patient-reported clinical outcomes and recovery-oriented outcomes during the second 6-month period than patients randomized to continued-TER.

For Hypotheses 4 and 5, the explanatory variable of interest will be group randomization status. No covariates will be included in the regressions beyond those required to account for stratification. Regression models will be specified with the appropriate distribution and link functions to match the dependent variable. Only the 12-month follow-up data for patients originally randomized to the TER intervention with ≤2 interactive video encounters in the first six months will be used for this analysis. The regression analysis will take into account stratification by clinic and disorder. For disorder-specific TER samples, the regression analyses will take into account stratification by clinic.

Hypothesis 6. Patient self-reported clinical outcomes and recovery-oriented outcomes will be moderated by minority race/ethnicity and older age (with better outcomes observed in TCC), and by high levels of baseline symptom severity and comorbidity (with better outcomes observed in TER).

Hypothesis 6 will be tested using interactions between group randomization status and the specific patient subgroups. The moderator variables will represent the pre-baseline time period and will not change over time. The moderator analysis will use the same regression specifications that were used to test Hypothesis 2. The hypothesized moderators will be added as a group as both main effects and as interaction effects (with group randomization status). The significance of the interaction effects will be used to determine whether the patient characteristic is a treatment moderator. A negative interaction term will be interpreted as a smaller positive (or larger negative) treatment effect for TCC and positive interaction term will be interpreted as a larger positive (or smaller negative) treatment effect. The presence of significant treatment moderators will be interpreted as evidence of treatment heterogeneity, and subgroup specific treatment effects will be estimated with associated confidence intervals and displayed using a funnel plot to characterize the degree of heterogeneity.

2.16. Statistical power

For Hypotheses 1 and 2 comparing TCC and TER, there will be > 80% power (α = 0.05) to detect a small effect size (Cohen's D = 0.21) for non-disease specific continuously measured outcomes (n = 700, assuming 30% lost to follow-up). For example, there will be > 80% power to detect a 2.1 point (σ = 10) difference in health-related quality of life (SF-12 MCS) between TCC and TER. Assuming a third of the sample screened positive for BD (n = 233, assuming 30% lost to follow-up) and two thirds for PTSD only (n = 466, assuming 30% lost to follow-up), there will be > 80% power to detect a medium effect size (Cohen's D = 0.29) for BD specific outcomes, and > 80% power to detect a medium effect size (Cohen's D = 0.26) for PTSD specific outcomes. For example, there will be > 80% power to detect a 0.2 point (σ = 0.7) difference in the SCL-20 (n = 233 BD patients) and a 3.4 point (σ = 12.9) difference in the PCL-5 (n = 466 PTSD patients). For Hypothesis 3 testing the treatment engagement mediators, we will have 80% power to detect a small effect size (Cohen's D = 0.21) for non-disease specific continuously measured outcomes (n = 700, assuming 50% of patients do not engage in care and 30% lost to follow-up). For Exploratory Hypothesis 4 and 5 testing whether the adaptive engagement intervention PER is more effective than TER, we will have 80% power to detect a medium effect size (Cohen's D = 0.43) for continuously measured outcomes (n = 175, assuming 50% of patients do not engage in care and 30% lost to follow-up). For Hypothesis 8 testing treatment heterogeneity, we will have 80% power to detect a medium difference in effect sizes (Cohen's D = 0.45) between patient groups assuming n = 700, α = 0.05, and the subgroup of interest represents 35% of the sample (e.g., minority status).

3. Preliminary baseline results

Recruitment and enrollment to date is depicted in the consort diagram (Fig. 3). Seventy eight percent of the patients screening positive for PTSD and/or BD were approached by clinic staff and 78% of those were determined to be eligible for the study. The most common reason (85%) for ineligibility was that the patient was already being prescribed a psychotropic medication(s) by a mental health specialist and did not need the interventions offered. Two thirds (63%) of eligible patients approached consented to be in the trial and 83% completed the baseline survey (roughly equal numbers by phone or web) and were randomized. Nearly two thirds (63%) of enrolled patients screened positive for PTSD only and the rest screened positive for BD (37%). Of those screening positive for BD, 92% also screened positive for PTSD.

Table 3 presents the baseline characteristics of the enrolled sample. The sample was middle aged, mostly (70%) female and a third (34%) were racial/ethnic minorities. Over a fifth (22%) did not graduate from high school, two thirds (66%) were unmarried, 81% were not employed full time, 7% were uninsured, 68% were Medicaid enrollees, 24.0% were Medicare enrollees, and 62% lived below 100% of the 2016 Federal Poverty Level (e.g., $11,880 for household size of one). Endorsed and Anticipated Stigma Inventory (EASI) scores suggest moderate disagreement with negative statements about mental health and mental health treatment-seeking. The vast majority (88%) had a perceived need for mental health treatment, and the average age for first seeking treatment was 21 for psychotherapy and 25 for pharmacotherapy. Almost all (92%) had a cell phone and most had a smartphone (76%), the most common type being Android (64%). Among those with a cell phone, there was no significant difference in the proportion of Android smartphone users in the two treatment groups (TCC = 64.7% and TER = 64.1%, p = .87). The average number of physical health comorbidities was four. Most (70%) were taking a psychotropic medication(s) prescribed by a primary care provider at baseline and those taking medications reported an average of seven moderate to severe side-effects. The majority screened positive for panic disorder (92%) and/or borderline personality disorder (79%), and the majority (78%) meet DSM-5 criteria for trauma exposure. Over half (56%) smoked tobacco in the last week, 18% screened positive for alcohol misuse, and 39% reported use of street or prescription drugs. The average Pittsburg Sleep Quality Index (PSQI) score was 14, which is considerably higher than the cutoff of five suggesting poor sleep quality.

In terms of clinical outcomes measured at baseline, the sample was > 2.5 standard deviations below the national mean on the SF-12 MCS score indicating substantially worse mental health-related quality of life. The average score on the Recovery Assessment Scale was 3, indicating that patients neither agreed nor disagreed with positive statements about their recovery. The average score on the SCL-20 depression scale was 2.4 indicating that they were bothered by depression symptoms moderately to quite a bit in the past two weeks. For patients screening positive for BD, the total score on the Altman Mania Rating scale was 5, indicating that they experienced manic symptoms occasionally in the past week. The results of the Internal State Scale indicated that most patients screening positive for BD were in a mixed state (41%), followed by a manic state (26%) and depressed state (23%). For patients screening positive for PTSD, the average score on the PCL-5 was 45, indicating they were moderately bothered by PTSD symptoms in the past month.

Virtually all (92%) of those screening positive for BD also screened positive for PTSD., Compared to those screening positive for PTSD only, those screening positive for BD were younger, were younger when first prescribed a psychotropic medication, were less likely to be unemployed, and were less likely to have a cell phone (though differences were not large). All other socio-economic characteristics were similar in both groups. Compared to trial participants screening positive for PTSD

Table 3
Baseline characteristics of patient enrolled in SPIRIT trial.

	PTSD Sub-sample (N = 637) N(%) or μ(SD)	BD Sub-Sample[1] (N = 367) N(%) or μ(SD)	P-value	Full Sample (N = 1004) N(%) or μ(SD)
Casemix				
Socio-Economic Characteristics				
Age	40.4 (13.4)	37.6 (11.7)	< 0.01	39.4 (12.9)
Gender				
Female	460 (72.2)	243 (66.2)	0.05	703 (70.0)
Male	168 (26.4)	117 (31.9)		285 (28.4)
Other	8 (1.3)	4 (1.1)		12 (1.2)
Missing	1 (0.2)	3 (0.8)		4 (0.4)
Race				
Non-Hispanic Caucasian	428 (67.2)	231 (62.9)	0.06	659 (65.6)
Hispanic Caucasian	56 (8.8)	22 (6.0)		78 (7.8)
Native American/Alaskan Native	25 (3.9)	11 (3.0)		36 (3.6)
African American	63 (9.9)	55 (15.0)		118 (11.8)
Asian/Pacific Islander	2 (0.3)	1 (0.3)		3 (0.3)
Arab/Middle Eastern	1 (0.2)	1 (0.3)		2 (0.2)
Multi-race	32 (5.0)	31 (8.4)		63 (6.3)
Something else, unspecified	24 (3.8)	11 (3.0)		35 (3.5)
Don't know	1 (0.2)	1 (0.3)		2 (0.2)
Missing	5 (0.8)	3 (0.8)		8 (0.8)
Marital Status				
Married/Living with partner	221 (34.7)	121 (33.0)	0.11	342 (34.1)
Widowed	28 (4.4)	8 (2.2)		36 (3.6)
Separated	38 (6.0)	35 (9.5)		73 (7.3)
Divorced	146 (22.9)	81 (22.1)		227 (22.6)
Single, never married	204 (32.0)	120 (32.7)		324 (32.3)
Refused to answer	0 (0.0)	1 (0.3)		1 (0.1)
Missing	0 (0.0)	1 (0.3)		1 (0.1)
Education				
≤8th grade	18 (2.8)	8 (2.2)	0.78	26 (2.6)
Some high school	124 (19.5)	72 (19.6)		196 (19.5)
High school graduate	196 (30.8)	119 (32.4)		315 (31.4)
Some college	211 (33.1)	128 (34.9)		339 (33.8)
College graduate	72 (11.3)	32 (8.7)		104 (10.4)
Any postgraduate work	15 (2.4)	7 (1.9)		22 (2.2)
Don't know	0 (0.0)	1 (0.3)		1 (0.1)
Refused to answer	1 (0.2)	0 (0.0)		1 (0.1)
Military Service				
No	600 (94.2)	349 (95.1)	0.63	949 (94.5)
Yes, but not currently on active duty/reserves	35 (5.5)	16 (4.4)		51 (5.1)
Other, unspecified	2 (0.3)	2 (0.5)		4 (0.4)
Employment				
Full-time	109 (17.1)	78 (21.3)	0.04	187 (18.6)
Part-time	85 (13.3)	40 (10.9)		125 (12.5)
Temporarily laid off/on-strike	10 (1.6)	4 (1.1)		14 (1.4)
Unemployed	308 (48.4)	201 (54.8)		509 (50.7)
Retired	74 (11.6)	24 (6.5)		98 (9.8)
Student	22 (3.5)	11 (3.0)		33 (3.3)
Don't know	9 (1.4)	4 (1.1)		13 (1.3)
Refused to answer	17 (2.7)	4 (1.1)		21 (2.1)
Missing	3 (0.5)	1 (0.3)		4 (0.4)
Household Income Below 100% Poverty	389 (61.1)	232 (63.2)	0.61	621 (61.9)
Health Insurance[2]				
Uninsured	50 (7.8)	21 (5.7)	0.25	71 (7.1)
Medicaid	426 (66.9)	258 (70.3)	0.21	684 (68.1)
Medicare	158 (24.8)	82 (22.3)	0.35	240 (23.9)
Government Insurance	23 (3.6)	17 (4.6)	0.44	40 (4.0)
Private Insurance	113 (17.7)	56 (15.3)	0.30	169 (16.8)
Endorsed and Anticipated Stigma Inventory (EASI)[3]				
Beliefs About Mental Health Treatment (range: 8–40)	18.5 (5.7)	18.5 (5.9)	0.94	18.5 (5.8)
Beliefs About Mental Health Treatment Seeking (range: 9–45)	21.2 (6.4)	20.6 (6.8)	0.21	21.0 (6.5)
Stigma Loved Ones (range: 9–45)	21.2 (8.5)	21.1 (9.5)	0.85	21.2 (8.9)
Health Literacy Screener (range: 3–15)[4]	6.3 (3.2)	6.2 (3.4)	0.59	6.3 (3.3)
eHealth Literacy Scale (eHEALS) (range: 8–45)[4]	25.6 (8.0)	25.7 (8.4)	0.85	25.7 (8.1)
Pew Survey of Telephone and Internet Access				
Has a cell phone	587 (92.2)	332 (90.5)	0.04	919 (91.5)
Has a smart phone	474 (74.4)	290 (79.0)	0.06	764 (76.1)
iPhone	137 (21.5)	82 (22.3)	0.35	219 (21.8)
Android	301 (47.3)	191 (52.0)		492 (49.0)
Blackberry	10 (1.6)	2 (0.5)		12 (1.6)
Windows phone	5 (0.8)	2 (0.5)		7 (0.7)
Some other type	9 (1.4)	3 (0.8)		12 (1.2)
Not sure	10 (1.6)	10 (2.7)		20 (2.0)

(*continued on next page*)

Table 3 (*continued*)

	PTSD Sub-sample (N = 637) N(%) or μ(SD)	BD Sub-Sample[1] (N = 367) N(%) or μ(SD)	P-value	Full Sample (N = 1004) N(%) or μ(SD)
Clinical Characteristics				
Number of Physical Health Comorbidities (Depression Outcomes Module Comorbidity Checklist)	4.1 (2.7)	3.9 (2.6)	0.28	4.0 (2.7)
Perceived need for treatment (NCS-R)	560 (87.9)	320 (87.2)	0.10	880 (87.7)
Treatment history (NCS-R)				
Past use of psychotropic medication	538 (84.5)	299 (81.5)	0.48	778 (84.2)
Age first used psychotropic medication	21.5 (13.1)	19.9 (11.5)	0.08	20.9 (12.5)
Past use of psychotherapy	493 (77.4)	279 (76.0)	0.94	718 (77.7)
Age first used psychotherapy	25.6 (12.8)	23.2 (11.1)	0.01	24.7 (12.3)
PTSD Trauma Criteria (Brief Trauma Questionnaire)	443 (69.5)	278 (75.7)	0.04	720 (77.9)
Borderline Personality (Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II))	462 (72.5)	333 (90.7)		795 (79.2)
Panic Disorder World Health Organization Composite International Diagnostic Interview	575 (90.3)	350 (95.4)	< 0.01	925 (92.1)
Tobacco Use (HSI modified)				
Smoker	335 (52.6)	222 (60.5)	0.01	515 (55.7)
Heaviness of smoking[5]	2.5 (1.7)	2.7 (1.8)	0.17	2.6 (1.7)
Drug Use (DAST10)				
No drug use	424 (66.6)	192 (52.3)	< 0.01	616 (61.4)
Low level (1–2)	133 (20.9)	89 (24.3)		222 (22.1)
Moderate level (3–5)	49 (7.7)	47 (12.8)		96 (9.6)
Substantial level (6–8)	22 (3.5)	27 (7.4)		49 (4.9)
Severe level (6–8)	9 (1.4)	12 (3.3)		21 (2.1)
Pittsburg Sleep Quality Index (PSQI)[6]	14.7 (3.4)	15.7 (3.1)	< 0.01	15.1 (3.3)
Outcomes				
Short Form (SF12)				
Mental Health Component Summary (range: 0–100)	25.2 (9.8)	23.8 (9.8)	0.04	24.6 (9.8)
Physical Health Component Summary (range: 0–100)	42.1 (13.1)	43.9 (13.8)	0.04	42.7 (13.3)
Recovery Assessment Scale (RAS)				
Overall (range: 1–5)	3.1 (0.6)	3.0 (0.6)	0.24	3.0 (0.6)
Personal Confidence and Hope (range: 1–5)	2.9 (0.7)	2.9 (0.8)	0.32	2.9 (0.8)
Willingness to ask for Help (range: 1–5)	3.3 (0.9)	3.3 (1.0)	0.47	3.3 (0.9)
Goal and Success Orientation (range: 1–5)	3.3 (0.8)	3.4 (0.8)	0.33	3.3 (0.8)
Reliance on Others (range: 1–5)	3.5 (0.8)	3.3 (0.9)	0.01	3.4 (0.9)
Not dominated by symptoms (range: 1–5)	2.2 (0.8)	2.1 (0.9)	0.10	2.2 (0.8)
Hopkins Symptoms Checklist (SCL-20) (range: 0–4)	2.3 (0.7)	2.6 (0.7)	< 0.01	2.4 (0.7)
Altman Mania Rating Scale (range: 0–20)	NA	5.1 (3.6)	NA	5.1 (3.6)
Internal State Scale, V2.0				
Hypo (Mania)	NA	94 (25.6)	NA	94 (25.6)
Mixed State	NA	152 (41.4)	NA	152 (41.4)
Euthymia	NA	36 (9.8)	NA	36 (9.8)
Depression	NA	85 (23.2)	NA	85 (23.2)
PTSD Checklist (PCL-5) (range: 0–80)	44.9 (17.3)	52.3 (17.7)	< 0.01	47.8 (17.8)
Generalized Anxiety (GAD-7) (range: 0–27)	13.9 (5.4)	16.3 (4.8)	< 0.01	14.8 (5.3)
Alcohol Use (AUDIT)				
Zone I (0–7)	526 (82.6)	300 (81.7)	0.27	826 (82.3)
Zone II (8–15)	64 (10.0)	33 (9.0)		97 (9.7)
Zone III (16–19)	20 (3.1)	8 (2.2)		28 (2.8)
Zone IV (20–40)	22 (3.5)	23 (6.3)		45 (4.5)
Unknown	5 (0.8)	3 (0.8)		8 (0.8)
Side Effects (SPIRIT Side Effects Assessment)				
Percent taking psychotropic medications	450 (70.6)	241 (65.7)	0.01	642 (69.5)
Average number of Moderate side effects	3.9 (2.7)	4.1 (2.6)	0.43	3.9 (2.7)
Average number of Severe side effects	2.9 (2.4)	3.5 (3.1)	0.06	3.1 (2.7)

[1] BD sub-sample includes patients screening positive for PTSD
[2] Categories not mutually exclusive
[3] Higher scores indicate more negative beliefs
[4] Higher scores indicate greater literacy
[5] Lower scores indicate heavier smoking
[6] Higher scores indicate worse sleep

only, those screening positive for BD were significantly more likely to screen positive for panic disorder, to be smokers, to use illegal drugs (or legal cannabis in WA state), to have worse sleep quality (PSQI), to have more severe depression (SCL-20), anxiety (GAD-7) and PTSD (PCL-5), and were more likely to meet DSM-5 criteria for trauma exposure. Those screening positive for BD also had significantly lower mental health-related quality of life (SF-12 MCS), and significantly higher physical health-related quality of life (PCS).

4. Discussion

This pragmatic trial with broad inclusion criteria and minimal exclusion criteria was designed to enroll large numbers of patients and to maximize the generalizability of the results to FQHC patients with complex psychiatric disorders. The large sample size provides sufficient statistical power to detect small to moderate effect sizes and for identifying treatment heterogeneity (i.e., treatment moderators).

The enrolled sample endures formidable socio-economic difficulties and clinical challenges. Nearly a quarter did not graduate high school, less than one in five are fully employed, and two thirds live in poverty. Patients in the sample were > 2.5 standard deviations below the national mean with regards to mental health-related quality of life. Study participants reported numerous symptoms of depression, anxiety, mania, and PTSD. The vast majority had a perceived need for mental health treatment, and two thirds were currently taking psychotropic medications prescribed by a PC provider at baseline. Over half smoked tobacco in the last week, one in five screened positive for alcohol misuse, and more than a third reported use of street or prescription drugs. Sleep quality was poor. This sample of patients is likely to be challenging to manage in the PC setting. It is unlikely that we will observe the high response and remission rates achieved by collaborative care trials that focus on treating uncomplicated depression [86]. However, the one previous trial of collaborative care for PTSD conducted in the FQHC setting found substantial improvement in symptom severity for both the intervention and usual care groups [87].

It is hypothesized that TER will have better outcomes for those who engage in care because the treatment is being delivered by mental health specialists (psychiatrists and psychologists) rather than the PC team. However, because of the negative beliefs about specialty mental health treatment and stigma associated with needing care from a provider specializing in mental health, we hypothesize a lower percentage of patients randomized to TER to engage care. Thus, from a population-level effectiveness or intent-to-treat perspective, it is hypothesized that patients randomized to TCC will have better outcomes than those randomized to TER. Treatment engagement is hypothesized to be the mechanism of action and will be tested in the mediation analysis. Engaging in TCC is somewhat different than engaging in TER, so to compare engagement across treatment arms this construct had to be specified somewhat generically (e.g., medication adherence and number of counseling visits). While the trial is not designed to consider capacity, the TCC model leverages scarce specialty mental health resources and therefore, has the capacity to reach more patients than the TER arm. Thus, if we find no significant differences in clinical outcomes between those randomized to TCC and TER, the former will be preferable from a population health perspective.

Another factor that could influence outcomes is treatment fidelity. Being a pragmatic trial, we are not controlling fidelity. This approach runs the risk of comparing two low quality treatments and finding equivalently poor outcomes in both arms of the trial. We tried to minimize the risk of this scenario using several methods. First, the TCC and TER intervention leads work with clinics to develop and refine strategies for scheduling and promoting attendance at appointments with telepsychiatrists and telepsychologists. Second, sites receive quarterly reports with site-specific and study-wide data extracted from CMTS about patient engagement in care (e.g., percent with an initial care manager assessment, percent with a telepsychology encounter, no show rates), as well as clinical outcomes combined across both study arms. Third, for the TCC arm, care managers receive intensive initial and ongoing training. Fourth, the telepsychiatrists and telepsychologists hold regular meetings to discuss patient care and operational challenges that need to be communicated to the clinic. Finally, we did intervene when the quality of care at one clinic fell below what we considered to be minimally acceptable (i.e., patient safety was at risk). Specifically, we alerted FQHC leadership about concerns we had with their care manager in the TCC arm and the high no show rate in the TER arm. This site ultimately stopped enrolling patients in the trial. Although not a pre-planned analysis, we anticipate examining variation across sites with regard to treatment engagement, fidelity, and outcomes. However, with 12 only FQHCs participating in the trial, we will not have sufficient statistical power to determine whether observed variation is due to differences in patient characteristics or organizational factors. Although not described in this protocol, we are also conducting qualitative interviews with PC providers and enrolled patients that may help us understand any observed variation in treatment engagement and outcomes.

Even if one model of care is found to be superior to the other with regard to average treatment effects, clinics may need to offer both models of care if we observe significant treatment heterogeneity. By offering both models of care, clinics can direct patients to the model that will benefit them the most based on predictions from the treatment heterogeneity analysis. Alternatively, clinics could adopt a stepped care approach whereby patients not responding to TCC are referred to TER [88]. A stepped care approach should maximize population-level cost-effectiveness [89] because the TCC model leverages scarce specialty mental health resources and therefore, has the capacity and potential to reach more patients than TER.

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