Project CARE: An Integrated Treatment Adherence Program for Bipolar Disorder at the Time of Prison Release - Pilot RCT

NCT04269772

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Please note: This study protocol includes details on this clinical trial registration and the open trial, developmental phase, which is a separate clinical trial registration (NCT03825640).

Project CARE (Community treatment Adherence at Re-Entry): An integrated treatment adherence program for bipolar disorder at the time of prison release

2. Lay summary

Bipolar disorder (BD) is a serious, disabling, and highly recurrent illness that is disproportionately represented in the criminal justice system. BD increases risk for several adverse outcomes for prisoners, including mood instability, suicide attempts, substance use relapse, and high rates of repeat incarceration. Despite these serious negative consequences, up to 70% of prisoners with BD do not receive mental health treatment upon prison release. Lack of engagement in ongoing mental health treatment for BD upon community re-entry represents one potent factor that perpetuates risk for adverse outcomes, and consequences of untreated BD (e.g., impulsivity, substance use) may greatly exacerbate difficulties in establishing stable living conditions (e.g., adequate housing, legal employment) at community re-entry. Thus, there is a critical need for interventions to facilitate engagement with treatment for BD during this vulnerable transition.

The primary aim of this pilot trial is to develop and establish the feasibility, acceptability, and potential for future uptake of the Community treatment Adherence at Re-Entry (CARE) program. CARE is an innovative intervention that will combine evidence-based cognitive-behavioral, family, and telephone outreach strategies to promote treatment engagement and improve clinical outcomes for prisoners with BD during the period of community re-entry. CARE will include 3-4 individual sessions in prison or in the community, 1 optional family session, and 11 brief telephone contacts for up to 6 months. Given its moderate intensity, adjunctive nature, use of community mental health counselors, and use of telephone administration for post-release follow-up, CARE has been designed with an eye toward community implementation. Its proposed mechanisms of action (i.e., increasing values-action consistency, enhancing social supports, and linkage to community treatment services) are further well matched to the practical and clinical needs of re-entering individuals.

The development phase of the study will result in a treatment manual, training manual, and fidelity scales, to be tested in an open trial of 12 prisoners with BD nearing prison release. The pilot study phase will examine the feasibility and acceptability of the proposed recruitment methods, research design, intervention, and training program by randomizing 40 prisoners with BD nearing prison release or recently released to treatment as usual (TAU), enhanced with monitoring and emergency referral, or to enhanced TAU plus CARE. The primary outcome will be mood symptoms in the 6 months follow-up window. Secondary outcomes include: suicidal ideation/behaviors, substance use, re-arrest rates, and employment and housing stability. We will also explore differential engagement of CARE's purported mechanisms of action. To our knowledge, this proposal represents the first attempt to develop and pilot a targeted transitional interventional for BD among prisoners, laying the groundwork for a larger clinical trial (R01) to evaluate the effectiveness of CARE for improving clinical outcomes for this seriously ill, high risk, understudied population during the vulnerable transition from prison to community re-entry.

3. Protocol narrative

Please note: We have approval from the [redacted] to conduct human subjects research at their site. In addition, the [redacted] IRB submitted this protocol to the U.S. Office of Human Research Protections (OHRP) for their certification of this research protocol.

3a. Aims:

The primary aim of this pilot effectiveness trial is to develop and establish the feasibility, acceptability, and potential for future uptake of CARE (Community treatment Adherence at Re-Entry), an innovative, moderate intensity intervention that combines evidence-based cognitive-behavioral, family, and telephone outreach strategies to promote community treatment engagement and thereby improve clinical outcomes for prisoners with bipolar disorder (BD) across the period of community re-

entry. Development of CARE will be informed by our experiences successfully piloting a similar intervention (the Integrated Treatment Adherence Program; ITAP[1]) for individuals with BD and comorbid substance dependence across another vulnerable transition, from inpatient to outpatient care in the community.[2] As an adaptation of ITAP for community re-entry, CARE will be designed to be delivered by a range of clinicians, providing advantages for scalability in the resource-poor criminal justice system. Its proposed mechanisms of action (i.e., increasing values-action consistency, enhancing social supports, and linkage to community treatment services, all to promote treatment engagement, thereby improving clinical outcomes) are further well-matched to the practical and clinical needs of re-entering individuals.

The secondary aim of this research will be to compare outcomes, within 95% confidence intervals, between CARE as an adjunct to treatment as usual (TAU) vs a TAU control condition. In keeping with ethical obligations, we will enhance TAU by providing post-release monitoring and emergency referral, as needed. We will explore future dissemination potential by using community mental health counselors for treatment delivery.

The *development* aims of this project are to:

1) Develop a comprehensive treatment manual, interventionist training program, and fidelity scales for CARE, comprised of 3-4 individual sessions prior to release, and 1 family meeting (when applicable), followed by a series of 11 brief telephone outreach contacts up to 6 months post-release.
2) Improve the clarity, content, acceptability, and feasibility of CARE through a small open trial (n=12) of prisoners with BD treated through 6 months post-release, followed by stakeholder interviews (participants, prison staff, community mental health partners) as part of the refinement process.

The *pilot study* aims of this project are to:

3) Conduct a randomized pilot trial in 40 prisoners with BD, comparing CARE to TAU to demonstrate the *feasibility* and *acceptability* of the proposed recruitment methods, research design, intervention, and counselor training program, with assessment at baseline, pre-release, and 1 and 6 months post-release. For those recruited post-release, assessments will be at baseline, 1 month and 6 months.
4) Examine 95% confidence intervals around differences between CARE and TAU for the following outcomes: reduced mood symptoms *(primary)*; suicidal ideation and behaviors, substance use, rates of re-arrest, and more stable employment and housing (*secondary*);
5) Examine 95% confidence intervals around differences between CARE and TAU to evaluate differential engagement of purported mechanisms of action: increased values-action consistency, practical and emotional social support, and increased treatment engagement (i.e., utilization and adherence).

3b. Methodology:

3.b.1. Description of study participants.

Participants will be sentenced prisoners who are incarcerated in the women's and men's minimum and medium security prison facilities at the [redacted]. In the development (open trial) phase, we will consent up to 36 prisoners in order to achieve our enrollment goal of 12 prisoners who meet study inclusion criteria for participation. In the pilot trial phase, we will consent up to 160 prisoners in order to achieve our enrollment goal of 40 prisoners who meet study inclusion criteria for randomization to conditions. Additional inclusion criteria across both phases include: 1) DSM-5 diagnosis of bipolar I, bipolar II, bipolar disorder not elsewhere classified, or schizoaffective disorder, bipolar type, as determined by the Structured Clinical Interview for DSM-5 Disorders (SCID-5); 2) 18 years or older; 3) Anticipated prison release within 4-10 weeks or recent prison release; 4) Expected release to or current living in locations anywhere within [redacted]; and 5) Willingness to sign an informed consent

document that describes study procedures. Exclusion criteria include: 1) Presence of current psychiatric symptoms severe enough to warrant separation from the general prison population; 2) Cognitive impairment sufficient to prevent successful completion of the baseline interview; and 3) Inability to understand sufficiently well to understand the consent form or assessment instruments when they are read aloud. Virtually all prisoners at the [redacted] speak English. Because a few prisoners may have reading difficulties, consent forms will always be read aloud and RAs will offer to read self-report measures aloud. As CARE is designed to be purely adjunctive and because release dispositions can change dramatically in the days leading up to release, participants will not be included/excluded based on post-release treatment plans (or lack thereof).

Those assigned to receive the CARE intervention (n= 12 in the open trial; n = 20 in the pilot randomized trial) will be invited to have a family member or significant other (heretofore referred to as SO) participate in the intervention with them. We highlight that this is not a requirement for participation of the prisoner participant, but will be optional. Hence, we will enroll up to 32 SOs into this study. In order to be eligible for participation, SOs must be over 18, speak and read English, have frequent (at least every other week) contact with the prisoner participant, be on the prisoner participant's visitor list at the [redacted] (for those prisoners recruited while still incarcerated), and consent to participate in treatment.

Finally, as part of the treatment development process, we will conduct brief (~30 min) stakeholder interviews with relevant parties (e.g., [redacted] staff and administrators, community mental health partners). We anticipate conducting up to 6 interviews with relevant stakeholders (2 each with [redacted] staff, administrators, and partnered community mental health center administrators), half of which will occur upon completion of the open trial and half of which will occur upon completion of the pilot randomized trial. In order to be eligible to participate in this interview, individuals must be: 18 years or older, currently employed in one of the stakeholder settings described above, able to speak English sufficiently well to participate in the interview, and to consent to participate in the interview.

Special classes. Because the purpose of this study is to develop and evaluate the feasibility and acceptability of CARE in prisoners during the vulnerable period of community re-entry, it is necessary to sample a prison population. Prisoners are an understudied population with complex treatment needs; hence the urgency for more research attending to the mental health concerns of this population. Incarcerated children 18-21 will be eligible. Recruitment procedures are described in more detail in the "Protection of Human Subjects" section.

3.b.2. Description of interventions.

Overview. In the open trial phase of the study, participants who provide informed consent and are determined to be eligible for participation will be assigned to receive the CARE intervention as an adjunct to enhanced treatment as usual (E-TAU). In the pilot trial phase of the study, participants will be randomized to the CARE intervention as an adjunct to E-TAU or to E-TAU alone.

Enhanced treatment as usual (E-TAU). To meet our ethical obligations for human subjects protections, we note that TAU will be enhanced with routine monitoring (i.e., through scheduled research assessments) and emergency referral, as clinically indicated. We will also provide all study participants a resource packet containing information about treatment and other supportive resources available in prison and in the community. In those respects, the control condition will be "enhanced TAU" because it provides a level of clinical monitoring and referral that is not typically available to re-entering prisoners as part of routine care, but will be available to all study subjects as part of their participation in human subjects research. Given the adjunctive nature of CARE, other treatments (e.g., medication management, counseling, case management, discharge planning, etc.) will be unrestricted, and in fact, encouraged. We acknowledge that TAU will be highly variable both in prison and after re-entry, ranging from any to no treatment for BD. We will carefully monitor and assess treatment utilization (e.g., initiation, maintenance, changes, discontinuation, adherence) and clinical severity for participants in both conditions at each study assessment time point. For treatments that participants report receiving, we will obtain signed release of information (ROI) forms for prison and community

treatment providers, so that we may communicate with them in cases of clinical need. Please see "Protection of Human Subjects" section for details re: our emergency referral procedures, as needed.

Community treatment Adherence at Re-Entry (CARE) intervention. CARE will begin within the 2 months preceding prison release, and will continue for 6 months following community re-entry. Or, for those enrolled post-release, CARE will begin right after enrollment and continue for 6 months. CARE will be comprised of: a) 3 individual sessions with the CARE counselor prior to prison release or right after prison release; b) either a fourth individual session or 1 family/significant other (SO) session either prior to prison release or as soon as possible after release into the community (when applicable); and c) a series of 11 brief (15-20 min) follow-up telephone contacts with prisoners and their SO. If a participant is released earlier than expected before finishing the in-prison sessions or if the participant is recruited after release from prison, we will complete the sessions by telephone, by zoom, or in person at our offices (or in any residential facility where the participant is located, with facility approval).

The CARE intervention will incorporate motivational strategies from existing interventions[3–5] in order to *clarify values and goals* to enhance motivation for behavior change. These strategies will be primarily derived from Acceptance and Commitment Therapy (ACT; note that this is different from Assertive Community Treatment), a "third wave" cognitive-behavioral approach that has demonstrated efficacy in a wide range of disorders, including mood disorders,[6] psychosis,[7,8] and SUDs.[9] ACT proposes that a discussion and clarification of the patient's personal values can facilitate motivation, hopefulness about the future, and behavior change. Values are defined as broad, personally defined verbal constructs that provide the context for more specific behaviorally consistent goals. Values provide a personal rationale that can help motivate individuals to remain committed to desired actions, even if they are associated with other undesirable consequences. In contrast, goals represent more narrowly defined desired consequences that can be impeded by various internal and external factors. Procedures have been developed to clarify values and goals in order to assess and decrease discrepancies (thereby promoting consistency) between patient values and daily actions. Such values strategies will inform the initial, sessions with the patient and SO, and culminate in an individualized "Re-entry Plan" document that clarifies important goals for re-entry that are in line with core values, potential obstacles to achieving these goals (e.g., non-adherence, substance misuse), early warning signs for mood/substance relapse or increased suicide risk, appropriate corrective actions, and a safety plan, particularly given the high risk for suicide in this population.[10]

CARE will also integrate strategies from existing *family models of intervention for BD* (e.g., Family Focused Therapy,[11] the McMaster Model of Family Functioning[12,13]) that are designed to improve family communication, social support, and problem-solving around BD illness management. The family/SO meeting will provide an opportunity to solicit feedback from and review the patient's "Re-entry Plan" with the family member, in order to enlist them in supporting the patient's specified values-consistent actions and goals as they

Table 1. Tentative CARE Session Schedule

Prison Sessions	
	Session Content
Individual Session 1	rapport building; orientation and psychoeducation; review of psychiatric, SUD, and criminal justice history; elucidate links between psychiatric symptoms, substance use, & criminal justice involvement, and need for treatment; introduce values discussion to motivate change
Individual Session 2	continued values discussion; highlight discrepancies between values and actions to generate list of short term, values-consistent behavioral goals; identify barriers to valued actions; elucidate links between treatment attitudes and beliefs, adherence, and values
Individual Session 3	formulation of an individualized "Reentry Plan," a document upon which therapist and patient can record values-consistent goals and actions, and specify the importance of consistent treatment in facilitating progress toward goals; includes space to record triggers and other early warning signs for mood symptoms, SUD, and other risk behaviors (e.g., suicide risk), ways to access treatment upon release, and a safety plan; referral information provided
Family/SO Meeting	review psychoeducational information with patient and SO; discuss SO's perspective on patient's psychiatric, SUD, & criminal justice history; review Re-Entry Plan and facilitate discussion about ways in which SO can support goals for reentry; if patient/SO conflict identified, additional referrals provided
Post-Release Phone Sessions	
Phone sessions (11)	15-20 minutes in length; conducted individually with patient and SO; follows schedule of decreasing frequency (weekly in first two months, biweekly in next two months, monthly thereafter); calls start with brief assessment of risk factors, with patient safety taking priority; problems around treatment engagement and adherence addressed next, with main strategy to engage in active service linkage, if required (e.g., facilitating intake appointments at the CMHCs where counselors are already employed) and also to facilitate communication between patient and SO; problems addressed in context of Re-Entry Plan values and goals; if a problem develops that cannot be addressed in this manner, therapist may obtain permission to contact patient's community treatment provider(s) (if already service connected) and/or temporarily increase frequency of contacts during times of crisis; SO contact proceeds in a similar manner

transition back to the community. A copy of the participant's "Re-entry Plan" will be mailed to his/her home after his/her release from prison or after completion if recruited post-release. The family intervention component will also be facilitated by the post-release telephone contacts between the provider and the patient and the SO.[1,2,14–16] Telephone contacts are used to: a) identify, monitor, and address problems in relevant areas (e.g., sobriety, treatment utilization), b) encourage additional support and open communication, and c) facilitate problem-solving and concrete service linkage to reduce barriers to treatment engagement and progress toward values-consistent goals.

Finally, within the context of the above intervention strategies, CARE will also incorporate *psychoeducation* to promote illness insight, early symptom detection, and to de-stigmatize treatment of BD and frequently comorbid substance use disorders (SUDs), combined with practical and active *service linkage efforts* by study counselors (e.g., assistance with intake appointment scheduling) in an effort to assist individuals in overcoming barriers to care. Because study counselors will already be employed in the systems that serve re-entering individuals (see Interventionists, below), they will be uniquely situated to provide this level of referral and linkage. Our group has combined similar therapeutic approaches harmoniously and effectively in prior intervention trials with other high-risk psychiatric populations, especially during care transitions in the community.[2,17,16]

3.b.3. Interventionists.

Our investigative team has benefited over the years from strong community partnerships, and especially so with [redacted] is the community mental health center that is contracted by the [redacted] to provide post-release mental health and substance use treatment services to re-entering prisoners. Through our clinical administration contacts at [redacted] we will solicit referrals and names of interested counselors, who will be required to: a) have a master's degree in a mental health-related field (e.g., counseling, social work), b) be independently licensed, and c) have at least 3 years of experience working with patients with severe mental illness in the community mental health setting, ideally at the intersection of community mental health and justice involvement. Interventionists will also be required to submit to and pass the [redacted] security clearance process for entry into the participating prison facilities for purposes of conducting study intervention sessions.

Prior to delivering the intervention, interventionists will be hired and trained during a one-day didactic training workshop co-led by [redacted] This workshop will include content on the phenomenology of BD, BD in prison, and how to conduct the individual, family, and phone sessions in a culturally sensitive manner. Training will also include role-plays of standard, challenging, and emergency situations. After the training, participants will be "certified" to deliver CARE in the open and randomized trials of this study. [redacted] will review therapists' taped sessions and provide feedback and guidance to therapists during weekly supervision, with assistance from [redacted]. Experiences in the open trial will contribute to development of fidelity rating scales to be used in the pilot randomized trial. In the pilot randomized trial phase, supervision will be complemented by ongoing fidelity ratings of intervention sessions, conducted by a blind rater.

3.b.4. Potential intervention issues.

Telephone access: Our research and others has shown that telephone interventions are feasible and acceptable for individuals with SMI[1,2,14,18,17] and for justice involved persons (see prelim studies).[19,20] A minority (< 10% at our recruitment site based on previous experience) may not have regular access to their own telephone, but have been able to provide a phone number for a family member or other locator that is accessible to them for use upon re-entry; reliance upon these contact methods is feasible.[19,20]

Significant others: Some patients may have difficulty identifying a family member or SO for study participation. Thus, our definition will be broad. For example, if there is no local SO available, we may identify an SO who is geographically distant, but otherwise available to participate in phone sessions. We may also consider inclusion of an alternative support person (e.g., case manager) who is willing to

participate if no family member or close friend is willing/able. If a participant has no SO available, we will omit this portion of the intervention. However, we will allow for the participation of an SO later in treatment, should one become available. Although we expect the family component of the intervention to be feasible, given our previous experience with prisoner re-entry,[19–21] assessing its feasibility/acceptability in the context of CARE will be part of the proposed study. In our previous studies with prisoners, 10-15% of participants have been unable to identify an SO.

Patient-SO conflict: In situations of mild-moderate relationship impairment, we will carry out CARE as outlined and identify relationship issues as one additional risk factor to be addressed. We will then engage the patient and the SO in problem-solving to determine what to do about their relationship issues (e.g., referral to marital/family treatment). In a minority of cases, there may be such severe impairment and/or abuse that facilitating increased involvement is not clinically appropriate. As in our previous studies of re-entering prisoners, we will work with the participant to identify another SO for participation and we will privately provide information about partner violence resources to participants as needed (see Human Subjects).

Illness severity: If the patient's symptoms (e.g., mania, psychosis, substance use) are so severe that he/she is unable to participate in the contacts, we will continue to work with the SO and with other providers (with a release of information) to help obtain adequate treatment for the patient. (see Human Subjects Protections)

3.b.5. Recruitment and Informed Consent.

Prisoner participants: Prison recruitment will follow procedures successfully used to recruit prisoners into our completed and ongoing trials at the study site over the past decade. Participants will either be recruited pre-release from women's and men's minimum and medium security prison facilities of the [redacted] or post-release in the community.

In-Person Recruitment at [redacted] will occur in one of three ways. First, with permission from prison treatment staff and security personnel, research staff will attend housing unit community meetings to briefly explain the study. Research staff will hand out "interest slips" of paper, on which participants can confidentially indicate interest or lack of interest in learning more about the study. We request that all prisoners complete the "interest slip," regardless of interest in participation, to ensure privacy of responses. Second, we will identify potentially eligible participants based on their time in prison and release dates from prison records and approach them privately. Third, with the assistance of [redacted] Director of Psychiatric Services at the [redacted] we will provide an in-service to prison psychiatrists and mental health counselors, and will distribute study brochures and flyers for them to place around treatment areas. Brochures will contain study details and guidance regarding how a participant can submit a confidential "interest slip" to request a meeting with an RA, if interested in learning more about the study.

Post-Release Recruitment will occur due to the COVID-19 pandemic and the inability to recruit participants in-person at [redacted] The following recruitment strategy is in place to continue study recruitment without in-person activities at [redacted] We will solicit referrals directly from [redacted] behavioral health workers (discharge planners, counselors, etc.), from probation and parole, and service organizations that that work directly with recently released inmates. Referral sites will be given our study materials (i.e. consent-to-contact form, etc.). They will present the forms to potential participants. Interested inmates will complete the consent-to-contact form, and referral sites will fax completed forms to our offices. As referral sites will be involved in our recruitment procedures, we will make every effort to minimize potential risks of coercion. There is a note in the consent-to-contact form explaining to potential participants that their decision whether or not to complete the form will not impact their privileges, relationship, or treatment with [redacted] probation and parole, and/or their service organization. Additionally, study RAs will be very clear to participants, as soon as possible after they make contact, that the study is voluntary and their relationship with [redacted] probation, parole, and/or their service organization will not be impacted if they decide not to participate. If they are interested, study RAs will screen them for study eligibility over the phone or by HIPAA complaint zoom. Due to the

COVID-19 pandemic, a waiver of documentation of consent will be utilized for post-release recruitment. We will consent participants over the telephone or via HIPAA complaint zoom. As part of the informed consent process, participants will always be informed that: (1) a decision to not participate in the research will have no impact on their status, access to treatment, or length of stay at the prison; (2) the study has a Certificate of Confidentiality; and (3) the study information will be kept confidential from prison staff, officers of the court, parole officers, or others in the criminal justice system. Study staff will also carefully review the limits to confidentiality, including the prison's mandatory reporting procedures (see page 16). Informed consent procedures have been developed to comply with the Code of Federal Regulations 45 CFR 46.116, *General Requirements for Informed Consent* and 46.117 *Documentation of Informed Consent*. Freedom to refuse to participate or to discontinue participation at any time without penalty will be emphasized. Participants will be asked to provide written permission for us to try to locate them through significant others, their appointed parole/probation officer, and/or post-release treatment program, but will not be excluded if they are unwilling to do so. Participants will be able to refuse or revoke locator consent. Because of the NIMH data sharing requirements, which we are bound to, we will need to obtain the participant's city or municipality of birth at the time of consent as well as the participant's full name a birth. This will be used to link the participant's data with any existing data they may already have in the National Database for Clinical Research Related to Mental Illness, using a global unique identifier (GUID) to protect the participant's privacy. Once a participant has agreed to participate in the research and signed the informed consent, s/he will undergo the baseline assessment phase. The participant will provide the RA with verbal consent over the phone or over HIPAA complaint zoom and the RA will document this consent on a blank consent form. These forms will be stored in a lockbox in the RAs homes and will be transported to the office in the lockbox. Once in the office, these consents will be filed with the other study consent forms in a locked file cabinet in our offices. We will also mail a copy of the consent form to the participant. Once a participant has agreed to participate in the research and provided informed consent, s/he will undergo the baseline assessment phase.

For in-person recruitment, participants who indicate potential interest in the study are approached privately in a confidential setting. Research staff will carefully explain all aspects of the study to a potential participant, including its voluntary nature, risks and benefits, the schedule of visits, and the expected duration of participation, and will elicit and answer any questions the participant may have. If still interested, we will request participant verbal permission to conduct a brief screen to determine if they meet initial eligibility for participation in the study (i.e., current age, remaining duration of prison sentence, expected location following prison release). If they meet initial eligibility criteria, we will ask them if they would like to continue with the informed consent process. We will ask participants if they would like us to read the consent forms aloud. As part of the informed consent process, participants will always be informed that: (1) a decision to not participate in the research will have no impact on their status, access to treatment, or length of stay at the prison; (2) the study has a Certificate of Confidentiality; and (3) the study information will be kept confidential from prison staff, officers of the court, parole officers, or others in the criminal justice system. Study staff will also carefully review the limits to confidentiality, including the prison's mandatory reporting procedures (see page 16).

Participants who give their consent will sign a copy of the document and will be given a signed copy of the informed consent document. Informed consent procedures have been developed to comply with the Code of Federal Regulations 45 CFR 46.116, *General Requirements for Informed Consent* and 46.117 *Documentation of Informed Consent*. Freedom to refuse to participate or to discontinue participation at any time without penalty will be emphasized. Participants will be asked to provide written permission for us to try to locate them through significant others, their appointed parole/probation officer, and/or post-release treatment program, but will not be excluded if they are unwilling to do so. Participants will be able to refuse or revoke locator consent. Because of the NIMH data sharing requirements, which we are bound to, we will need to obtain the participant's city or municipality of birth at the time of consent as well as the participant's full name a birth. This will be used to link the participant's data with any existing data they may already have in the National Database for Clinical Research Related to Mental Illness, using a global unique identifier (GUID) to protect the

participant's privacy. Once a participant has agreed to participate in the research and signed the informed consent, s/he will undergo the baseline assessment phase.

SO participants: Once participants have been determined to meet eligibility criteria through study assessment, and have completed 2 of the 4 individual sessions with their CARE counselor, the CARE counselor will work collaboratively with the participant to identify an appropriate SO for participation. In addition to the standard inclusion criteria described above, for those participants recruited while in prison, we will require that this individual be on the patient's approved visitor list at the [redacted] for both practical (i.e., in order to attend the family/SO session prior to release) and also safety (i.e., because this person will have been cleared by the [redacted] for entry) purposes. With written permission from the participant, the CARE interventionist will contact the SO over the telephone to describe the program and to explain all aspects of the study to the potential SO, including the risks and benefits, and invite him/her to attend the family session. The family session may occur either prior to release in prison, or after release in the community. If the session occurs after release from prison, the session may take place either by telephone, by zoom, or in person (e.g. our offices or a residential facility, with their approval). Immediately prior to the family session, a study RA will meet the SO in person to obtain the SO's written consent for participation, following our standard informed consent procedures as described above. If the family session will take place by telephone or zoom, a waiver of documentation of consent will be utilized for the SO. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context since the SO is only participating in a family session and brief phone sessions to support the participant. SOs are not completing any assessments nor is the treatment focused on the SO. We will try to consent SOs in person whenever possible. When a waiver of documentation of consent takes place, a study RA will send a copy of the consent form to the SO and then review it together during a telephone or zoom call, which will take place after the initial recruitment call. The SO will provide the RA with verbal consent over the phone or zoom and the RA will document this on a blank consent form. These forms will be filed with the other SO consent forms in a locked file cabinet in our offices.

Stakeholders as key informants: Using the [redacted] staff directory, we will individually and confidentially reach out to stakeholders internal to the [redacted] Other community stakeholders will be identified through the [redacted] of which [redacted] is a member. Prison counselors, staff, and administrators who indicate potential interest in stakeholder interview participation will be approached privately and treated as key informants for purposes of conducting the proposed research. We will emphasize that participation has no impact on their employment or affiliation with the [redacted] or their community mental health center. All stakeholders will be reminded that there is no penalty for participants who choose to not participate or to withdraw from these stakeholder interviews.

3.b.6. Participant Timeline.

After providing informed consent, and if the participant is determined to be eligible for continued participation, the appointment structure in each study phase is described below:

In the Open Trial Phase, if a participant is determined to be eligible following the baseline assessment, s/he will be assigned a CARE interventionist. Eligible participants will receive 3 individual sessions in prison in the time between the baseline assessment and the anticipated date of release from prison. A family/SO session (as applicable) will take place either in prison prior to release or as soon as possible after release either by telephone or in person (e.g., at our offices or in any residential facility where the participant is located, with facility approval). Ideally, the first two sessions will be delivered within 1 week, the third session will be delivered within the following week, and the family/SO session will be delivered within the week after that. However, we acknowledge that time to release will be variable, and the session schedule may be compressed or spread out depending upon length of time available to complete the sessions between the baseline assessment and the prison release date.

Following prison release, the counselor will initiate the phone follow-up calls, delivered across the first 6 months post-release. The schedule for phone follow-up will be: weekly for the first month, biweekly for the next 2 months, and then monthly for the final 3 months. Calls will be made separately to the prisoner participant and to the identified SO (if applicable).

In addition to the baseline assessment in prison, outcome assessments will occur on the following schedule: a) following the in-prison sessions, prior to prison release (~1-2 weeks prior to prison release); b) 1 month after prison release; and c) 6 months after prison release, immediately post-treatment. To enhance feasibility and therefore retention, we will aim to complete all post-release follow-up assessments by telephone, using procedures we have in place for other studies (see "Human Subjects Protections"). However, there may be some circumstances that might make it difficult for a participant to complete the follow-up assessment by telephone (e.g., rearrest and reincarceration, participation in a residential treatment program). In such cases, we will complete the follow-up assessment in person.

In the Pilot Randomized Trial Phase, if a participant is determined to be eligible following the baseline assessment, s/he will be randomized to either E-TAU plus CARE or to E-TAU alone. **Randomization** will be determined in a 1:1 ratio, with 2 stratification variables, the maximum number advisable in a sample of this size: sex (male vs. female) and polarity of most recent mood episode (depression vs. (hypo)mania) using a randomization table.

Participants randomized to receive CARE will receive 4 counseling sessions. The first 3 sessions will be individual sessions that take place in prison in the time between the baseline assessment and the anticipated date of release from prison; or they will take place after release for those enrolled post-release. A fourth session will either be an individual counseling session or a family/SO session (as applicable). This session will take place either in prison prior to release or as soon as possible after release either by telephone, by zoom, or in person (e.g., at our offices or in any residential facility where the participant is located, with facility approval). Ideally, the first two sessions will be delivered within 1 week, the third session will be delivered within the following week, and the fourth session will be delivered within the week after that as either an individual session or a family/SO session. However, we acknowledge that time to release will be variable, and the session schedule may be compressed or spread out depending upon length of time available to complete the sessions between the baseline assessment and the prison release date. Following prison release (in prison enrollment) or completion of the initial sessions (post-release enrollment), the counselor will initiate the phone follow-up calls, delivered across the first 6 months post-release (in prison enrollment) or 6 months post-baseline (post-release enrollment). The schedule for phone follow-up will be: weekly for the first month, biweekly for the next 2 months, and then monthly for the final 3 months. Calls will be made separately to the prisoner participant and to the identified SO (if applicable).

Assessments will occur on the following schedule: For participants recruited in person at [redacted] prior to release: a) baseline assessment; b) following the in-prison sessions, prior to prison release (~1-2 weeks prior to prison release); c) 1 month after prison release; and d) 6 months after prison release, immediately post-treatment. For participants recruited post-release: a) baseline assessment; b) 1 month after baseline; and c) 6 months after baseline, immediately post-treatment. The post-release enrollment baseline would include any additional questionnaires/items from the pre-release assessment that were not already included in the baseline assessment. To enhance feasibility and retention, we will aim to complete all post-release follow-up assessments by telephone or zoom, using procedures we have in place for other studies (see "Human Subjects Protections"). However, there may be some circumstances that might make it difficult for a participant to complete the follow-up assessment by telephone or zoom (e.g., limited phone minutes, participant rearrest and reincarceration, current enrollment in a residential treatment program). In such cases, we will complete the follow-up assessment in person in our offices at [redacted] or in the facilities where the participant may be located (e.g., jail or prison, residential treatment facility). Additionally, if a participant is released earlier than expected before finishing the in-prison assessment, we will complete the assessment by

telephone, by zoom, or in person at our offices or in the facility (e.g., residential treatment program) where the participant is located.

Appointments for participants randomized to the E-TAU condition will consist of the regularly scheduled research assessments. For participants recruited in person at [redacted] prior to release: baseline, pre-release, 1 month post-release, and 6 months post-release. For participants recruited post-release: baseline, 1 month after baseline; and 6 months after baseline. The post-release enrollment baseline would include any additional questionnaires/items from the pre-release assessment that were not already included in the baseline assessment.

3.b.7. Audio recording.

We will audio record all assessment interviews in order to perform reliability checks. Participants may refuse audio recording of assessments but still participate in the study. We will audio record all intervention sessions in order to monitor therapist adherence to the CARE manual. Participants may refuse audio recording of sessions and still participate in this study. With [redacted] permission to bring them into the prison facilities, we will utilize small, credit-card sized audio recorders that are password-protected and encrypted for purposes of safe transportation between the [redacted] facilities and [redacted] offices.

3.b.8. Assessment procedures.

Participants enrolled prior to release will be assessed at: intake, just prior to prison release (4-10 weeks later, depending upon timing of baseline and scheduled release date), and then at 1 and 6 months post-release. Participants enrolled post-release will be assessed at: intake, and then at 1 and 6 months post-release. The post-release enrollment baseline will consist of any items in the pre-release that were not included in the baseline. In addition to demographics, we will assess psychiatric diagnosis (primary inclusion criterion), psychiatric symptom severity, substance use history, psychosocial functioning, proposed mechanisms of action for the intervention (i.e., values-action consistency, social support, mental health and substance use treatment utilization and adherence), and treatment satisfaction. Assessments are listed in Table 2. RAs will also call to verify/update locator information monthly after release.

All interview and self-report assessment measures were chosen because they have strong psychometric properties for measurement of the constructs of interest to the study, and have been used in other NIH-funded clinical trials and prospective studies. With signed releases of information (ROIs) obtained at the baseline assessment, we will supplement interview and self-report data with criminal justice and medical records chart review to assess for recidivism and community treatment utilization, respectively.

Table 2: Pre-Release Enrollment Schedule of Assessments	**Type**	**Baseline**	**Pre-release, 1mo & 6mo post-release**
Diagnosis: Structured Clinical Interview for DSM-5[22]	Interview	X	
Psychiatric Symptom Severity			
LIFE – PSRs for depression and mania[23,24]	Interview	X	X
Quick Inventory of Depressive Symptomatology[25]	Self-report	X	X
Altman Self-Rating Scale for Mania[26,27]	Self-report	X	X
LIFE – suicidal ideation and behavior[28–30]	Interview	X	X
Substance Use			
Alcohol Use Disorders Identification Test[31]	Self-report	X	1 & 6 mo only
Drug Use Disorders Identification Test[32]	Self-report	X	1 & 6 mo only
Psychosocial Functioning			
SF-12 from RAND Medical Outcomes Study[33]	Self-report	X	X

Job Security Index/Job Satisfaction Scale[34]	Self-report		1 & 6 mo only
Housing Security Scale[35]	Self-report		1 & 6 mo only
Criminal Justice Records Review	Objective		X
Targeted Mechanisms of Action			
Valued Living Questionnaire[36]	Self-report	X	X
Multidimensional Scale of Perceived Social Support[37]	Self-report	X	X
NIH Toolbox Instrumental Support Fixed Form Age 18+ v2.0[38]	Self-report	X	X
Treatment History Interview-4[39]	Interview	X	X
Brief Adherence Rating Scale[40]	Interview	X	X
Medical Records Review	Objective	X	X
Participant Satisfaction			
Client Satisfaction Questionnaire-8[41,42]	Self-report		6 mo only
End of Intervention Questionnaire	Self-report		6 mo only
Exit Interview	Interview		6 mo only
COVID-19			
Coronavirus Impact Scale			6 mo only

Please note: The post-release enrollment assessments are the same as the pre-release enrollment assessments. However, the schedule of assessments is slightly different. Post-release enrolled participants will not complete a pre-release assessment. Items specific to the pre-release assessment that are not already included in the baseline assessment are added to the baseline for post-release enrolled participants.

3.b.9. Data analysis.

For this pilot effectiveness study, assessment of feasibility and acceptability of the intervention and research procedures is the primary goal. Nonetheless, pilot data can be used to demonstrate whether the effects of treatment look promising across a set of outcome variables, to begin to examine distribution of outcome variables to inform future analytic strategies, and to suggest, in concert with results from larger scale clinical trials in related fields, the range of effect sizes that would be reasonable to expect in a future trial.

Study Feasibility and Treatment Feasibility/Acceptability. One of the primary goals of a pilot study is to demonstrate the feasibility of the proposed treatment and of the study and recruitment methods. As a result, we will assess the feasibility of the research procedures by examining study recruitment and refusal rates, participants' willingness to be randomized, follow-up rates, reliability and range of responses to study questionnaires, and success of the interventionist training program. We will assess the feasibility and acceptability of CARE by examining rates of treatment attendance, rates of treatment completion (attending at least 3 of the 4 initial sessions and completing 6 out of the 11 scheduled post-release telephone calls) and drop-out, and reports on the End of Intervention Questionnaire. We will also examine reasons for termination for consistent patterns. We will examine the acceptability of both CARE and E-TAU using data from CSQ-8 treatment satisfaction and end of intervention questionnaires and detailed exit interviews.

Primary Outcomes: Using multilevel modeling of group by time, we will calculate the effect size and 95% CI for percent time symptomatic using the LIFE, with percent time symptomatic in the 90 days prior to study enrollment as a covariate. We will calculate similar exploratory tests for symptom severity using the QIDS and ASRM total scores, with baseline scores as covariates.

Secondary Outcomes: Using multilevel modeling of group by time, we will calculate the effect sizes and 95% CIs for: (1) percent time suicidal, as assessed by the LIFE, (2) alcohol and drug use severity using the AUDIT and DUDIT, respectively, and (3) overall functioning, employment stability, and housing stability, using the SF-12, JSI, and HSS, respectively. All assessments will use baseline scores, including percent time suicidal in the 90 days prior to study enrollment, as covariates. Potential group differences in rate of re-arrest will be calculated using simple chi-square analysis.

Target engagement/mechanisms of action. In this study, we will explore potential group differences in CARE's purported mechanisms of action. To that end, we will rely upon multilevel modeling of group

by time to calculate effect sizes and 95% CIs for change in VLQ, NIH Toolbox Instrumental Support, MSPSS, THI, and BARS scores across study time points. Across the four assessment time points, we will also evaluate associations between change in these intermediary constructs and primary/ secondary outcome measures, using multilevel models.

3.b.10. Material inducements.

We will compensate participants $40 for each of the three follow-up assessments for pre-release enrolled participants (immediate pre-release, 1 month post-release, 6 months post-release) in the form of a money order or a gift card (if they do not have state or federal identification to cash the money order). For post-release enrolled participants, they will be compensated $40 for each of their completed assessments (baseline, 1 month follow-up, and 6 month follow-up). In total, participants may receive up to $120 if they complete all study assessments. Compensation for the pre-release assessment will be mailed to an address of the participant's choosing after it is confirmed that the participant has been released from prison. If a follow-up is completed in jail or prison, we will provide the participant the following options: a) us mailing the compensation once they are released, or b) mailing it to a family member or significant other of their choosing, or c) depositing it into their commissary account at the [redacted]

3.b.11. Training of research personnel.

All research personnel will have formal training in research with human subjects (e.g., CITI training, GCP training). [redacted] will provide training to and supervise research assistants. RAs will have a bachelor's or master's degree, and will receive training in the informed consent process and their ethical responsibilities when conducting research, with a particular focus on the ethics involved with research in perinatal populations. All interviewers will receive specific training in the assessment instruments to be administered and in all study-related safety protocols. With assistance from study [redacted] will supervise the study therapists.

3c. Protection of Human Subjects

Please see section 3.b.1 for a detailed description of study participants. Special classes. Because the purpose of the application is to develop and evaluate the feasibility and acceptability of CARE in prisoners during the vulnerable period of community re-entry, it is necessary to sample a prison population. Prisoners are an understudied population with complex treatment needs; hence the urgency for more research attending to the mental health concerns of this population. Because the target population for this study is constituted by sentenced prisoners with BD, the Prisoner Checklist for research has been included as an appendix to this application. It is anticipated that, once approved, the [redacted] IRB will apply to OHRP for project certification. Incarcerated children 18-21 will be eligible.

3.c.1. Inclusion of Women and Minorities

Because the purpose of this application is to develop and pilot an intervention for prisoners with bipolar disorder (BD) around the period of community re-entry, the study population will consist of sentenced male and female inmates who meet criteria for BD. The study sample will also include participating family members/significant others (SOs). Equal numbers of male and female prisoners and SOs will be recruited.

Extant data from prisoners at participating facilities in [redacted] have been used to estimate the racial and ethnic distribution of the 104 participants (52 prisoners; 52 SOs) in the open and randomized trials. For females, the overall racial distribution will be approximately 66% White, 17% African American, 2% Asian, 4% American Indian or Alaska Native, and 11% other. The overall ethnic distribution for women will be approximately 17% Hispanic or Latina and 83% Non-Hispanic or Latina. For males, the overall racial distribution will be 48% White, 28% African American, 2% Asian, 4% American Indian or Alaska Native, and 18% other. The overall ethnic distribution for men will be approximately 24% Hispanic or Latino and 76% Non-Hispanic or Latino.

If the minority distribution of our participants falls below the targeted minority distribution (i.e., if

halfway through the study, the proportions of African Americans or Hispanics recruited are less than two thirds of the proportion of that minority distribution for the [redacted]), then we will conduct additional outreach to the group that fell below their targeted enrollment numbers. We will also attempt to obtain feedback on why individuals for that group may refuse to participate in the study. Based on the feedback, we will take corrective action. All subjects will be asked to identify their race and ethnicity separately, by self-report, at the time of study entry, when demographic information is collected. We plan to conduct analysis to determine whether minority status is associated with any of the treatment utilization or clinical outcome data collected as part of this investigation.

3.c.2. Inclusion of Children

Individuals aged 18-21 who meet our inclusion criteria will be included in this study. Individuals younger than 18 will not be included. This study includes children 18-21, but does not include anyone under 18 years of age (the age of emancipation in [redacted]) because adolescent developmental issues would confound outcomes of interest to the study. Additional instruments and study methods would also be required to assess the unique mental health needs of a younger population. Thus, the current research is not applicable to children under the age of 18.

Because children ages 18-21 are of legal age, they will be treated as adults and will be able to consent and agree to participate in the study themselves. Our consent procedures are conducted face-to-face, with trained interviewers guiding eligible subjects step-by-step; materials are written at a Grade 7 level and the interviewers ensure that each element is understood. In addition, consent forms will be read aloud.

3.c.3. Potential Risks

There are three major sources of low to moderate risk associated with participation in the proposed study.

1. Potential coercion. It is possible that individuals may feel coerced into participating. This is a particularly important risk to minimize with incarcerated individuals.
2. Increased distress due to assessment or intervention procedures. It is possible that some participants will experience increased intrapersonal or interpersonal psychological distress as a result of participating in assessment or intervention. In the vast majority of cases, we believe that any increased distress experiences will be mild and transitory in nature.
3. Confidentiality and loss of privacy. The greatest potential risks to those participating in the research are legal or social, caused by the inadvertent loss of confidential information obtained during the data collection process. That is, a participant's identity may be inadvertently exposed or questionnaire material may be released or disclosed to unauthorized persons. In the case of such a breach, serious personal and social consequences could conceivably occur. However, such risks can be minimized by instituting the proper procedures to protect confidentiality and by having resources in place to provide counseling and referrals. We have extensive experience taking appropriate measures to safeguard confidential information in research with criminal justice populations. These measures are described below.

3.c.4. Protection Against Risks

All aspects of the study will be conducted in accordance with HIPAA regulations. Data and safety monitoring will take place to assure the safety of subjects (see below). All participants will be reminded that their participation is voluntary and that they can withdraw at any time without penalty. Additionally, the risks described above will be minimized by the following procedures:

1. We will minimize the risk of potential coercion by following standard procedures for obtaining informed consent (please see section 3.b.5). We will begin this process during the intake where we will clarify the nature of the study and possible alternatives upfront. Prior to enrolling participants in the research, we will fully explain the study procedures, risks, benefits, and alternatives to participants,

emphasizing that participation has no impact on the other services they receive at the prison, the terms or length of their confinement, or any other community services that they receive post-release. Also, participants who do not consent or who withdraw will receive appropriate referrals (e.g., for mental health treatment), if needed. All participants will be reminded that there is no penalty for participants who choose to not participate or to withdraw from the study. All reimbursements for participating will be commensurate with participants' time required for participating in the research.

2. We will minimize the risk of distress. Incarcerated individuals with BD who serve as participants in this research face the risk of increased distress during assessment procedures or study intervention. All participants will be informed that they do not have to answer questions that they find too distressing and will be reminded that they can discontinue participation at any time. Moreover, clinical backup will be provided during all assessments and intervention sessions by a licensed clinician to help facilitate the stabilization and referral process for participants who decompensate during study procedures. The need for additional services will also be monitored during each clinical (assessment or intervention) contact. Participants will be formally assessed while they are in prison (intake, pre-release) and after release (1 and 6 months post-release). Incarcerated participants who report significant homicidal ideation or suicide risk, or who manifest significant manic or psychotic symptomatology, will be referred to appropriate clinical prison staff for evaluation, per [redacted] policy. For assessments in the community, a licensed clinician (the PI or her covering clinician) will be available at all times by cell-phone. Research staff will contact the licensed clinician if there are any safety concerns.

3. We will minimize potential risks due to loss of confidentiality of research data by having all information collected and handled by research staff, including study interventionists, trained to deal appropriately with sensitive clinical issues. All participants will be informed about the limits of confidentiality concerning suicidal intent, homicidal intent, suspected child abuse, suspected elder abuse, and prison-required mandatory reporting issues (i.e., sexual contact within the prison, weapons in the prison, prison escape plans). All information will be treated as confidential material and will be available only to research staff. All information will be kept in locked file cabinets at [redacted]. Computer data files will be kept on [redacted] secure research servers, will be available only to authorized personnel, and no names or obvious identifying information will be stored in data files. No participant will be identified in any report of the project. Written consent will be obtained to contact other persons for the purpose of locating the participant for follow-up and participants can refuse or revoke such requests. Participants will update their contact information and contact person for the post-release period at each assessment point to ensure that this information remains appropriate. To further protect participants, a **Federal Certificate of Confidentiality** will be granted by the NIH at the time of the Notice of Grant Award. Potential subjects will be informed that a Certificate of Confidentiality has been obtained for this project and that this certificate will protect the investigators from being forced to release any research data in which participants can be identified, even under court order or subpoena, although this protection is not absolute. Potential participants will be informed of the situations in which they may not be protected under the Certificate of Confidentiality. No information about participants will be released without their permission or where required by law.

Audio recording is necessary to rate reliability of the interview assessments and also study interventionists' fidelity to the treatment. As in our past 10 years of prison research, audio recording is accomplished through the use of credit-card size digital audio recorders, which have password-protection *and* encryption capabilities thereby protecting their contents during transport between the [redacted] and our research offices. These digital recordings are regularly transferred to [redacted] secure computer server (designed to hold and protect digital audio and video recordings for clinical trials) via USB connection and secure file transfer to [redacted] secure audio server, and the recorders are wiped. This is the same procedure that has been used in our completed and ongoing intervention studies with prisoners and jail detainees at the recruitment site. Participants will be asked to give informed written consent to audio recording at the time of intervention study entry. To assure the confidentiality and protection of participants with respect to audio taping, the following steps will be taken: a) each recording will be labeled with the participant's study identification number, the intervention

provider's/interviewer's name, and the session/interview date; b) all recordings will be stored on a secured computer server designed to hold and protect research data; and c) access to the audio recordings will be limited to research staff who need access to the recordings to perform their duties.

3.c.5. Data Monitoring Plan

Data management and data entry will be conducted by the investigative team, who will establish a participant tracking and data monitoring system. Research assistants will be trained in interviewer-administered instruments (e.g., SCID, LIFE, THI) at [redacted] using established procedures. RAs complete follow-up assessments and will be blind to intervention condition. All assessments will be audiotaped and reliability checks for RA-administered interviews will be made monthly throughout the study.

Data will be collected using standardized paper forms or (if collected by telephone or zoom) will be directly entered into a REDCap database, and will only be identified with the study's ID of the participant. REDCap is a secure, web-based application developed by Vanderbilt University for building and managing surveys and databases. REDCap is designed to support online or offline data capture for research studies, quality improvement, and operations. REDCap provides easy data manipulation (with audit trails for reporting, monitoring, and querying participant records), real-time data entry validation and an automated export mechanism to common statistical packages.

The codes that link the name of the participant and the study ID will be kept confidential by [redacted] in a secured cabinet. Collected forms will be transported to [redacted] data entry center. Data quality will be monitored by random inspection of the completed forms by one of the research assistants and any problems detected will be discussed with the PI. Standard data checking procedures will include checking forms for missing data, daily back-up copies of computer files, and examination of key variables for skewness, variability, missing data, and outliers. Study statistician [redacted] will analyze the data using SAS or SPSS.

The computer systems used for data entry and analysis are protected by passwords and secure logon and data communications procedures to minimize the potential for disclosure of research information either inadvertently or as a result of external attack. Within each computer system, only those users authorized to access the data for a given study are able to do so. Research records are stored in areas that are locked when staff is not present.

3.c.6. Safety Monitoring Plan

[redacted] will be responsible for overseeing the safety of all participants. [redacted] (who maintains her clinical license in RI) will be available to serve as clinical back-up for [redacted], when required. [redacted], study co-investigator, is a board-certified psychiatrist who will serve as the medical advisor. Participant safety will be monitored in two ways: (a) during the intake or ongoing assessments by the research staff, or (b) during intervention sessions. Research assessments will be conducted in the prison at study intake, at pre-release (4-10 weeks later), and in the community at 1 and 6 months post-release. We will monitor all participants for significant suicidal ideation (SI), homicidal ideation (HI), and clinical deterioration at each time point.

During incarceration the [redacted] standards for mandatory reporting of suicide risk specify that we are required to report anyone who has had suicidal ideation within the past 24 hours (as determined by a QIDS item 12 score > 1, LIFE PSR > 2, or reporting any current desire to hurt oneself to any member of the research staff). If the participant reports this level of SI within the past 2 weeks, but not in the 24 hours prior to the assessment, a voluntary referral will be offered. Participants meeting the prison's SI mandatory reporting criteria (or those who elect the voluntary referral) will be referred to a prison mental health clinician for evaluation, who will follow prison procedures. Standard prison procedures include: (1) checking in the prison's electronic medical record to see if the person has already been flagged as having SI; (2) having a licensed mental health clinician check in with the person and do a suicide risk evaluation; and/or (3) if needed, putting the person on psychiatric observation within the prison. If the prison mental health professional determines that someone's risk has gone down, that person will leave

psychiatric observation and return to the general population. All of these procedures are set and executed by the prison, which follows its own ethical and legal requirements. We will clearly describe this in our consent form. Homicidal risk will be defined by reporting any desire to hurt another person or member of the study staff. Standard mandatory reporting procedures (e.g., contact prison mental health staff) will be followed. Clinical deterioration will be defined using the QIDS (for depression) and ASRM (for mania) questionnaires at each assessment time point. Clinical deterioration for depression will be defined as a QIDS score of ≥ 16. Clinical deterioration for mania will be defined as an ASRM score ≥ 8 (threshold for suspected hypo/mania). If someone meets these criteria for clinical deterioration while still incarcerated, a referral will be made to the prison's mental health staff, who will follow procedures similar to those describe for suicide risk management above. Additionally, if a participant reports any escape plans, any sexual contact with anyone while incarcerated, or any ongoing child or elderly abuse or neglect, we are required to report this information to the [redacted]

During the post-release period (in the community), definitions of suicide risk, homicide risk, and clinical deterioration will be the same those described above; however, we will rely upon our standard study procedures (vs. [redacted] mandatory/voluntary reporting criteria) to facilitate clinician referral and safety assessment, as needed. If any study staff member identifies an individual with significant clinical deterioration or who report any suicidal or homicidal ideation in the course of standard assessment procedures, the staff member will immediately contact [redacted] (or the licensed covering clinician). The covering clinician will evaluate the participant over the telephone, by zoom, or in person. First, they will conduct a suicide and homicide risk assessment to determine whether it is necessary to take immediate action to prevent the participant from causing harm to self or others. If needed, actions that the covering clinician may take include escorting the person to the emergency [redacted] at [redacted] (if the person is in our offices), having a family member transport the person to [redacted] or another hospital, or calling the local police who may conduct a welfare check and evaluate the need to transport an individual to the closest emergency room for further evaluation.

If a study participant has experienced significant deterioration, but is not in immediate danger to self or others, we will take the following actions. First, we will inform the participant about procedures for contacting emergency services should they find themselves at risk for self-harm. Second, with the participant's knowledge and release of information, we will contact their community psychiatric or primary care providers to inform them of the deterioration. We will urge the participant to make an appointment with their outpatient provider(s); if they are not in active treatment with an outpatient provider, referrals will be provided. Third, and consistent with the CARE protocol, we will speak with the participant's SO so that he/she can be aware of the seriousness of the patient's symptoms and the agreed-upon treatment plan.

The study will reply upon the NIH's definitions for Common Adverse Events (AEs) and Serious Adverse Events (SAEs) for clinical research, and definitions will be operationalized in the approved study protocol document and manual of procedures (MOP). We will require that all study staff, study interventionists, and study participants report any adverse events to [redacted] immediately. These include, but are not limited to, psychiatric hospitalization and/or suicide attempt. Consistent with procedures utilized in our other psychosocial treatment studies for prisoners, jail detainees, and other high risk psychiatric samples, [redacted] will be available by telephone, by zoom, or in person during all participant assessments in the event that immediate consultation is needed for an emergent mental health or other problem. If an AE occurs, [redacted] will complete an Adverse Event form and report the event to the [redacted] IRB per their reporting guidelines and timeline. [redacted] will also review the adverse event form with the investigator team. They will gather any information needed to investigate the event and to determine subsequent action; this will also be reported to the IRB. We will inform NIH of any significant action taken as a result of any adverse event report. Anticipated and less serious adverse events will be submitted annually in reports to the IRB.

3.c.7. Data Safety and Monitoring Board

An external local DSMB will be assembled to evaluate the data and safety to participants enrolled in the study. We will recruit 3 [redacted]-affiliated board members who have experience in clinical trials and/or BD treatment research and/or research with criminal justice samples as well as the ethical issues involved with a randomized control study. The external DSMB will convene twice in Year 1, and then at the end of each year in Years 2-3 for a meeting. Initially, the Board will convene with the PI and study Co-Is to review the study protocol and review the guidelines for data and safety monitoring. At this meeting and at each subsequent meeting, the DSMB will evaluate recruitment, the progress of the trial, subject retention, data quality and confidentiality. In addition, they will review participants' clinical status, rates of adverse events and whether or not there have been any changes in risk to participants.

3.c.8. Benefits of the Proposed Research to the Subjects and Others

The potential risks associated with participation in this study appear to be mild to moderate. Although there is a risk for distress, the procedures proposed for monitoring distress should ensure that participants who require a higher level of care receive it. The study provides additional screening, assessment, and referral to emergency services, as needed, for all study participants, and in no way restricts or limits the treatment individuals would have received had they not participated in the study. Moreover, participants are helping other incarcerated individuals with BD by providing information that will improve treatments for this population. Thus, the potential benefits outweigh the potential risks of the study.

3.c.9. Importance of Knowledge to Be Gained

To our knowledge, this proposed study represents the first attempt to develop and pilot a targeted intervention for BD treatment engagement – with the aim of improving mood symptom and functioning outcomes – surrounding the period of community re-entry. This pilot study will lay the groundwork for a larger, stage II clinical trial (R01) to evaluate the effectiveness of CARE for increasing treatment engagement, and thus improving clinical outcomes, among this seriously ill, high risk, understudied population during the vulnerable transition from prison to the community. The risks involved in the study are minimal compared to the need for treatments for this population.

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