STUDY PROTOCOL

Official Title: Treatment Engagement in Families with Substance Use and Psychosis: A Pilot Study

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Detailed Protocol

Protocol Title and Date:
Treatment Engagement in Families with Substance Use and Psychosis: A Pilot Study
March 28, 2024

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Study Performance Site: Admissions Building and McLean Imaging Center, McLean Hospital, 115 Mill St., Belmont, MA 02478

I. Background and Significance

Treatment Engagement Challenges: Psychosis and Substance Use Disorders. Co-occurring substance use disorders significantly increase the likelihood of treatment dropout for people with first episode psychosis (FEP) (Conus et al., 2010). This is a critical concern, because approximately 50-70% of people with FEP have a lifetime history of substance use disorder (Cather et al., 2018; Shinn et al., 2015), endorse recent tobacco, alcohol, and cannabis use (Oluwoye et al., 2019), and approximately 30% of people with FEP disengage from treatment (Dixon et al., 2016; Doyle et al., 2014). Though evidence-based treatments are available for FEP and substance use (e.g., Kane et al., 2016), they cannot be effective if clients are not engaged in treatment. Insufficient readiness to engage in substance use treatment likely contributes to poor outcomes among clients with co-occurring substance use disorders and FEP. These results call for novel strategies to increase substance use disorder treatment engagement, which has the potential to make a significant impact on reducing substance use in this population.

Treatment Engagement Intervention. Community Reinforcement Approach and Family Training (CRAFT) is an evidence-based intervention that increases treatment engagement for substance use disorders regardless of diagnosis (Meyers et al., 1999). CRAFT acknowledges that people with substance use disorders may not be ready to change their substance use, and it capitalizes on the motivation of concerned significant others (CSOs e.g., family members) as agents of change. Such families often seek additional support, as they experience elevated family distress associated with the identified patient's (IP) addiction and psychosis (Orford et al., 2013). CRAFT has not been studied with CSOs of individuals with co-occurring substance use and psychosis to date. Targeting CSOs may decrease family distress and facilitate greater substance use treatment engagement in FEP IPs. In this context, the CSOs are the subjects of intervention.

Many individuals with FEP have frequent contact or live with family (Drapalski et al., 2018), but time, transportation, finances, and childcare are barriers to family members accessing additional services. Utilizing telemedicine (e.g., video conferencing) mitigates these barriers, and such technology typically achieves similar results to in-person therapy (Hulsbosch et al., 2017; Tse et al., 2015). å

Phase 1: We will first develop a CRAFT for FEP delivered via telemedicine (CRAFT-FT) manual/training protocol by conducting an open-label cross-over feasibility pilot test in families with substance use and FEP with subjects (N=14) completing the first half of sessions in-person and the second half via telemedicine in counterbalanced order; we will also recruit corresponding FEP clients (N=14). Second, we will collect interview/focus group feedback on feasibility/delivery preferences to refine the manual. Third, we will further test

the manual feasibility and collect feedback in a second two-arm pilot (CRAFT-F N=7; CRAFT-FT N=7); we will also recruit corresponding FEP clients in each condition (CRAFT-F N=7; CRAFT-FT N=7). FEP clients will complete assessments only, as the study intervention is targeted toward family members.

In light of COVID-19 guidelines and subject/staff safety concerns, we may forego the cross-over and randomized designs involving in-person visits to have family subjects participate in the CRAFT-FT via virtual visits only.

Phase 2: After developing the above intervention, we will take the adapted CRAFT-FT protocol, now termed CRAFT for early psychosis (CRAFT-EP), and conduct a small pilot randomized controlled trial comparing CRAFT-EP plus treatment as usual (TAU) to TAU alone. Family members (N=40) will be randomized to CRAFT-EP + TAU (N=20) or TAU alone (N=20). The CRAFT-EP intervention nis targeted toward family members, but given participant feedback from the development stage of the study, FEP clients will now have the option for limited intervention participation if their family member is randomized to CRAFT-EP + TAU. We will also recruit FEP clients (up to N=40) for assessment purposes for CRAFT-EP + TAU (N=20) and TAU alone (N=20). If a FEP client subject does not have a family member participating in the study, the FEP client will be automatically be assigned to the TAU alone group. Total target enrollment is N=80 (N=40 family members and up to N=40 FEP clients). To account for potential attrition, an additional N=12 participants (N=6 family member and N=6 FEP clients) may be recruited, and the overall total enrollment would be up to N=92 (N=46 family members and N=46 FEP clients).

II. Specific Aims

Phase 1:

Develop a feasible telemedicine and in-person Community Reinforcement Approach and Family Training (CRAFT) protocol to improve treatment engagement for families with substance use and psychosis.

Hypothesis 1A: The adapted CRAFT protocol will be feasible as measured by session completion rate (%) and participant satisfaction questionnaire/interview assessments.

Phase 2:

Test preliminary efficacy of CRAFT-EP plus TAU compared to TAU alone.

Hypothesis 2A: CRAFT-EP will improve IP substance use treatment engagement compared to TAU as measured by FEP client readiness to change substance use and past 30-day sessions attended %.

Hypothesis 2B: CRAFT-EP will reduce FEP client substance use more than TAU as measured by self-report past 30-day use, and biological verification of use (e.g., urine) when available.

Hypothesis 2C: CRAFT-EP will result in greater improvements in family wellbeing compared to TAU, as measured by self-report mood, anxiety, happiness, and family relationship measures.

III. Subject Selection

Family members:

Phase 1 Inclusion:

1) Ages 18-70.
2) Having a relative who:
    a. Is a patient with early course psychosis (DSM-5 schizophrenia, schizoaffective disorder, schizophreniform, psychosis NOS, delusional disorder, brief psychotic disorder, major depression with psychosis, and bipolar disorder with psychosis) with first onset in the past 6 years, and
    b. Used tobacco, alcohol, or cannabis in the past 90 days and/or has no apparent immediate interest in abstinence (responding "No" to "Do you think they want to quit right now?" in reference to overall substance use).
3) The person(s) who can best describe the client with first episode psychosis (FEP).
4) At least 4 days per month contact with the client.
5) Access to a computer with internet or mobile phone with video conferencing capabilities.
6) Ability to provide written informed consent.
7) Speak and read English.

Phase 1 Exclusion:

1) DSM-5 moderate or severe substance use disorder in the past year
2) Lifetime psychotic disorder
3) History of domestic violence with the IP

Psychiatric, cognitive, or medical impairments that would interfere with the ability to follow through with the treatment plan.

Phase 2 Inclusion:

1) Ages 18-70.
2) Having a relative who:
    a. Is a patient with early course psychosis (schizophrenia, schizoaffective disorder, schizophreniform, psychosis NOS, delusional disorder, brief psychotic disorder, major depression with psychosis, and bipolar disorder with psychosis (as reported by family member, clinician, or chart review)) with first onset in the past 6 years, and
    b. Used alcohol or cannabis in the past 30 days and/or has no apparent immediate interest in abstinence (responding "No" to "Do you think they want to quit right now?" in reference to overall substance use).
    c. Family member has concerns about the relative's substance use.
    d. Is 18-35 years of age
3) The person(s) who can best describe the client with first episode psychosis (FEP).
4) At least 4 days per month contact with the client.
5) Access to a computer with internet or mobile phone with video conferencing capabilities.
6) Ability to provide written informed consent.
7) Speak and read English.

Phase 2 Exclusion:

1) DSM-5 moderate or severe substance use disorder in the past year.
2) Lifetime psychotic disorder.
3) History of domestic violence with the IP that would interfere with the ability to safely follow through with the intervention plan.
4) Psychiatric, cognitive, or medical impairments that would interfere with the ability to follow through with the intervention plan.
5) Prior participation of a family member of the FEP client in the study
6) Significant prior experience with CRAFT (e.g., having completed a CRAFT course prior to study enrollment)

FEP clients:

Phase 1 Inclusion:

1) Ages 18-35.
2) FEP in the past 6 years with a Diagnostic and Statistical Manual (DSM)-5 diagnosis of affective (bipolar disorder or major depressive disorder with psychotic features) or non-affective psychosis (schizophrenia spectrum disorder) as assessed by the Structured Clinical Interview for DSM-5, Research Version (SCID-5; First et al., 2015).
3) Used tobacco, alcohol, or cannabis within the past 90 days and/or no apparent immediate interest in abstinence (Responding "No" to "Do you want to quit right now?" in reference to overall substance use).
4) Ability to provide informed consent (or assent with their legal guardian providing informed consent).
5) Speak/read English.

Phase 2 Inclusion:

1) Ages 18-35.
2) FEP onset in the past 6 years with a Diagnostic and Statistical Manual (DSM)-5 diagnosis of affective (bipolar disorder or major depressive disorder with psychotic features) or non-affective psychosis (schizophrenia spectrum disorder) as assessed by the Structured Clinical Interview for DSM-5, Research Version (SCID-5; First et al., 2015)
3) Used alcohol or cannabis within the past 30 days and/or no apparent immediate interest in abstinence (Responding "No" to "Do you want to quit right now?" in reference to overall substance use).
4) They or others have concerns about the client's substance use.
5) Ability to provide written informed consent (or assent with their legal guardian providing informed consent).
6) Speak/read English

In **Phase 1**, Participants (N = 56) Participants will be recruited from families in the McLean OnTrack or similar first episode psychosis clinics or inpatient units using clinician referral, flyers, groups, medical record pre-screening (e.g., EPIC), and participants who completed SBDP research studies and agreed to be contacted about future research opportunities. Prior to consenting inpatient participants, the physician in charge would complete the Clinical Capacity form. Eligibility screening will be completed prior to recruitment. Participants will be screened and recruited through McLean Hospital's Schizophrenia and

Bipolar Disorder Research Program (Dost Öngür, MD, PhD, Director). The PI, Julie McCarthy, clinic, and/or research staff will identify appropriate early psychosis families and supervise a research assistant who will assist with screening, recruitment, and scheduling.

In **Phase 2**, Participants (N = 92) will be recruited from families in the McLean OnTrack or similar first episode psychosis or general outpatient clinics, clinical evaluation centers, inpatient units using clinician referral, assertive community treatment, partial hospital, and residential programs. Participants will also be recruited from the community, newsletters, list serves, flyers, groups, medical record pre-screening (e.g., EPIC), and participants who completed SBDP research studies and agreed to be contacted about future research opportunities. This study is also included in protocol 2022P002927, the Registry of Research Participants for the Psychotic Disorder Division. We will access the registry to identify participants that might be eligible for the study. We will also invite participants and potential participants that we screen to consent to the registry if they are interested. Clinicians from any of the above settings may notify their patients and families about the research study and refer them to the study team to obtain information about the study. Referrals can be done in person, by phone, email, video conferencing, or in the course of routine medical care or by providing a flyer, brochure, other IRB-approved written or electronic recruitment materials/links, or name and contact information of research staff to patients and family members. When making referrals, clinicians may share the name and contact information of potential participants with the research staff for those individuals who want the research staff to contact them directly. Further recruitment will occur online (e.g., via Rally, MAPNet, Facebook, Instagram, and Reddit) and a REDCAP CRAFT-FT Eligibility Survey (Prescreen) link with preliminary eligibility questions to facilitate subsequent phone screening. Phone screens may be conducted by telephone and/or video conferencing To facilitate recruitment of family dyads, if a potential participant requests that research staff contact their family member who may be interested, research staff may contact that family member directly. Prior to consenting inpatient participants, the physician in charge would complete the Clinical Capacity form either on paper or digitally via REDCap. Eligibility screening will be completed prior to recruitment. The Discussion of Clinical Appropriateness form will be used to obtain permission to contact inpatients after discharge if they would prefer to be enrolled after their hospitalization. Participants will be screened and recruited through McLean Hospital's Schizophrenia and Bipolar Disorder Research Program (Dost Öngür, MD, PhD, Director). The PI, Julie McCarthy, clinic, and/or research staff will identify appropriate early psychosis families and supervise a research assistant who will assist with screening, recruitment, and scheduling.

For **Phases 1 and 2**, adults will be recruited. For this study all subjects meeting criteria for participation (as detailed in the protocol) will be offered participation in this research study. We welcome all subjects whose data would be relevant to the study regardless of race, sex, ethnicity, religious beliefs, or sexual orientation.

IV. Subject Enrollment

The PI or trained research staff will conduct the informed consent procedures. The informed consent interview may take place in person and/or via virtual visit to minimize participant burden and time on campus. **Virtual visits** refer to videoconferencing, telephone, and/or online questionnaires. Whenever possible, virtual visits will be conducted using the Partners HIPAA-compliant Zoom platform. For subjects unable to use Zoom, virtual visits will be conducted by telephone. If conducted in person it will take place in a quiet, private room

where the subject will be given another opportunity for questions or concerns. The purposes, procedures, risks of the study, and that subject's right to withdraw from any procedures at any time will be explained by research staff verbally and with a written document to be read by subjects. Subjects will be encouraged to read through and consider the informed consent form; we will give subjects all the time they need to do so. The PI and research staff will be available to subjects to answer any questions related to the study. Consent will be documented by the subject's signature (witnessed) on the written document. Individuals under legal guardianship will need their legal guardian provide consent and the individual will need to provide their assent to participate in the study.

When digital consent will be used remotely or in-person, we will use REDCap or Adobe Sign and return the signed consent in-person or electronically with the REDCap survey Login feature or SEND SECURE. REDCap and Adobe Sign are validated password-protected and Partners-approved signature platforms. Though it is not always possible to validate the identity of the individual "on the other end of the computer" or for remote consent by mail, the present protocol is considered minimal risk, and in-person and remote digital signatures are generally approved for low risk research, according to the PHRC consent policy.

As with all consent procedures, the consent form will be reviewed and the subject will complete the Informed Consent Survey to ensure that they understand the consent form and can have any questions answered. The research staff member conducting the consent will also sign and date the version of the consent form reviewed with the subject. Documentation of remote consent will be entered into the subject file.

Written consent will be obtained in all cases using forms approved by the Partners IRB, except participants who choose to enroll in only the medical records portion of the study or joining a family member's coaching session* will complete verbal/implied consent documented in the Medical Records Fact Sheet or Session Fact Sheet* with Documentation of Verbal Consent completed, as appropriate. Any subject who does not agree to participate (or who the PI deems is not able to provide informed consent) will not be enrolled.
*Consent procedures involving joining a coaching session and Session Fact Sheet apply to **Phase 2** only.

V. Study Procedures

Phase 1 Study Procedures:

The study may consist of 3 in-person assessments, 6-8 therapy sessions (in-person or virtual visit), and 1 follow-up assessment (follow-up). Assessments may completed in person and/or during a virtual visit. **Virtual visits** refer to videoconferencing, telephone, and/or online questionnaires. Whenever possible, virtual visits will be conducted using the Partners/MGB HIPAA-compliant Zoom platform. For subjects unable to use Zoom, virtual visits will be conducted by telephone. We may ask subjects to complete the procedures detailed below, including activities/questionnaires using a computer, tablet, or pencil and paper, interviews, audio/video recording, an intervention, and urine and breath measures. If subjects have completed certain interviews, questionnaires, or tasks in the past month (or year for SCID-5) as part of another Schizophrenia and Bipolar Disorder Program study, they may not have to repeat them again for this study to reduce subject burden.

a) Consent procedures
b) Substance use screening (FEP clients only)

c) Clinical interview
d) Self-report questionnaires asking about preferences, daily life experiences (e.g., drug use), and symptoms (e.g., depression)
e) Intervention (family members only)
f) Focus group (family member only)

FEP clients who have been pre-screened for eligibility will also have the option to participate by granting access to medical record data including psychiatric diagnosis, symptoms, and use of treatment services by agreeing to participate by completing the Medical Records Fact Sheet (and Contact Sheet if opting for payment in the form of a gift card) in lieu of the full set of research procedures.

Substance Use Screening
FEP subjects may complete breath samples** to detect recent alcohol use (Alco-Sensor IV, Intoximeters, Inc.) and recent smoking (Micro Smokerlyzer, Bedfont). FEP subjects may also provide a urine sample** to screen for recent drug use). FEP subjects will complete substance use screening in person whenever possible. In the event that in person screening is not possible (e.g., to minimize in person contact during the COVID-19 pandemic), a drug and/or nicotine test, as appropriate, may be mailed to subjects. The principal investigator or trained research staff would be in communication with subjects about administration and results of the tests. The results of the test would be presented to study staff, either during a virtual visit or sent as a photo via email, so the results are clearly visualized by staff.

Clinical Interview
Subjects may complete the following measures in person and/or via virtual visit, and the interview may be audio/video recorded:

Structured Clinical Interview for DSM-5 (SCID-5-RV)
Positive and Negative Syndrome Scale (PANSS)
Montgomery-Asberg Depression Rating Scale (MADRS)
Young Mania Rating Scale (YMRS)
Fagerstrom Test for Nicotine Dependence (FTND)
Substance Use Questionnaire – Family (SUQ-Family)*
Substance Use Questionnaire – Client (SUQ–Client)**
Timeline Followback (TLFB)**
Treatment Satisfaction Interview*

Questionnaires
Subjects may complete questionnaires about demographic/medical information, menstrual (for women), and substance use history, as well as several questionnaires about symptom severity, mood, family distress, and feedback about the intervention throughout the study. Subjects may complete questionnaires in person and/or remotely via REDCap.
These include:

Demographic Form
Beck Depression Inventory – II (BDI-II)
State-Trait Anxiety Inventory-Short Form (STAI-SF)
Happiness Scale
Relationship Happiness Scale (RHS-Family)*
Relationship Happiness Scale – (RHS-Client)**
Readiness Scale – Family*

Readiness Scale – Client**
Readiness to Change Questionnaire – Family (RCQ-Family)*
Readiness to Change Questionnaire – Client (RCQ-Client)**
Treatment Engagement Survey – Family (TES-Family)*
Treatment Engagement Survey – Client (TES-Client)**
Credibility/Expectancy Questionnaire (CEQ)*
Session Survey*
Working Alliance Inventory – Short Revised (WAI-SR)
Motivation and Pleasure Scale – Self-Report (MAP-SR)
Drinking Motives Questionnaire – Revised (DMQ-R)**
Marijuana Motives Measure (MMM)**
Motives for Smoking Scale (MSS)**
Five Facet Mindfulness Questionnaire (FFMQ)
Perceived Stress Scale (PSS)

*Measures for family members only.
** Measures for FEP clients only.

Intervention (only family members)
We will tailor CRAFT for FEP with in-person (CRAFT-F) and telemedicine delivery (CRAFT-FT) in 6-8 sessions of approximately 45 minute therapy. Topics include building motivation, self-care, communication, and understanding family interactions. The sessions will be in person and/or virtual visits (video conferencing) and audio/video recorded. The audio/video recording will include identifiable information (e.g., face and potentially first names), but we will label the recordings with codes instead of names. We will store the recordings indefinitely, and they will not be erased. The audio recording will be sent securely to trained coders who will review sessions for therapist quality assurance and training purposes. At any time, subjects may request (verbally or in writing) to have their audio/video recordings erased. Session notes will be documented with:

Notes Template
Functional Analysis Worksheet (when conducting functional analysis exercise)

Focus group (only family members)
We may conduct 1-2 in person or virtual focus groups with subjects who are available at a mutual time following each Part 1 and Part 2 of the pilot to validate proposed changes to the manual and collect feedback to inform further manual improvements. The Focus Group Questions and responses from the treatment Satisfaction Survey and Session Surveys will be used to guide the semi-structured interview. The group may be audio/video recorded. Regarding confidentiality, subjects will be asked to not take screenshots, photographs, or recordings of any kind with any electronic equipment, refrain from using last names, and to keep information shared during the group confidential. The audio recordings may be sent securely to a MGB-approved transcription service in order to obtain research grade transcriptions for analysis.

Timing of Measures
Study assessment procedures will take approximately the following durations to complete:

Visit 1: 3 hours
Visit 2: 1 hour
Visit 3: 1 hour
Follow-up: 30 minutes

Focus Group: 30-60 minutes

If virtual visit assessments are used, number of visits may vary to reduce participant burden and time on campus. If subjects have completed certain study procedures as part of another Schizophrenia and Bipolar Disorder Program study within the past 30 days (e.g., clinical interview,) or past year for the SCID-5, they may not be repeated to reduce participant burden. FREQUENCY: The Informed Consent Survey Family/Client, Demographic Form, SCID-5, DMQ-R**, MMM**, and MSS** may be assessed at baseline, the Treatment Satisfaction Interview* may be assessed at the final session or post-treatment, the Focus Group Questions* may be assessed once any time after post-treatment for each subject, and the Functional Analysis* will be assessed once during treatment. The CEQ* may be assessed at baseline and post-treatment, the WAI may be assessed once at mid-treatment for Clients and session 2 and post-treatment for Families. The PANSS, MAP-SR, MADRS, YMRS, and substance use screening** may be assessed at baseline, mid-treatment, and post-treatment. The PSS and FFMQ may be assessed at baseline and post-treatment (and at follow-up for Families). The Session Survey may be assessed following each intervention session. Remaining measures may be collected at baseline and repeated mid-treatment (approximately week 3), and post-treatment (approximately week 6-8), and measures may be assessed via online survey or phone/virtually at 3-month follow-up.

Study intervention procedures will take approximately 45 minutes weekly for a total of 6-8 sessions in person and/or via virtual visits.

Phase 2 Study Procedures:

The study may consist of 3 in-person assessments, 8 coaching sessions (in-person or virtual visit), and 1 follow-up assessment (follow-up). Assessments may be completed in person and/or during a virtual visit. **Virtual visits** refer to videoconferencing, telephone, and/or online questionnaires. Whenever possible, virtual visits will be conducted using the Partners/MGB HIPAA-compliant Zoom platform. For subjects unable to use Zoom, virtual visits will be conducted by telephone. We may ask subjects to complete the procedures detailed below, including activities/questionnaires using a computer, tablet, or pencil and paper, interviews, audio/video recording, an intervention, and urine and breath measures. If subjects have completed certain interviews, questionnaires, or tasks in the past month (or year for SCID-5) as part of another Schizophrenia and Bipolar Disorder Program study, they may not have to repeat them again for this study to reduce subject burden.

g) Consent procedures
h) Substance use screening (FEP clients only)
i) Clinical interview
j) Self-report questionnaires asking about preferences, daily life experiences (e.g., drug use), symptoms (e.g., depression), and debriefing
k) Intervention (family members, option for client-relative participation)
l) Focus group (family member only)

FEP clients who have been pre-screened for eligibility will also have the option to participate by granting access to medical record data including psychiatric diagnosis, symptoms, and use of treatment services by agreeing to participate by completing the Medical Records Fact Sheet (and Contact Sheet if opting for payment in the form of a gift card) in lieu of the full set of research procedures.

Substance Use Screening

FEP subjects may complete breath samples** to detect recent alcohol use (Alco-Sensor IV, Intoximeters, Inc.) and recent smoking (Micro Smokerlyzer, Bedfont). FEP subjects may also provide a urine sample** to screen for recent drug use). FEP subjects will complete substance use screening in person whenever possible. In the event that in person screening is not possible (e.g., to minimize in person contact during the COVID-19 pandemic), a drug and/or nicotine test, as appropriate, may be mailed to subjects. The principal investigator or trained research staff would be in communication with subjects about administration and results of the tests. The results of the test would be presented to study staff, either during a virtual visit or sent as a photo via email, so the results are clearly visualized by staff.

Clinical Interview
Subjects may complete the following measures in person and/or via virtual visit, and the interview may be audio/video recorded:

Structured Clinical Interview for DSM-5 (SCID-5-RV)
Positive and Negative Syndrome Scale (PANSS)**
Montgomery-Asberg Depression Rating Scale (MADRS)
Young Mania Rating Scale (YMRS)**
Fagerstrom Test for Nicotine Dependence (FTND)
Substance Use Questionnaire – Family (SUQ-Family)*
Substance Use Questionnaire – Client (SUQ–Client)**
Timeline Followback (TLFB)**
Satisfaction Interview*

The audio recordings from this study may also be used for training purposes, i.e., to train research staff (e.g., research assistants, postdoctoral fellows, etc.) and students on SCID and scales administration. Trainees may include research staff and students who are not directly involved in this study (i.e., members of the lab who are not study staff.) Any audio recordings used for training purposes will be stored in a Partners Dropbox folder that is shared only with the specific individuals who are undergoing the training. Trainees will be given view-only access (vs. edit access) and will be instructed that they are not permitted to download any of the audio files.

Questionnaires
Subjects may complete questionnaires about demographic/medical information, menstrual (for women), and substance use history, as well as several questionnaires about symptom severity, mood, family distress, and feedback about the intervention throughout the study. Subjects may complete questionnaires in person and/or remotely via REDCap.
These include:

Demographic Form
Beck Depression Inventory – II (BDI-II)
State-Trait Anxiety Inventory-Short Form (STAI-SF)
Happiness Scale
Relationship Happiness Scale (RHS-Family)*
Relationship Happiness Scale – (RHS-Client)**
Readiness Scale – Family*
Readiness Scale – Client**
Readiness to Change Questionnaire – Family (RCQ-Family)*
Readiness to Change Questionnaire – Client (RCQ-Client)**
Treatment Engagement Survey – Family (TES-Family)*

Treatment Engagement Survey – Client (TES-Client)**
Credibility/Expectancy Questionnaire (CEQ)*
Session Survey*
Working Alliance Inventory – Short Revised (WAI-SR)
Motivation and Pleasure Scale – Self-Report (MAP-SR)
Drinking Motives Questionnaire – Revised (DMQ-R)**
Marijuana Motives Measure (MMM)**
Motives for Smoking Scale (MSS)**
Stigma Resistance Scale – Family (SRS-Family)
Stigma Resistance Scale – Client (SRS-Client)
Perceived Stress Scale (PSS)
Patient Health Questionnaire 9 (PHQ-9)
Generalized Anxiety Disorder 7 (GAD-7)
Family Questionnaire
World Health Organization Quality of Life - BREF (WHOQOL-BREF)
Generalized Self-Efficacy Scale
Debriefing Interview

*Measures for family members only.
** Measures for FEP clients only.

Intervention (family members, optional client participation)
We will tailor CRAFT for FEP with telemedicine delivery (CRAFT-FT) in 8 sessions of approximately 60-minute coaching. Topics include building motivation, self-care, communication, and understanding family interactions.

CRAFT-FT is now termed CRAFT for early psychosis (CRAFT-EP). Participants will be randomized to treatment as usual or treatment as usual + CRAFT-EP to assess preliminary efficacy of the intervention. Given focus group feedback, we will have eight standard coaching sessions offered, with the option for one in-person visit when hospital policies allow for in-person care without masks. FEP clients will have the option to participate in one coaching session to communicate their needs or provide feedback to their family member if both parties are interested in a joint session. If the FEP client chooses to participate in a session without full participation in the larger study, they will be asked to complete a verbal consent after reviewing the Session Fact Sheet with research staff, who would document the verbal consent.

The sessions will be in person and/or virtual visits (video conferencing) and audio/video recorded. The audio/video recording will include identifiable information (e.g., face and potentially first names), but we will label the recordings with codes instead of names. We will store the recordings indefinitely, and they will not be erased. The audio recording will be sent securely to trained coders who will review sessions for therapist quality assurance and training purposes. At any time, subjects may request (verbally or in writing) to have their audio/video recordings erased.

Session notes may be documented as needed with:

Notes Template
CRAFT-EP Session Checklists:
    Session 1 Introduction and Self-Care

Session 2 Communication
Session 3 Functional Analysis
Session 4 Positive Reinforcement
Session 5 Treatment Engagement
Session 6 Natural Consequences
Session 7 Problem Solving
Session 8 Final Session

CRAFT-EP Worksheets that to be shared and potentially completed with subjects:

Happiness Scale
Communication Worksheet
Functional Analysis Worksheet (when conducting functional analysis exercise)
Positive Reinforcement Worksheet
Natural Consequences Worksheet
Problem Solving Worksheet
Next Steps Worksheet

CRAFT-EP informational handouts to be shared with subjects also include:

Program Outline
Milestone Conversations
Psychosis and Substance Use
Goal Setting Guidelines
Communication Guidelines
Communication Examples
Treatment Engagement
Problem Solving Guidelines
CRAFT-EP Resources**
Email Template

** CRAFT-EP Resources will also be offered to family members in the control condition and to interested client relatives at the conclusion of their study participation. Relevant resources from the CRAFT-EP Resources sheet may also be offered to potential participants who were deemed ineligible on the phone screen and/or the REDCAP eligibility prescreen survey.

Focus group (only family members)

We may conduct 1-2 in person or virtual focus groups with subjects who are available at a mutual time following each Part 1 and Part 2 of the pilot to validate proposed changes to the manual and collect feedback to inform further manual improvements. The Focus Group Questions and responses from the Satisfaction Survey and Session Surveys will be used to guide the semi-structured interview. The group may be audio/video recorded. Regarding confidentiality, subjects will be asked to not take screenshots, photographs, or recordings of any kind with any electronic equipment, refrain from using last names, and to keep information shared during the group confidential. The audio recordings may be sent securely to a MGB-approved transcription service in order to obtain research grade transcriptions for analysis.

Timing of Measures

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Follow-up: 30 minutes

Focus Group: 30-60 minutes

If virtual visit assessments are used, number of visits may vary to reduce participant burden and time on campus. If subjects have completed certain study procedures as part of another Schizophrenia and Bipolar Disorder Program study within the past 30 days (e.g., clinical interview,) or past year for the SCID-5, they may not be repeated to reduce participant burden. FREQUENCY: The Informed Consent Survey Family/Client, Demographic Form, SCID-5, DMQ-R**, MMM**, and MSS** may be assessed at baseline, the Debriefing Interview and Satisfaction Interview* may be assessed at the final session or post-intervention, the Focus Group Questions* may be assessed once any time after post-intervention for each subject, and the Functional Analysis* will be assessed once during intervention. The CEQ* may be assessed at baseline and post-intervention, the WAI may be assessed once at mid- intervention for Clients and session 2 and post- intervention for Families. The PANSS, MAP-SR, MADRS, YMRS, and substance use screening** may be assessed at baseline, mid-, and post-intervention. The PSS and the SRS may be assessed at baseline and post-intervention (and at follow-up for Families). The Session Survey may be assessed following each intervention session. Remaining measures may be collected at baseline and repeated mid-intervention (approximately week 4), and post-intervention (approximately week 8), and measures may be assessed via online survey or phone/virtually at 3-month follow-up.

Study intervention procedures will take approximately 60-90 minutes weekly for a total of 8 sessions in person and/or via virtual visits.

VI. Biostatistical Analysis

Interviews and questionnaires mentioned above are all variables that will be analyzed.

The study will be considered complete when 20 family member subjects and up to 20 FEP clients have completed the tasks outlined above for the development **phase 1**, and 40 family member subjects and up to 40 FEP clients have completed the tasks outlined above for the randomized controlled trial **phase 2** (we will enroll up to 148 total participants across phases 1 and 2 (74 family members and 74 FEP clients to account for potential attrition).

Phase 1 outcome measures for statistical analysis will include:

Primary

1. **Title:** Percentage of Sessions Completed
   Description: Percentage of sessions completed during the intervention
   Time Frame: Post-intervention, approximately Week 6-8

Secondary

2. **Title:** Mean Session Satisfaction Rating
   Description: Participants will report weekly satisfaction ratings following each session on the Session Survey. Ratings will range from 1 (poor) to 5 (excellent) for overall experience and convenience.
   Time Frame: Up to 8 weeks
3. **Title:** Percentage of Participant Preference for In-person, Telemedicine, or Both Session Formats
   Description: Percentage of participant preference for in-person, telemedicine, or both sessions formats as assessed categorically during the Treatment Satisfaction Interview.

Time Frame: Up to 8 weeks

Descriptive statistics will assess the preliminary feasibility with respect to participant satisfaction with the initial version of the CRAFT-F/FT protocol and session completion % at post-intervention. We will also review recorded interview/focus group data as qualitative feedback to inform a feasible revised protocol tailored to the unique needs of families with co-occurring substance use disorders and FEP. Following iterative feasibility testing of the revised protocol, we will again conduct descriptive statistics and collect feedback to confirm its feasibility. GLM and correlational analyses will be used to explore preliminary efficacy of the intervention and its relationship with sample characteristics.

Phase 2 Outcome measures for statistical analysis include:

Primary

Outcome 1

Title: Mean readiness to change substance use

Description: Mean readiness to cutdown/quit using [most problematic substance] for the client with psychosis using importance-confidence-readiness rulers (0 = not at all to 10 = extremely).

Time Frame: Baseline, mid-intervention (week 4), post-intervention (week 8)

Secondary

Outcome 2

Title: Percentage of Session Attendance

Description: Percentage of treatment sessions attended by the client with psychosis in past 30 days.

Time Frame: Baseline, mid-intervention (week 4), post-intervention (week 8)

Outcome 3

Title: Substance Use

Description: Client Timeline Follow Back (TLFB) past 30 day substance use, urine toxicology screen for drugs of abuse.

Time Frame: Baseline, mid-intervention (week 4), post-intervention (week 8)

Outcome 4

Title: Family Wellbeing: Depression

Description: Beck Depression Inventory-II total; scores range from 0 to 63 with higher scores representing more severe depressive symptoms.

Time Frame: Baseline, mid-intervention (week 4), post-intervention (week 8)

Outcome 5

Title: Family Wellbeing: Anxiety

Description: State-Trait Anxiety Inventory-Short Form; total scores range from 6 to 24 with higher scores representing more severe anxiety symptoms.

Time Frame: Baseline, mid-intervention (week 4), post-intervention (week 8)

Outcome 6

Title: Family Wellbeing: Relationship

Description: General Happiness item on Relationship Happiness Scale; scores range from 1 to 10 with higher scores representing greater relationship happiness.

Time Frame: Baseline, mid-intervention (week 4), post-intervention (week 8)

For the randomized controlled trial phase, repeated measures random regression analyses comparing the rate of change between groups (CRAFT-EP + TAU vs. TAU alone) for the primary analyses (treatment engagement: FEP client readiness to change substance use), as well as secondary analyses (treatment engagement % session attendance, substance use outcomes, and family wellbeing measures). We will use a model for the mean of the

outcome variable that includes terms for intervention, time, and the intervention-by-time interaction, and we will use generalized estimating equations to adjust standard errors for the correlation of observations within individuals. The coefficient for the intervention-by-time interaction term at after session 8 quantifies the difference between groups at session 8, adjusted for baseline. In separate analyses, we will use linear regression to explore the association between baseline predictor variables with treatment engagement, substance use, and family wellbeing outcomes. We will perform exploratory analyses of the 3-month follow-up time point and potential moderating effects of sex to inform the design of future studies.

Power. N/A

VII. Risks and Discomforts

One potential risk is a breach of confidentiality. This could lead a subject's employer, insurance company, or others to learn about their participation in the research study.

It is possible that some of the questions in the medical, personality or psychiatric assessments and tasks may cause subjects to become fatigued or emotionally upset and distressed, but this is unlikely and would be expected to be very mild should it occur. Subjects will be informed that they may take a break at any time or refuse to answer any questions that they wish. Study personnel will be trained to manage any distress that arises.

VIII. Potential Benefits

There are no known direct benefits to subjects. For participants assigned to the CRAFT-EP intervention, possible benefits may include gaining additional support and coping skills. Families with a history of psychosis and/or substance use may benefit in the future from what we learn in this study.

IX. Monitoring and Quality Assurance

The PI will have responsibility for continuous monitoring of data and safety of subjects in the study. Data and safety monitoring will take place continuously throughout the study during weekly study meetings, and we will review deviations and adverse events in monthly meetings. We will report both adverse events and all serious adverse events that occur during the study to the Partners IRB. We will provide the Partners IRB with a summary of any unexpected and related adverse events as well as any other unanticipated problems that occurred at the time during the annual continuing review.

Suicidality: If participants spontaneously report suicidality during the phone screen or study visit or if they endorse suicidality on an instrument (MADRS response 4 or 6 on item 10; SCID-5 response of 2 or 3 on A17 or affirmative response on OP9-OP12 and OP14; BDI-II response 2 or greater on item 9), research staff will implement the study suicidality standard operating procedures.

Domestic Violence: If participants spontaneously report a history of domestic violence with a member of their current household or if they endorse such a history on an instrument (phone screen domestic violence question affirmative response involving a member of their

current household, SCID-5 response L1-8 affirmative response with respect to domestic violence involving a member of their current household), research staff will implement the study domestic violence standard operating procedures.

All adverse events and unanticipated problems involving risks to subjects or others will be investigated by the PI and reported to the PHRC in accordance with the PHRC adverse event and unanticipated problems reporting guidelines.

The PI will ensure that the study adheres to the IRB-approved protocol and will frequently monitor the overall progress of the study.

X. References

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