Pilot Study of Motivational Interviewing for Loved Ones (MILO)

ClinicalTrials.gov number: NCT04010747
Protocol Version Number: 1
Protocol Version Date: 3 March 2021
NCT04010747
Funding Mechanism: NIMH K23 MH118373
Principal Investigator: Emily Kline
Phone: 412-298-8839 (cell)
E-mail: Emily.kline@bmc.org

Statistical Analysis Plan pages 15-17

TABLE OF CONTENTS

1 List of Abbreviations

Abbreviation	Abbreviation definition
MILO	Motivational Interviewing for Loved Ones
IP	Individual with Psychosis
PCSO	Parents and Concerned Significant Others

2 Protocol Summary

Title:	**Pilot Study of Motivational Interviewing for Loved Ones (MILO)**
Population:	Caregivers (age 18 or older) of individuals ages 15-35 experiencing early course psychotic disorders; N = 100
Intervention:	Motivational Interviewing for Loved Ones, "MILO" MILO consists of four 60-minute sessions of communication skills training delivered by a trained provider in person or via secure telehealth
Objectives:	Evaluate the effectiveness of MILO for (1) facilitating the engagement of IP with evidence-based treatments and (2) reducing distress among PCSO
Design/Methodology:	Participants will be randomly assigned to either receive MILO (50%) or the waitlist condition (50%) as a partial cross-over design.
Total Study Duration:	3/1/21-7/31/23
Subject Participation Duration:	Four to six months, depending on whether participant is assigned to immediate intervention vs. waitlist condition as well as the pace

3 Background/Rationale & Purpose

3.1 Background Information

First Episode Psychosis (FEP) often represents a time of crisis for young people and their families. Since peak onset occurs during late adolescence and early adulthood, the onset of serious mental health challenges can disrupt plans for education, relationships, and other milestones of independence. Although some psychoses are brief and self-limiting, more often these symptoms portend a potentially chronic and disabling psychiatric disorder such as schizophrenia. FEP can also be acutely dangerous: youth with FEP are far more likely to die in the year following their diagnosis relative to the general population of 16-30-year old's in the United States. Approximately 100,000 youth in the United States experience FEP every year. Young people identified by providers as experiencing FEP often slip through the cracks before they reach appropriate treatment. A review of privately insured adolescents and young adults in the US showed that 62% of young people in the US with FEP filled no outpatient prescriptions, and 41% received no outpatient psychotherapy, in the year following their index diagnosis. Among those who do have an initial encounter with specialized FEP outpatient care, high

attrition is a common problem, with 30% of individuals initially enrolled in first episode programs dropping out prior to completing treatment.

Many individuals experiencing psychosis are reluctant to seek mental health treatment due to lack of insight and fear of psychiatric interventions. Young adults may be torn between distress and dissatisfaction relating to their symptoms and functioning, and mistrust of mental health providers and irritation with their parents' concern. Motivational Interviewing (MI) techniques are designed to elicit this ambivalence through nonjudgmental listening, so that discrepancies between current behaviors and ideal outcomes can be explored. Clinician-delivered MI has been identified as effective for enhancing adherence once individuals with psychosis are involved in care, and MI may also be useful for engaging those who are not yet interested in treatment. Several studies have found positive results in training and deploying non-professionals to use MI to influence others' health behaviors. MI training for parents and concerned significant others (PCSO) is a promising venue through which PCSO can specifically influence their loved one's decision to seek care and adhere to treatment plans.

The PI (Dr. Kline) has developed a brief 4-5 session training course for caregivers called "motivational interviewing for loved ones" (MILO). Each training session lasts 45-60 minutes and consists of teaching the participant an MI based communication skill, reviewing previously discussed skills, or offering referral information for treatment for their IP. The training can be done in-person or virtually. In a feasibility focused pilot, the intervention was found to be highly valued by participants, with 94% of consented participants completing at least three sessions. This application represents the continuation of a pilot efficacy trial that was initiated at Beth Israel Deaconess Medical Center and which the PI would like to continue at Boston Medical Center.

This study will be conducted in compliance with the protocol, applicable regulatory requirements, and BMC/BU Medical Campus Human Research Protection policies and procedures.

3.2 Rationale and Purpose

MILO aims to address the critical problem of delayed treatment and under-treatment in early course psychosis by offering a motivational interviewing (MI) based skills intervention for parents or other concerned significant others (PCSO) of individuals with psychosis (IP) who refuse treatment. This intervention will offer psychoeducation and concrete skills for communicating with the IP about the potential benefits of seeking care. The primary aim of the intervention is to increase the likelihood of IP engaging with evidence-based treatment. Secondary outcomes include reductions in PCSO distress and increases in PCSO well-being.

4 Objectives

4.1 Study Objectives

The initial aim of this pilot study is to evaluate feasibility of the intervention. The secondary aims are to evaluate the effectiveness of MILO for (a) facilitating the engagement of IP with evidence-based treatments and (b) reducing distress among PCSO. We hypothesize that the intervention

will be superior to control condition for both enhancing IP engagement with mental health services and reducing PCSO distress.

4.2 Study Outcome Measures

4.2.1 Primary Outcome Measures

Feasibility will be analyzed using the following descriptive metrics: # participants screened; # Eligible; # Enrolled; # not enrolled and corresponding reasoning; # Meeting DSM-5 Adjustment Disorder criteria; Percentage of study sessions completed; study Satisfaction; % assessments completed; Duration of assessments. A demographics questionnaire, a clinician-administered assessment containing information relevant to the DSM-5 diagnosis of adjustment disorder, and the Client Satisfaction Questionnaire will be used.

4.2.2 Secondary Outcome Measures

Measurement of secondary outcomes will occur using the instruments in the table below.

Measure	Study Objective	Time Point
Absolute Worth and Autonomy Scale	Aim 2b: Reducing distress among PCSO	Baseline, Waitlist Condition, Post Intervention, 8 Week FU, 12 Week FU
Perceived Stress Scale	Aim 2b: Reducing distress among PCSO	Baseline, Waitlist Condition, Post Intervention, 8 Week FU, 12 Week FU
Conflict Behavior Questionnaire	Aim 2b: Reducing distress among PCSO	Baseline, Waitlist Condition, Post Intervention, 8 Week FU, 12 Week FU
SCORE-15 Index of Family Functioning	Aim 2b: Reducing distress among PCSO	Baseline, Waitlist Condition, Post Intervention, 8 Week FU, 12 Week FU
Parenting Self Agency	Aim 2b: Reducing distress among PCSO	Baseline, Waitlist Condition, Post Intervention, 8 Week FU, 12 Week FU
Family Questionnaire	Aim 2b: Reducing distress among PCSO	Baseline, Waitlist Condition, Post Intervention, 8 Week FU, 12 Week FU
Motivational Interviewing Skills Questions	Aim 2a: Feasibility	Baseline, Post- Intervention
Mental Health Service Use History	Aim 2a: Facilitating engagement of IP in treatment	Baseline
Past Month Service Use History	Aim 2a: Facilitating engagement of IP in treatment	Baseline, Waitlist Condition, Post Intervention, 8 Week FU, 12 Week FU
Change Questionnaire	Aim 2b: Reducing distress among PCSO	Post Intervention, 12 Week FU

10 Minute Audio Recorded Role Play	Aim 2a: Feasibility	Baseline, Waitlist Condition, Post Intervention

5 Study Design

The study population is parents and concerned significant others (PCSO) of individuals experiencing psychosis (IP) who are not currently engaged with treatment. The IP has to have a recent onset of psychosis within the past 5 years. MILO is a structured brief intervention that seeks to accomplish two aims. The primary aim is to facilitate the engagement of IP with evidence-based treatments. The secondary aim is to reduce the distress and increase the wellbeing of PCSO. The intervention will be trialed for feasibility and then tested against a small waitlist condition control arm. Participants will be randomly assigned to either receive MILO (50%) or the waitlist condition (50%) in a cross over design.

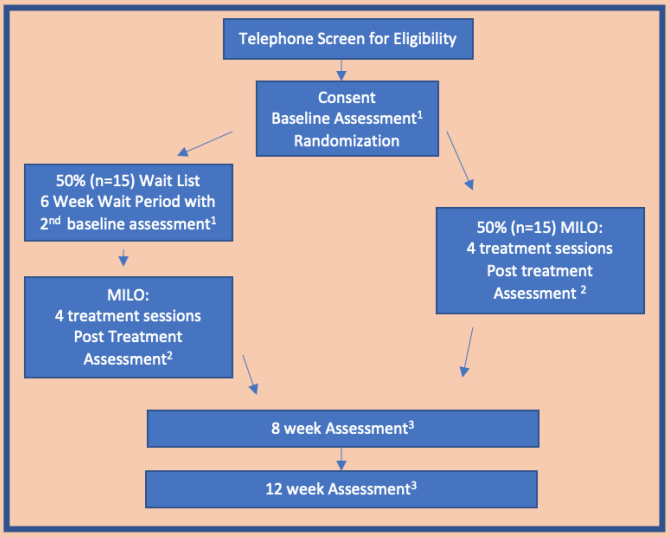
The study is designed to minimize participant burden. Concerns about the ethics of randomization are allayed by the fact MILO is untested (effectiveness is not proven), and that the control condition represents treatment as usual. Thus the risk benefit ratio, even for those assigned to "treatment as usual/waitlist", is favorable given that typically no particular assistance is offered in the community for parents/significant others attempting to connect their loved one with care. Phase 1 of the study was completed at its initial site at Beth Israel Deaconess Medical Center. Phase 2 was also started at the previous sight and will be completed at Boston Medical Center.

We will be collecting data through REDCap surveys administered via email link to the participants. Those assigned to the MILO treatment condition will be assessed at 4 time points (study entry, post intervention, 8 week follow up, 12 week follow up). Those in the waitlist condition will be assessed at 5 time points (study entry, end of waitlist, post intervention, 8 week follow up, 12 week follow up). Please see the following measures:

- Participants Contact Information
- Demographics questionnaire
- SCID-5 Adjustment disorder module
- Absolute Worth and Autonomy Scale
- Perceived Stress Scale
- Conflict Behavior Questionnaire
- SCORE-15 Index of Family Functioning
- Parenting Self-Agency
- Family Questionnaire
- Motivational Interviewing Skills Questions
- Mental Health Service Use History & Past month Service Use History Forms
- Modified Client Satisfaction Questionnaire
- Change Questionnaire

- 10-minute audio-recorded standardized patient role play (at study entry and post-intervention and waitlist time points only; role-plays will be scored using the Motivational Interviewing for Loved Ones Skills Assessment.

Figure 1. "Phase 2" Study Consort



[1]Contact information, Demographics, Perceived Stress Scale, Conflict Behavior Questionnaire, Score 15 Functioning, Parenting Self- Agency, Family Questionnaire, Absolute Worth and Autonomy Scale, Motivational Interviewing Quiz, Service Use History, Past Month Service Use, MI Role Play
[2]Percieved Stress Scale, Conflict Behavior Questionnaire, Score 15 Functioning, Parenting Self-Agency, Family Questionnaire, Absolute Worth and Autonomy Scale, Motivational Interviewing Quiz, Past Month Service Use, Client Satisfaction Questionnaire, MI Role Play
[3]Percieved Stress Scale, Conflict Behavior Questionnaire, Score 15 Functioning, Parenting Self-Agency, Family Questionnaire, Absolute Worth and Autonomy Scale, Past Month Service Use

6 Potential Risks and Benefits

6.1 Risks

Potential risks to PCSO participating in MILO include: 1) There is a potential risk that confidential health information collected during the course of the study may be disclosed to others. 2) Participating PCSO may at times feel inconvenienced by the time required to complete the sessions and/or research assessments. 3) Participants may experience frustration or anxiety in learning to use the motivational interviewing communication skills. They may experience sadness or discomfort when discussing personal problems or in interacting with a family member. Discussing or experiencing the IP's psychiatric problems may be upsetting to the family. 4) There is a potential risk that participants will be subjected to stigma or undue anxiety from identification with the study. 5) The individuals with psychosis will be discussed in detail during study sessions. These individuals might find it distressing to know that their circumstances are the topic of their loved ones' research participation.

The PI and study staff will take the following steps to protect against risks:

1) Confidentiality will be maintained by assigning each participant a study number, and coding all data collected with that number. Identifying information and study data will be stored separately on secure BMC servers. To protect the confidentiality of the IP being discussed, his/her name will not be written down anywhere. All computer databases will be password protected, and hard copies of all data and records will be stored in locked filing cabinets. All study personnel will be certified to conduct research with human subjects and will be aware of the importance of maintaining strict confidentiality. Audio recordings of participants will be saved in digital files on a secure BMC server. Audio files will be destroyed at the conclusion of the study unless explicit consent to use audio files (e.g. for training purposes) is obtained from participants.

2) The assessment battery has been designed to minimize participant burden.

3) The study PI is a very experienced clinician and will provide ongoing supervision to each individual working on the protocol to ensure that they are equipped to provide appropriate support when necessary and to recognize signs of distress and discomfort. It is not expected that participants will feel any more sadness or discomfort talking about personal problems or interacting with a family member than they would at home or if they took part in psychotherapy in the community. If participants or family members experience frustration or distress, the PI, will offer participants emotional support and validation. She will also offer strategies for managing the situation and accompanying emotional responses. Participants will also be informed that they can receive and follow-up on outside referrals for counseling outside of the study at any time without being dropped from the protocol.

4) The PI will review each participant carefully with study staff. Study participants who are judged by the PI to be in need of additional psychiatric or psychological evaluation/treatment or medical consultation will be referred as clinically indicated. This includes endorsement of self-harm and suicidality which will be addressed immediately. The participants will be frequently asked whether they desire additional referral or consultation for their own or their loved one's safety. If imminent danger is reported, participants will develop a safety plan with Dr. Emily Kline as described below.

5) The PI will meet with stuff staff and clinicians at least weekly for supervision. Staff will be trained to recognize signs of distress (for instance, hopeless statements) and will report to the PI both the content of interactions with participants as well as any concerns about their mood or concerning statements. If needed, study staff will provide crisis intervention, recommendations or referrals for adjunctive medical/pharmacological interventions, and when necessary, referral to emergency or inpatient treatment facilities. The PI will closely supervise or personally provide any crisis intervention. Staff will seek written release to coordinate care with other mental health providers prior to the start of treatment to avoid need for acute care when increased outpatient supports may be sufficiently garnered. Participants will be told they may decline to answer any questions or participate in any component. Staff will make the study assessments and MILO sessions as pleasant as possible by developing rapport and going at an appropriate pace so that participants do not become frustrated.
6) The PI does not believe this study poses significant risks to participants and does not anticipate any serious adverse events as a result of the study. However, first episode psychosis is associated with increased mortality in the community. Any safety concerns

relating to either the PCSO's or IP's wellbeing will be carefully discussed with the participant. Whenever reason for concern arises, the PI or other licensed clinician will evaluate safety risks and create a plan in collaboration with the participating PCSO to address such risk. This could involve calling 911 in cases of imminent safety threats. There is no reason to suspect that rates of illness complications will be higher if the parents or significant others of IP participate in the study.

7) Risks to subjects will be closely monitored as described in Section 6.1. Adverse events will be documented and reported per BMC/BUMC HRPP policies. Any event or set of events meeting the definition of Unanticipated Problem (UP) will be reported in an expedited timeframe (within 7 days) of the study team learning of the UP.
8) Staff will maintain regular contact with the IRB regarding study protocol, consents, recruitment materials, and human subject protection plan.

6.2 Potential Benefits

If it is effective, the intervention has tremendous upside to both participants and their loved ones with psychosis. The goals of the intervention are to shorten DUP, increase service utilization by the IP, and reduce caregiver distress. These parents and other loved ones are often desperate to seek help on behalf of the IP. Learning MI skills may benefit participants by reducing their stress, helping them to feel more confident in their caregiving role, and giving them information about how they can better facilitate the IP's connection or adherence to treatment.

Those randomized to the waitlist will be offered a 30-minute consultation during which the PCSO is provided with information about treatment options (e.g., community mental health and FEP coordinated specialty care programs) and contact information for an active NAMI chapter in in his/her area. This will be done in person or by telephone. This consultation represents the minimum standard of care for caregivers of individuals with recent-onset psychosis being treated at BMC. Additionally, waitlist participants will have the opportunity to receive MILO training after a six-week wait.

Concerns about the ethics of randomization are allayed by the fact MILO is untested (effectiveness is not proven), and that waitlisted participants will also be offered the MILO intervention after a short waiting period.

6.3 Analysis of Risks in Relation to Benefits

This study will be of minimal risk to participants. There is a relatively low risk of harm to individuals receiving family therapies. Prior studies of family therapies with this and similar populations have demonstrated tolerability and efficacy. There are no physical risks of participating in this study and the study is not expected to be harmful or dangerous in any way. There are no manipulations of drug treatments. Pharmacotherapy is not required and if participants opt for it, they will be referred to appropriate providers. Thus the risk benefit ratio, even for those assigned to "waitlist", is favorable.

7 Study Subject Selection

7.1 Subject Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

- PCSO is 18 years or older
- PCSO is able to communicate in English
- PCSO is a primary care giver or an individual who has ≥20 hours weekly contact with an IP
- PCSO is able to provide informed consent by demonstrating that they understand the aims and structure of the study

Although the individual with psychosis will not participate in MILO, study staff will establish via the participating PCSO that the individual with psychosis is:

- Aged 15-35
- Has been diagnosed with a DSM-5 psychotic disorder by a health professional, OR has clearly observable (by the PCSO) symptoms/behaviors indicating psychosis
- Experienced onset of observed symptoms or first psychosis diagnosis occurred within past five years
- Is not optimally engaged in outpatient treatment

Identifiable information about the individual with psychosis is not kept in study records. The information gathered about the IP is based on participants' reporting and perceptions.

Subject Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study:

- Current mental health crisis: if study staff determine that the potential participant is in serious emotional distress during the eligibility determination and consent process, staff will consult with the PI to determine whether the participant should be referred to psychiatric care to address their distress prior to participating in MILO

8 Study Intervention

The active intervention includes four to five 45-60 minute sessions. Sessions will be conducted individually with the clinician, or if two or more PCSO (e.g., parents) wish to participate together, they will meet at the same time with the clinician. The first two sessions will focus primarily on teaching through concept review, demonstration, and role play. In the third and fourth sessions, the clinician will learn about PCSOs' efforts to initiate a conversation about treatment with the IP using, and will provide feedback, problem-solving, and encouragement regarding the PCSO's

efforts. A fifth session may be offered upon request to provide additional coaching, consultation, and psychoeducation relevant to MILO topics. See Table 1 for details about session content.

Session	Content
1	Participants talk with a study clinician about the IP's illness history and how the experience has impacted them and their family. Treatment and psychoeducational resources are offered (e.g. NAMI support groups). Study staff teach participants about the philosophy of motivational interviewing and the potential value of listening and asking questions instead of giving advice or solving the problem.
2-3	Study staff teach participants core MILO communication skills (reflections, questions, asking permission before offering advice) and practice the skills during the session.
4-5 (5th session optional depending on participants' preference)	Participants review their attempts to use MILO skills with the IP and receive feedback and encouragement from MILO clinicians. Participants have the opportunity to role play with the clinician to obtain additional practice.

The waitlist condition offers a one-time consultation session to participants while they are on a 6-week waitlist condition to receive MILO sessions. This involves a 30 minute consultation with a clinician experienced psychosis treatment with the goal of providing some psychoeducational resources. These resources include links to NAMI handouts, a directory of psychosis early intervention clinics, and information about psychiatric emergency services. This is similar to content addressed the first half of session 1 of MILO. Participants may decline this consultation and wait for the MILO intervention instead.

9 Study Procedures

See the Appendix for the schedule of events.

Event	Protocol
Contact	Potential participant contacts study staff via email or phone communication. This is a dedicated study phone number. Study staff schedule a 10 minute phone call with potential participant to review study details and complete pre-screen.
Pre-Screen	Study Staff confirm that potential participant is interested in learning more, reads the Consent to Phone Screen, asks eligibility criteria questions
Eligibility Determination	Study staff review the answers to the eligibility questions, if any answer is unknown or needs clinical input, study staff contacts the Principal

	Investigator. If contact is ineligible, they are told why and given other resources to consider.
Consent	If potential participant is eligible, they are offered a time to review the study consent with study staff. Once study details have been reviewed and study staff have made sure participants have no lasting questions, then study staff send the REDCap consent link to the participants. Participants are given study staff contact information if they have any more questions before signing the document via REDCap. If participants do not have access to necessary technology to complete a remote consent, they will be invited to Dr. Emily Kline's office. All in person operations will follow BMC's COVID procedures.
Baseline Assessments	Participants are sent a REDCap survey link after consent is complete via email and asked to schedule a 15 minute phone call with study staff to complete their baseline real play assessment
Randomization	Once baseline assessments are complete, study staff randomize participant into MILO or waitlist condition.
IF Waitlist Condition	Participants randomized to waitlist condition, are emailed the date that their waitlist period ends and offered a 30 minute treatment consultation with one of the MILO trainers before the 6 week waitlist period is complete. This treatment consultation can be completed over the phone, over a BMC Zoom, or in person at Dr. Emily Kline's office. All in person visits will follow BMC's COVID procedures. At the end of the waitlist period, they are sent REDCap surveys and asked to complete another real play assessment over the phone (first done at baseline).
MILO Treatment	Participants randomized to immediate MILO, as well as those who have already finished the waitlist period, are scheduled for their first MILO training session. Sessions are offered via a secure telehealth platform, HIPAA compliant Zoom or in person if the participant does not have access to appropriate technology. All in person operations will follow BMC's COVID procedures. Sessions are 45-60 minutes and participants are offered 4-5 sessions. All sessions are conducted by trained study staff. Study staff receive weekly individual supervision from the PI.

	Study staff utilize detailed guides to ensure high fidelity to the MILO intervention. Details of the intervention are described in the table above in section 8.
Post-Intervention Assessments	Once participants have completed MILO intervention, they are emailed their post-intervention REDCap survey and asked to schedule their last real play audio recorded exercise over the phone.
8 Week Follow Up	Participants are emailed a REDCap survey 8 weeks after their last MILO session.
12 Week Follow Up	Participants are emailed their last REDCap survey 12 weeks after their last MILO session.

9.1 Definitions

The following definitions will be used in the assessment of safety:

Adverse Event (AE) is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

Serious Adverse Event (SAE) is any adverse event that

(1) Invasion of privacy
(2) Breach in confidentiality
(3) Breach in the protection of participant data
(4) Any abnormal or harmful behaviors

Unanticipated Problem is defined as an event, experience or outcome that meets **all three** of the following criteria:

- is unexpected; AND
- is related or possibly related to participation in the research; AND
- suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research

Unexpected means the nature, severity, or frequency of the event is not consistent with either:

- the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol–related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or

- the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

9.2 Safety Review

Both the risks listed in Section 4.1 and unknown risks will be monitored as follows:
Study staff who are meeting with participants will participate in weekly supervision with the PI. Staff are trained to identify signs of acute participants' distress and potential suicidality. Via direct observation or supervision, the PI will monitor participant distress and clinical state and address concerns at the time they are raised or observed. Any and all adverse events will be reported to the IRB. Any adverse events will be evaluated by the PI who is a licensed PHD psychologist in accordance to IRB requirements and changes will be made to the protocol to prevent future adverse events if deemed necessary by research staff and/or the IRB. The PI will seek consultation from the IRB and/or her department chair Dr. Henderson if she has any question about whether to report an event to the IRB immediately or during annual review.

9.3 Reporting Plans

The Principal Investigator at BMC/BU Medical Campus will report Unanticipated Problems, safety monitors' reports, and Adverse Events to the BMC/BU Medical Center IRB in accordance with IRB policies:

- Unanticipated Problems occurring at BMC/BU Medical Campus will be reported to the IRB within 7 days of the investigator learning of the event.
- Reports from safety monitors with recommended changes will be reported to the IRB within 7 days of the investigator receiving the report.
- Adverse Events (including Serious Adverse Events) will be reported in summary at the time of continuing review, along with a statement that the pattern of adverse events, in total, does not suggest that the research places subjects or others at a greater risk of harm than was previously known.
- Reports from safety monitors with no recommended changes will be reported to the IRB at the time of continuing review.

9.4 Stopping Rules

A subject will be withdrawn from the study if adverse event(s) occur that per the PI's judgment require subject withdrawal. Examples would be a participant who endorses suicidal ideation or reports a violent altercation with the IP.

There are no specified stopping rules.

10 Data Handling and Record Keeping

10.1 Confidentiality

Confidentiality will be maintained by assigning each participant a study number, and coding all data collected with that number. Identifying information will be saved separately from study data. To protect the confidentiality of the IP being discussed, his/her name will not be written down anywhere. Databases containing both PHI and non-PHI study data will be stored on securely on the BMC Network and REDCap. Any papers containing study notes or participant information will be stored in locked filing cabinets in the PI's BMC office. All study personnel will stay updated on CITI-based human subjects' research training and will be aware of the importance of maintaining strict confidentiality and data security. Audio recordings of participants will be saved in digital files on a secure BMC server. Transcriptions of audio files will be performed by BMC research staff and stored on secure BMC servers. Audio files will be destroyed at the conclusion of the study unless explicit consent to use audio files (e.g. for training purposes) is obtained from participants during the informed consent process.

Study monitors or other authorized representatives of the sponsor (i.e. NIMH) may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the subjects in this study. The clinical study site will permit access to such records.

The study is registered and regularly updated on clinical trials.gov, NCT04010747.

10.2 Source Documents

Source data and source documents will be stored on BMC secure servers. They include study team administrative notes, study clinician notes and progress checklists, recorded data from automated instruments including REDCap, audio files and audio transcription documents. Data generated by the methods described in the protocol will be recorded in the subjects' study progress notes.

10.3 Case Report Forms

CRFs will not be used for this study. All data will be saved in REDCap, most of which will be inputted by participants themselves.

10.4 Study Records Retention

All records will be saved on BMC's secure servers electronically and retained at least seven years after completion of the study. At the completion of the study, any paper notes will be scanned and uploaded as electronic documents to the BMC server. Within the informed consent process, participants indicate whether their audio recordings can be used for research and teaching purposes. Examples on how they may be used include during training new study staff on the measure or used as an example during a research presentation. Audio recordings of participants who say that their recordings can be used will be retained and others will be deleted at the end of the study. Any identifying information disclosed within the audio files will be removed by editing, the files themselves are de-identified.

11 Statistical Plan

11.1 Study Hypotheses

1. The MILO intervention will be feasible and acceptable for participants.

2. The MILO intervention will impact outcomes of interest (e.g., proficiency using MILO skills, confidence, stress, caregiving attitudes, and caregiver-reported IP treatment engagement).

3. Participants attending MILO sessions will show more improvement with regard to outcomes of interest within the first six weeks of study participation relative to those on the waitlist.

4. After attending MILO sessions, waitlisted participants will "catch up" to those randomized to receive the intervention immediately with regard to changes on outcomes of interest.

5. Gains in MI proficiency as demonstrated via scored audio recordings will mediate the impact of the intervention on other outcomes such as reduced conflict and stress and increased confidence and caregiver-reported IP treatment engagement.

11.2 Sample Size Determination

The overall target for recruitment is 100 participants. 52 participants will be recruited for the protocol once approved by BMC (48 participants were recruited at Beth Israel Deaconess Medical Center which was the original recipient of the K23 funding support). This study is a pilot intended to test feasibility and preliminary effectiveness of the MILO intervention. Although true "pilot" studies focus an on intervention's feasibility, rather than effects per se, the current study reflects a two-phase hybrid of priorities balancing the need to focus on feasibility while also investigating whether the intervention impacts the hypothesized treatment targets (MI skills, self-efficacy) and whether it is more effective in achieving the primary outcome (IP engagement in FEP treatment) than a control condition representing "treatment as usual" and a waiting period. The control group will be small relative to the active treatment group, thus maximizing the feasibility-focused sample. Thus the study may be somewhat underpowered to detect statistically significant effects, but has been designed to yield high quality feasibility metrics, highlight important factors for implementation, and provide a rough estimate of effect size that will inform a later, fully powered RCT.

11.3 Statistical Methods

Feasibility will be analyzed using the following descriptive metrics: # participants screened; # Eligible; # Enrolled; # not enrolled and corresponding reasoning # Meeting DSM-5 Adjustment Disorder criteria; Percentage of Treatment sessions completed; Treatment Satisfaction; % assessments completed; Duration of assessments.

The outcomes of interest will be compared between the intervention and waitlist groups, and also within the waitlist group (comparing the pre-post intervention changes to the pre-post waitlist time changes. Prevalence of IP treatment seeking in each group will also be analyzed via odds ratios. Secondary outcomes, i.e. changes in PCSO distress and quality of life, will be

assessed via repeated measures ANOVAs examining group-by-time changes. Similarly, hypothesized mediators of effects (MI skill proficiency and self-efficacy) will be examined via repeated measures ANOVAs examining group-by-time changes. Analyses will be conducted using SPSS software.

12 Ethics/Protection of Human Subjects

This study is to be conducted according to applicable US federal regulations and institutional policies (which are based in federal regulations, guidance, and ICH Good Clinical Practice guidelines).

This protocol and any amendments will be submitted to the Boston Medical Center and Boston University Medical Campus IRB, for formal approval of the study conduct. The decision of the IRB concerning the conduct of the study will be made in writing to the investigator. A copy of the initial IRB approval letter will be provided to the sponsor before commencement of this study.

All subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. The consent form will be submitted with the protocol for review and approval by the IRB. The consent of a subject, using the IRB-approved consent form, must be obtained before that subject is submitted to any study procedure. Consent will be documented as required by the IRB.

13 Literature References

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