Integrated Cognitive Behavior Therapy to Improve Work Outcomes in Schizophrenia

NCT01992913

May 14, 2017

A. **Protocol Title**
1. Integrated Cognitive Behavior Therapy to Improve Work Outcomes in Schizophrenia (Short Name: BEST Vet – Building Employment Skills through Therapy for Veterans)

2. **Date of Protocol Summary and Version #:** Date 05/04/2017; Version # 17

B. **Principal Investigator's Full Name and Degree:** Steven Sayers, Ph.D.

C. **Co-Investigator's Full Name and Degree**: Paul Grant, Ph.D.

D. **Financial Sponsor** (Provide the name of the agency, organization, company or person providing funds for the research study.) **VA Rehabilitation R&D**

E. **Grant** (Provide the name of individual who holds the grant and the grant number, if applicable.) **Steven L. Sayers, Ph.D., grant number D1157-R**

F. **Protocol Number** (Provide the financial sponsor's protocol number, if applicable.) **D1157-R**

G. **Institution(s) responsible for the project:**
1. For single-site studies - CMCVAMC is the only institution involved. Yes ☒ No ☐
2. For multi-center studies.
2.1. CMCVAMC is the Coordinating Center in which the PI is the lead investigator. Yes ☐ No ☐ N/A ☒
2.2. Provide the name of the Coordinating Center. Yes ☐ No ☐ N/A ☒
2.3. List the name of the other sites involved. **Not Applicable.**
2.4. Provide the FWA numbers for each of the other sites involved. **Not Applicable.**

THE FOLLOWING INFORMATION MUST BE CMCVAMC-SPECIFIC, THAT IS, SPECIFIC TO WHAT WILL BE DONE WITH CMCVAMC-RECRUITED VETERANS.

H. **Background and Significance** (Describe succinctly and clearly the past findings which justify the plan for this project. A summary of the relevant literature in the area of interest and reports of previous studies should be included.)**:** **[1]Between two and three million American adults currently suffer from schizophrenia.[2] The modal onset occurs in early adulthood, and roughly two-thirds of affected individuals experience a chronic or fluctuating course of illness.[3] This latter group is amongst the most expensive receiving psychiatric services, with the overall direct treatment costs and indirect costs incurred due to unemployment and lost productivity approaching $63 billion in the United States.[1] Although antipsychotic medications have been readily available for more than half a century, the impact of these agents on functional outcomes has been modest, even when medication regimes have been optimized.[4] By contrast, psychiatric rehabilitation programs have been shown to improve psychosocial functioning.[5] Vocational rehabilitation services, in particular supported employment (SE), have the best evidence base. As compared to those patients not participating in such services, patients successfully engaged in SE are more likely to be working competitive jobs, working full time, earning higher wages, and reporting a higher quality of life.[6] Furthermore, steady employment has been shown to generate significant savings in the use of mental health services use compared to patients who are minimally employed.[7] Given the impressive benefits of SE programs, it is disappointing that so few eligible patients agree to participate in them. Patients who do not engage in treatment achieve the poorest outcomes,[8] have the lowest quality of life, and are at risk for symptom exacerbation, recurring hospitalization, persistent homelessness, violence toward others, and suicide.[9] Indeed, "providing appealing**

and effective treatment to those who could derive benefit but who choose to avoid treatment remains an ongoing challenge"[9] in schizophrenia.

Our group has responded to this challenge by developing a new integrated Cognitive Behavior Therapy (iCBT) protocol designed for low functioning patients with schizophrenia who are not participating in psychiatric rehabilitation services such as SE. It is pragmatic, multimodal, recovery-oriented, and extends to some of the most challenging patients (e.g., those with the predominant negative symptoms and/or low insight). Our recent article in the *Archives of General Psychiatry* demonstrates that this approach is efficacious at improving functional outcomes and increasing motivation relative to standard treatment when delivered by PhD therapists in a university setting.[10] The current proposal aims to compare usual care to iCBT to see if there are differences in their ability to improve work outcomes achieved by VA patients with schizophrenia enrolled in SE. Not being enrolled in SE or being enrolled but not active both produce little benefit. The goal of adding iCBT or usual care is to increase the patients' motivation to achieve their own recovery goals and direct their own engagement in constructive activity such as utilization of SE.

I. **Purpose of the Project** (Clearly provide the purpose of this research project.)**: The objective of the current proposal is to improve work outcomes and functional outcomes of veterans with functional disability who are not participating in psychiatric rehabilitation services that are available to them.**

J. **Describe the Research Questions or Hypotheses** (that is, what questions are you trying to address by conducting the research.)**: The objective of the current proposal is to evaluate whether iCBT vs. treatment as usual can improve engagement and success in an existing SE program among the most functionally disabled patients with schizophrenia.**

K. **Primary Outcome Variable(s)** (Define the primary outcome variable(s) used to support the study objectives (e.g. if the objective is to show that treatment A is superior to treatment B in the treatment of subjects with essential hypertension, the primary outcome variable is blood pressure measurement.)**: Our *primary specific aim* is to determine whether iCBT will significantly improve work outcomes at post-treatment to a greater extent than usual care in low functioning patients with schizophrenia who are enrolled in SE. The primary outcome measures are several work-related indices of work participation across the 18 months of active study involvement, including the following: 1) instances of job attainment, 2) average days worked per week while employed, 3) average number of hours worked per week while employed, 3) total weeks worked , and 4) a composite of these indices.**

L. **Secondary Outcome Variable(s)** (Define the secondary outcome variables. Such measured variables should also include the timing of measurement.)**: The second trial outcome measures will include the Work behavior Inventory (WBI) and the Specific Levels of Functioning Scale (SLOF). A significant ITT difference on the WBI and the total SLOF score across 6 and 12 months would support the hypothesis that ICBT is more efficacious than usual care at improving functioning by the end of treatment (Secondary Aim 1). Similarly, WBI score and the SLOF total score at 18 months is a secondary outcome, and the separate ITT effects on functioning at 18 months with the respective month-treatment interaction in favor of iCBT would support the hypothesis that it promotes better functioning than usual care during the 6 months after the completion of treatment (Secondary Aim 3).**

M. **Study Design and Methods:**

1. Is this a clinical trial? ☐YES ☒NO (Randomized non-drug/non-medical device intervention)
   - 1.1. If yes, what type? Check all that apply.
     ☐ **Phase I** ☐ **Phase II** ☐ **Phase III** ☐ **Phase IV**
   - 1.2. If yes, this study must be registered on Clinicaltrials.gov.

2. **Design**

2.1. What research methods will be used in the project? Check all that apply.

☒ Surveys/Questionnaires	☒ Interviews	☐ Audio Taping
☒ Behavioral Observations	☒ Chart Reviews	☒ Video Taping
☐ Focus Groups	☒ Randomization	☐ Double-Blind
☒ Control Group	☐ Placebo	☐ Withhold/Delay Treatment
☐ Specimen Collection	☐ Deception	☐ Telephone Survey
☐ Other (Describe)		

2.2. Describe how randomization or other treatment assignment will be made. **Randomization will occur on a 1:1 basis to one of the two study conditions (iCBT or usual care) using a permuted block randomization with randomly varying block sizes of 2, 4 and 6 and stratification by gender (because females with schizophrenia have a better course and may respond better to traditional CBT). The study biostatistician will generate randomization lists based on the above procedure. The encrypted randomization file will be located on a server (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work) that is not accessible to the study personnel who make subject contact during the randomization procedure. S/He will access the file and provide the randomization token. S/He will not have subject contact nor know which condition is being assigned. Further, s/he does not have a stake in the outcome of the study.**

2.3. For retrospective research studies, provide the "look-back" period. (e.g., December 1, 1999 through December 31, 2008.) **Not Applicable.**

3. **Study Duration**

3.1. Provide the estimated length of time to enroll all subjects and complete the study. **To allow that not all identified patients will qualify and not all qualifying patients will elect to participate, we will conduct more baseline screenings than required. We propose, accordingly, to consent to the baseline assessment 48 patients in the first year of the study (months 6 to 12), 96 patients in the second year (months 13 to 24), and 48 patients in the third year (months 25 to 30), producing 24 randomized patients in year 1, 48 in year 2, and 24 in year 3, for an estimated total of 96 randomized subjects (48 per group). All 96 subjects will be randomized by middle of the third year. Data collection will be complete after the middle of the fourth year.**

3.2. Explain the expected duration of subject participation including any follow-up. **iCBT will be delivered as a group therapy for 12 months of weekly or biweekly sessions (see below). Usual care (and iCBT) will entail continued access to all treatments available to all Veterans receiving treatment at the CMC VAMC Mental Health Clinical without restriction. Blind, reliable independent assessors, who are part of the study team, will reassess participants every 6 months after participants begin treatment over an 18-month participation period, producing mid-treatment (6 month) end-of-treatment (12 month), and post-treatment (18 month) assessments.**

3.3. Specify the projected date of completion of the proposed study. **We plan to complete the study at the end of fiscal year 2018.**

4. **Drug Information** (If not applicable state, "Not Applicable.") **Not Applicable.**

4.1. Specify if the drug or biological agent is:

4.1.1. FDA approved

4.1.2. Used for off-label purposes

4.1.3. Not yet FDA approved.

4.2. Include the FDA Investigational New Drug (IND) number for all non-FDA approved and off-label drugs, biological agents or nutritional supplements. If not applicable state, "Not Applicable."

4.3. Provide all relevant information about the drug

4.4. Explain any wash-out periods, rescue medications permitted and any type of medications not permitted while enrolled in the study.
4.5. Describe blinding and un-blinding procedures.
4.6. Include the dosage, route of administration, previous use, and the safety and efficacy information on any drug used for research purposes.
4.7. Describe rationale for the dosage in this study.
4.8. Justify why the risks are reasonable in relation to anticipated benefits and/or knowledge.

4.9. Describe where drug preparation will be done.
4.10. All drugs for CMCVAMC subjects must be dispensed through the VA investigational pharmacy.
4.11. Describe where the study treatment will be administered.
4.12. Describe plan for tracking a non-compliant treatment study subject.
4.13. Summarize any pre-clinical data.
4.14. Describe the process for the storage, security, dispensing and return of an investigational drug.

5. **Investigational Device** (If not applicable state, "Not Applicable.") **Not Applicable.**
5.1. The Investigational Device Exemption (IDE) number must be submitted for all significant risk devices and if an IDE exists for a non-significant device.
5.2. Significant Risk or Non-significant Risk - If a device is not approved by the FDA, specify whether or not the sponsor has determined this device to be a "significant risk" or "non-significant risk" as defined by the FDA.
5.3. Provide all relevant information about the device.
5.4. Describe blinding and un-blinding procedures.
5.5. Specify if device is:
5.5.1. FDA approved
5.5.2. Used for off-label purposes
5.5.3. Not yet FDA approved.
5.6. Explain if the investigational device will be delivered and/or stored by the Principal Investigator or Pharmacy Services.
5.7. Describe the process for the storage, security, dispensing and return of an investigational device.
5.8. For research involving an investigational device, describe the SOP or plan for device control.
5.9. Address how the device will be stored in such a way that only research staff associated with the protocol will have access to the device.
5.10. Describe measures that will be put into place to ensure that the device will only be used in participants of this research protocol.

N. **Does this project involve international research?** ☐YES ☒NO
1. *For further instructions refer to VHA Directive 2005-050, Requirements for Conducting VA-Approved International Research Involving Human Subjects, Human Biological Specimens, or Human Data*
2. *VHA Handbook 1200.05 definition of international research - VA international research is any VA-approved research conducted at international sites (not within the United States (U.S.), its territories, or Commonwealths); any VA-approved research using either human biological specimens (identified, de-identified, or coded) or human data (identified, de-identified, or coded) originating from international sites; or any VA-approved research sending such specimens or data out of the U.S. (see par. 56).* ***NOTE:*** *For the purposes of this Handbook, research conducted at U.S. military bases, ships, or embassies is not considered international research.*

O. **Study Procedure**
1. **Study Procedures**

1.1. Outline all study procedures - (*If necessary, include a table or flow chart, showing the schedule of the procedures and interactions. Distinguish between interventions that are experimental and carried out for research purposes vs. those that are considered standard of care. Routine procedures that are performed solely for research purposes should also be identified.)*

Consenting patients will be administered a baseline assessment battery (diagnostic, work outcomes, functional outcomes, symptom, neurocognitive, and attitude measures) to determine eligibility. Baseline assessment procedures will take approximately 4-5 hours. (Please see section O.2.1 for full descriptions of the assessment battery.) Subjects will be notified of their eligibility status for the treatment component of the research by phone within 2 weeks of their baseline assessment.

The research team will seek permission to obtain the contact information of a secondary contact person, to assist in maintaining contact with the veteran over the course of the 18 active months of the study. Though participants will be encouraged to provide this information, they may refuse to do so and still remain in the study. The research team will not disclose any information to this secondary contact person.

Eligible subjects who give a second informed consent will be randomly assigned to receive either iCBT or to usual care. All randomized participants will enter into supportive employment at the CMCVAMC. iCBT will be delivered as a group therapy for 12 months of weekly or biweekly sessions (see below). iCBT sessions will take approximately 1 hour. Blind, reliable independent assessors will reassess participants every 6 months after participants begin treatment groups over an 18-month participation period, producing mid-treatment (6 month) end-of-treatment (12 month), and post-treatment (18 month) assessments. Follow-up assessment procedures will take approximately 3-4 hours. The Research Coordinator will conduct a 15-minute Check-In at baseline to gather information about medications and services being received outside of this research study; the Supported Employment Specialists or Independent Assessors will conduct the 15-minute Check-In every 3 months after participants begin treatment groups (i.e., at 3-, 6-, 9-, 12-, 15-, and 18-months). The SE Specialists will also conduct the assessment of employment variables at these Check-Ins using the Workforce Participation form using an informal interview assisted by the use of a calendar and review of holidays and other activity anchors, supplemented by the ongoing assessment they conduct as part of the SE activities.

We are proposing a prospective randomized controlled trial with participants recruited from the CMCVAMC. We will randomize 96 patients (48 patients per condition). Independent assessors will be blinded to participant treatment group allocation. Assessment sessions will occur at baseline, and at 6, 12, and 18 months after therapy groups begin; brief check-ins will occur at each assessment session, and also at months 3, 9, and 15 after therapy groups begin.

Subjects in the iCBT condition will receive weekly or twice weekly group sessions for 12 months. iCBT follows a treatment manual developed by Perivoliotis, Grant, & Beck. The manual details the approach (engagement, behavioral activation, cognitive remediation/restructuring, maintenance) and individualized treatment planning. It also describes strategies and techniques to deal with positive and negative symptoms, mood symptoms, and suicidality. Included in these strategies are mindfulness exercises, designed to assist the participant in identifying feelings and biological processes that accompany a stimulus (i.e.,

food and/or drink). It incorporates cognitive remediation strategies. iCBT sessions will be video recorded, for purposes of quality control and supervision.

Subjects in both conditions will participate in the existing SE program at CMCVAMC.

All participants will continue to receive any services (medical, psychiatric, case management) they were already receiving.

The primary outcome measure will be the work participation indices, including 1) instances of job attainment, 2) average days worked per week while employed, 3) average number of hours worked per week while employed, 3) total weeks worked, and 4) a composite of these indices Secondary outcomes measures will be total score of the Work Behavior Inventory (WBI) at the 6, 12, and 18 month follow up and the total score on the Specific Levels of Functioning scale (SLOF) measured at post-treatment 6, 12, and 18month follow-up.

Treatment conditions
Usual Care - Usual care will entail continued access to all treatments available to all Veterans receiving treatment at the CMC VAMC Mental Health Clinical without restriction.

iCBT - Subjects in the iCBT condition will receive sessions of group therapy scheduled at least once every week for up to 12 months following randomization. iCBT will follow a treatment manual developed by Perivoliotis, Grant, & Beck[74] based upon conceptualizations developed in Schizophrenia: Cognitive Theory, Research, and Therapy.[21] The manual details the modular approach (engagement, behavioral activation, maintenance) and individualized treatment planning. It also explains in detail strategies and techniques for negative symptoms, hallucinations, delusions, anxiety, depression, and suicidality. It also gives guidelines for when and how to incorporate the UCLA social skills role-plays[37] and cognitive remediation strategies.[75] The employment specialists will be masters level clinicians and will provide the iCBT. iCBT sessions will be video recorded, for purposes of quality control and supervision.

i. **Cognitive remediation - Cognitive remediation refers to programs that target specific cognitive domains and aim to improve them, often through thousands of repetitions of the same task, an approach called "drill and practice."[38] There is substantial evidence that cognitive remediation significantly improves performance on cognitive batteries in people with schizophrenia[39], and (perhaps by extension) improves measures of functioning. Several recent meta-analyses of cognitive remediation programs have found moderate effect sizes for improvement in cognitive functioning[40], social cognitive functioning,[41] and psychosocial functioning.[40] Kurtz conducted a literature review of studies that reported neurocognitive data in the context of different psychosocial interventions. He concluded that global cognition, and attention, memory, and problem-solving domains, were associated with outcome variables in people with schizophrenia enrolled in vocational rehabilitation programs.[42]. Five randomized control trials have been conducted integrating cognitive remediation and vocational rehabilitation. McGurk et al. reviewed 4 of the 5 trials in a 2008 review article, and subsequently published the results of another trial. In her review, and in the 2009 trial, she concluded that the combination of cognitive remediation and vocational rehabilitation improved both cognitive functioning and vocational rehabilitation outcomes.[43, 44]**

The cognitive remediation program we will use, Brain HQ by Posit Science (https://portal.brainhq.com/?study=best_vet), is a series of computer "games" developed by neuroscientists to target particular areas of cognition, for instance verbal and visuo-spatial memory, working memory, sustained attention, set-shifting, planning and problem solving, and others. The program is designed to provide practice on these cognitive areas in the form of interactive and engaging computer games. Brain HQ software is commercially available and targeted at a healthy adult population looking to improve cognitive skills that are already within the normal range of performance. It has also been developed for clinical populations with a unique training set for people with schizophrenia, and it has programs with more gradual increases in challenge level, less emphasis on timed tests, and a new interface for facilitators working with patients.

The cognitive remediation module lasts 4 months. During this module, participants will meet twice weekly for hour-long sessions. 40 minutes of those sessions will be devoted to computerized cognitive remediation using Brain HQ. The cognitive domains practiced by the subjects will be individually tailored to the areas of greatest cognitive weakness of each subject. During the cognitive reappraisal portion (see below), the challenges and gains of the subjects using Brain HQ will be discussed and the relationship of the skills mastered to employment situations will be discussed. The employment specialists will perform the cognitive remediation. Consistent with cognitive remediation programs already in place at CMCVAMC, the Brain HQ patient kiosk is connected to the local network, and provides access to the Internet; patients will be monitored by the Supported Employment Specialist during computer use. The name, email address, and password requested when logging on this site will be that of the Supported Employment Specialist (SES), who will then enter a subject code for each subject. Thus no identifiable information about the subject is being entered for use of this computer program.

ii. **<u>Cognitive reappraisal skills.</u> During the cognitive remediation and cognitive reappraisal module, participants will meet twice weekly. The cognitive reappraisal portion will occur 10 minutes prior and 10 minutes after cognitive remediation. The difficulties and gains encountered during cognitive remediation will be discussed. In particular, cognitive restructuring will be conducted around expectancies and attitudes that might block goal achievement. This will involve training patients to *recognize negative automatic thoughts* ("I can't do it," "I do not have the energy), to *identify thinking errors* (e.g., emotion based reasoning such as "if it feels like I can't do it, then I can't do it"), and to *generate alternative explanations* to specific unhelpful or inaccurate thoughts and beliefs. All skills are taught in a fun and engaging manner.**

<u>March 2016 Amendment</u>
This protocol was initially submitted with a study objective to evaluate whether iCBT vs. Psychoeducation (PE) can improve engagement and success in an existing SE program among the most functionally disabled patients with schizophrenia.

We decided to change the control group from Psychoeducation (PE) to usual care. We made this change because experts in randomized clinical trials (RCT) design have recently argued that control condition that is "active" in an effort to

equalize the attention association with the experimental intervention can reduce the power of the design to detect that impact of the intervention.[87] Thus, a control condition that is also active may lead to biasing the study against detecting a difference compared to the experimental group. Psychoeducation is often used as a minimally active control condition in lieu of usual care. Unfortunately, psychoeducation has been demonstrated to reduce relapse, reduce and shorten hospital admissions, and improve medication compliance[76]. It is an active comparator to iCBT, given its significant improvements in areas related to functional outcome. Again, this may in fact reduce the ability to detect a positive impact of iCBT.

This study change was approved by the Sponsor (See Request for Administrative Modification of a Rehabilitation Research and Development Service (RR&D) Project form signed by Patricia Dorn, Director, RR&D)

Plans for subjects already enrolled in the study: Prior to this change in the control arm, we were in the initial stages of existing participants who have been randomized and remain active (3 iCBT group, 3 Psychoeducation group). Since the Psychoeducation participants expect a group, will offer all these participants the iCBT group. Because those two participants who had been randomized to the Psychoeducation group would be offered the iCBT outside the original design, their data will be excluded from data analysis. They will otherwise receive all the benefits of the study.

All existing consented and randomized participants will be re-consented describing the new design just specified, with a usual care arm (that does not involve any group treatment). Again, those participants who want to participate in a group treatment (or an additional group if they are in iCBT arm), have the treatment resources of the Mental Health Clinic that they can access outside of their involvement in this study.

Supported Employment (SE). SE is the standard clinical intervention that is offered to Veterans with severe mental illness. Therefore, SE is not a research intervention. However, the supported employment specialists will be a part of the research team. Subjects randomized to either treatment group (i.e., iCBT, usual care) will participate in SE. All participants will also continue receive psychiatric care. Case management will continue for subjects already receiving such services. The SE program will adhere to the IPS model adopted by the CMCVAMC in 2005 as part of a national initiative (see Background, above). The IPS model has been well described [18] and training occurs through a mentor-trainer model. Multiple studies have demonstrated the importance of high fidelity scores on SE program evaluation in terms of employment outcomes[77].

1.2. Explain if and how the follow-up of subjects will occur. **The baseline assessment is designed to: a) determine baseline levels of work functioning, psychosocial functioning, symptomatology, cognitive impairment, and dysfunctional belief endorsement, and b) determine whether participants are eligible for the treatment phase of the study.**

The research team will strive to form treatment groups as quickly as possible. However, it may take several weeks to accumulate enough eligible and willing participants to form a treatment group (i.e., 6-8 participants). The intention of the follow-up assessments and check-ins is to measure the impact of treatment on the study measures. Therefore, the follow-ups and check-ins are tied to the beginning of the treatment groups.

All participants who are eligible and consent to randomization will participate in three additional assessment sessions. The mid-treatment and post-treatment assessments are designed to measure change from baseline that occurred during the treatment period and will consist of a re-administration of the baseline measures. The follow-up assessment occurs 6 months after the end of the treatment period (18 months after treatment groups begin). The Research Coordinator will conduct the 15-minute check-in at baseline; the Supported Employment Specialists or Independent Assessors will conduct the check-in every 3 months after treatment groups begin (i.e., at 3-, 6-, 9-, 12-, 15-, and 18-months).

1.3. Describe where, how and who will be conducting study procedures. **The primary purpose of the follow-up assessments is to determine the durability of change post-treatment. Table 1 depicts the study assessment timetable. Baseline study assessments will be carried out by the study Research Coordinator, while follow-up assessments will be carried out by the Independent Assessors. The Research Coordinator will conduct the 15-minute check-in at baseline; the Supported Employment Specialists or Independent Assessors will conduct the check-in every 3 months after treatment groups begin (i.e., at 3-, 6-, 9-, 12-, 15-, and 18-months).**

Table 1: Assessment measures and administration timeline

Measure	Baseline	3 Month (after groups begin)	6 Month (after groups begin; mid treatment)	9 Month (after groups begin)	12 Month (after groups begin; end of groups)	15 Month (after groups begin; post groups)	18 Month (after groups begin; post group follow up)
SCID	X		-		-		-
WHODAS	X		-		-		-
Work Readiness	X						
Risk Assessment	X						
Data from WBI	X		X		X		X
SLOF	X		X		X		X
BNSS	X		X		X		X
SAPS	X		X		X		X
DAS	X		X		X		X
ABS	X		X		X		X
BSES-SF	X		X		X		X
QOLI	X		X		X		X
BCIS	X		X		X		X
CNB	X		X		X		X
B-CATS	X		X		X		X
UPSA	X		X		X		X
Check-in	X	X	X	X	X	X	X
Workforce Participation	X	X	X	X	X	X	X
			Note. "X" = measure administered				

1.4. If a survey study, specify the estimated amount of time that subjects will need to complete the questionnaires/tools. **The baseline assessment will take approximately 4-5 hours. The follow-up assessments will take approximately 3-4 hours. The check-ins will take approximately 15 minutes.**

1.5. If a blood draw, specify the amount of blood to be drawn in milliliters and in teaspoonfuls or tablespoonfuls and specify how often and where the blood will be drawn. **Not Applicable.**

2. **Data Collection** (Include all questionnaires and survey tools with the submission.)

2.1. Provide

2.1.1. the mode of data collection, e.g. telephone, in-person, questionnaire, interviews: **Interview tools include: The Structured Interview for DSM-IV-TR Axis I Disorders, Clinical Trials Version (SCID); World Health Organization Disability Assessment Scale v. 2.0 (WHODAS),Work Behavior Inventory (WBI),Specific Level of Functioning Scale (SLOF), Brief Negative Symptom Scale (BNSS), Scale for the Assessment of Positive Symptoms (SAPS), the Check-In, and the Work Readiness Assessment The 15-minute check-in is a tool developed by the research team to capture information about medications and services being received outside of the study, and will include measures of workforce participation. Training of assessors on the clinical interview will follow the UCLA model of initial training, competency (ICC ¬> .80 with a minimum of 10 cases), and prevention of rater drift (sessions every 6 months).**

Questionnaires include: Dysfunctional Attitude Scale (DAS),[63] Asocial Beliefs Scale (ABS),[64] Beck Self-Esteem Scales – Short Form (BSES-SF),[65] the Quality of Life Inventory (QOLI),[66] and the Beck Cognitive Insight Scale (BCIS).[67]

Cognitive and Functional Tests include: the Computerized Neurocognitive Battery (CNB), the Brief Cognitive Assessment Tool for Schizophrenia (B-CATS), and the USCD Performance-Based Skills Assessment – Brief (UPSA-B).

Specific Levels of Functioning Scale (SLOF).[56] The SLOF is a self-report behavioral rating scale used to assess mentally ill patients' level of functioning in the community and in mental hospitals. The 30-item scale emphasizes subjects' everyday behaviors rather than emotional or mental capacity, and it focuses on subjects' tangible strengths and skills rather than on subjects' weaknesses. Subjects rate their typicality of certain behaviors and self-sufficiency regarding basic tasks on a 5-point scale, in the areas of interpersonal relationships, social acceptability, activities, and work skills. A high total suggests a higher level of functioning in the subject, while a low total suggests relatively lower functioning. The SLOF is considered to be one of the best scales for measuring functional outcomes in terms of reliability, convergent validity, sensitivity, and practicality.[60]

World Health Organization Disability Assessment Schedule 2.0 (WHODAS).[56] The WHODAS is an interviewer-administered assessment designed to determine the level of functioning in subjects with schizophrenia. The WHODAS measures a number of areas, including cognition, mobility, self-care, sociability, life activities, work/school activities, and participation. Each item is measured on a 5-point scale, with higher totals indicating higher levels of dysfunction. Schennach-Wolff et al.[61] found the WHODAS to have predictive validity for early response, response, remission, and symptomatic outcome.

Brief Negative Symptom Scale (BNSS).[57] The BNSS is a 13-item interviewer-scored instrument for assessing the negative symptoms of schizophrenia. Each item is rated on a 7-point scale: "Normal/No Impairment" (0), "Questionable/Very Slight Impairment" (1), "Mild/Mild

Deficit" (2), "Moderate/Moderate Deficit" (3), "Moderately Severe/Moderately Severe Deficit" (4), "Severe/Marked Deficit" (5), "Extremely Severe/Severe Deficit" (6). The items are organized into six subscales: Anhedonia (3 items), Distress (1 item), Asociality (2 items), Avolition (2 items), Blunted Affect (3 items), and Alogia (2 items). The total score is the sum of the 13 items, with the total possible score ranging from 0 to 78. Higher scores are indicative of greater negative symptomatology.

Scale for the Assessment of Positive Symptoms (SAPS).[58] The SAPS is a 34-item interviewer-scored instrument for assessing the positive symptoms of schizophrenia. Each item is scored on a 6-point scale ("Absent" (0), "Questionable" (1), "Mild" (2), "Moderate" (3), "Marked" (4), "Severe" (5)). There are four subscales: Hallucinations (6 items), Delusions (12 items), Bizarre Behavior (4 items), and Positive Formal Thought Disorder (8 items). In a manner similar to the SANS, each SAPS subscale is also assigned a global rating. Participants' positive symptom levels will be indexed by the global SAPS score, which is the sum of the four subscale global ratings. The range of the SANS global score is 0 to 20, with higher scores indicative of greater negative symptomatology. Additionally, the global score of the SAPS Psychotic factor is defined as the sum of the Hallucinations and Delusions subscale global scores, while the global score for the SAPS Disorganized factor is defined as the sum of the Bizarre Behavior and Positive Formal Thought Disorder global scores. Andreasen and colleagues have shown that the SAPS can be reliably administered with people diagnosed with schizophrenia, and a recent consensus statement has proposed the SAPS as a standard measure of positive symptoms.[62]

Check-In. The check-in is a tool developed by the research team to capture information about medications and services being received outside of the research study. There are six main sections: (1) mood, (2) medications, (3) current treatment, (4) hospitalizations, (5) legal issues, and (6) demographics. The Check-In will include measures of workforce participation (as described below).

Workforce Participation. This report form is also completed during the check-in and reflects the timing of job attainment, average days worked per week while employed, average number of hours worked per week while employed, and total weeks worked, These indices reflect common and accepted variables that reflect the degree of success in obtaining competitive employment and at a competitive compensation rate.

The Work Readiness Assessment. The Work Readiness Assessment was developed by David Loveland at the Human Service Center in Peoria, IL, and is based on the Transtheoretical Model of Change and the principles of motivational interviewing (http://www.bhrm.org/guidelines/motiveint.pdf). It is comprised of two scales: the Understanding of Benefits scale and the Work Motivation scale. Participants are asked to rate items on a 3-point scale (i.e., "disagree," "not sure," "agree") regarding their understanding of benefits, and a 4-point scale (i.e., "disagree," "somewhat agree," "mostly agree," "strongly agree") regarding their motivation to work. Assessors will use this data to determine a participant's overall work readiness on the following scale: Pre-contemplation about working, Contemplation for

working, Determination/preparation for working, Active stage of job seeking, and Maintaining job seeking activities or working.

Risk Assessment. The Risk Assessment is a tool developed by the study team to evaluate the potential risks (to the participant and study staff) in enrolling the participant into phase 2 of the research study. The risk assessment will be completed as part of the baseline/screening assessment, and then as clinically indicated throughout study participation (e.g., when a subject moves, after an inpatient hospitalization, etc.).

Questionnaires. Belief endorsement and quality of life, questionnaires include: Dysfunctional Attitude Scale (DAS),[63] Asocial Beliefs Scale (ABS) ,[64] Beck Self-Esteem Scales – Short Form (BSES-SF),[65] the Quality of Life Inventory (QOLI),[66] and the Beck Cognitive Insight Scale (BCIS).[67]

Dysfunctional Attitude Scale (DAS).[63] The DAS consists of 40 statements rated on a 7-point scale: "Agree Totally" (7), "Agree Very Much" (6), "Agree Somewhat" (5), "Neutral" (4), "Disagree Somewhat" (3), "Disagree Very Much" (2), and "Disagree Totally" (1). Participants are instructed to select the option that describes how they think most of the time. Sample items include: "If I do not do as well as other people, it means I am an inferior human being"; "If I fail at my work, then I am a failure as a person"; "If I fail partly, it is as bad as being a complete failure"; "If you cannot do something well, there is little point in doing it at all"; "Making mistakes is fine because I can learn from them (reverse keyed)." The DAS is composed of two subscales: Defeatist Performance Attitudes and Dysfunctional Need-for-Acceptance attitudes. The DAS can be reliably administered and its utility in outpatient samples diagnosed with schizophrenia has been established.[22]

Asocial Beliefs Scale (ABS).[64] The ABS is composed of 15 items self-reported as "True" or "False" (scored "1" or "0") that tap attitudes and preferences related to spending time with other people. Sample items include: "I prefer watching television to going out with other people," "people sometimes think I am shy when I really just want to be left alone," and "I could be happy living all alone in a cabin in the woods or mountains." In both patient and control populations, the ABS has been shown to be internally consistent and have high test-retest reliability.[68] Grant and Beck have shown that these items, which are a subscale of the larger Revised Social Anhedonia Scale (RSAS), predict current and future social functioning.[31]

Beck Self-Esteem Scales – Short Form.[65] Beck Self-Esteem Scales – Short Version.[65] The BSES-SF is a 12-item questionnaire that assesses beliefs about the self and others' impressions of the self. Domains queried include superior/inferior, likeable/unlikeable, strong/weak, secure/vulnerable, efficient/helpless, and powerful/powerless. Responses are made to each bipolar set of adjectives on a 10-point scale (anchors are "very much", "average", and "very much"). Modifications to the original form include: (1) the measure was shortened to capture the essence of self-esteem, and (2) seven of the twelve adjectives have been modified to better suit this population based on clinical experience.

Quality of Life Inventory (QOLI).[66] The QOLI consists of 32 self-reported items that tap subjective functioning. Participants are presented with descriptions of 16 life domains: health, self-esteem, goals-and-values, money, work, play, learning, creativity, helping, love, friends, children, relatives, home, neighborhood, and community. For each domain, the subject makes an importance judgment on a 3-point scale -- "Not Important" (0), "Important" (1), "Very Important" (2) -- and a satisfaction judgment on a 6-point scale -- "Very Dissatisfied" (-3), "Dissatisfied" (-2), "Somewhat Dissatisfied" (-1), "Somewhat Satisfied" (1), "Satisfied" (2), "Very Satisfied" (3). QOLI scores for each domain are determined by multiplying the importance rating by the satisfaction rating. The total QOLI score is the sum of the 16 individual domain scores; higher scores reflect higher reported quality of life.

Beck Cognitive Insight Scale (BCIS).[67] The BCIS is a 15-item measure of two components (factors) of cognitive insight—the capacity and willingness to observe one's experiences and consider alternative explanations (self-reflectiveness) and the overconfidence in the validity of one's beliefs (self-certainty). Sample items include, "There is often more than one possible explanation for why people act the way they do" and "My interpretations of my experiences are definitely right." In the original study with inpatients of varying diagnoses, the BCIS showed adequate convergent and discriminant validity and internal consistency (α = .60-.68). The original psychometrics and factor structure have now been replicated several times.[69] Taken together, the research on the BCIS suggest that cognitive insight has important clinical significance for people with schizophrenia, that it may be a mediating variable in cognitive therapy for the disorder, and that it should therefore be assessed and addressed in clinical trials.[69]

Collection of information from the Work Behavior Inventory (WBI).[55] The WBI is a 35-item scale specifically designed to assess the work behaviors of individuals suffering from severe mental illness. The WBI is completed as a routine standard of care measure during Supported Employment procedures. As part of usual care, the SE Specialists observes the patient in his/her work setting and also speak to the subject's supervisor (when the veteran allows this). As part of the research study, we will collect information from the WBI at the time of the baseline and follow-up assessments. The measure will have a value of '0' at points in which the participants are not working. WBI data may be missing if research participants refuse to allow the SE specialist to observe at the worksite and/or speak to employers. Data from the WBI will be analyzed along with other research data whenever available. The WBI is broken down into specific areas, including social skills, cooperativeness, work habits, work quality, and personal presentation. Each item is scored on a 5-point scale, with higher totals indicating stronger work performance. The WBI has been found to have good validity and reliability[55] and predicts vocational outcomes and productive activity after discharge from rehabilitation.

Performance measures

a) Cognitive

The Computerized Neurocognitive Battery (CNB). The CNB, developed by Ruben Gur and colleagues, is widely used and validated.[70] The version we will use evaluates both accuracy and speed of performance in the following 5

domains: abstraction and mental flexibility (Penn Conditional Exclusion Test), attention and working memory (Letter-n-Back), spatial memory (Visual Object Learning Test [VOLT]), spatial processing (Computerized Judgment of Line Orientation), and sensorimotor dexterity (Computerized Finger-Tapping Task and Motor Praxis test). Participants will be given standard instructions and practice trials with feedback to assure comprehension. Collected data are uploaded automatically to the VA MIRECC secure server using PGP encryption and reviewed for validity. Accuracy and response time for each trial are recorded and the domain scores for accuracy and speed are available in a relational database. The scoring code has been validated against manually scored tests. This procedure is fully automated.

Brief Cognitive Assessment Tool for Schizophrenia (B-CATS).[71]: The B-CATS is a 10-12 minute measure of global cognitive function designed for clinicians to administer and interpret. The B-CATS is composed of 3 neurocognitive tests, Trail Making Test (parts A and B), animal fluency, and Digit Symbol.

b) Functional capacity
The UCSD Performance-Based Skills Assessment-Brief (UPSA).[72] :The UPSA assesses functional capacity -- that is, the expected ability of subjects to function in a variety of real-world settings. This measure assesses skills in two areas: a) Communication (making phone calls, making emergency calls, rescheduling a medical appointment, and others), and b) Finance (e.g. counting change, writing checks, and paying bills). The brief UPSA (10 -15 min) has been shown to correlate at 0.91 with the scores on the full UPSA.[73]

2.1.2. the precise plan for how data is to be collected or acquired **At the baseline assessment interview, a member of the research team (PI, Co-I, or research coordinator) will administer a comprehensive, face-to-face interview that allows for a reliable diagnosis of schizophrenia and queries patient psychosocial functioning levels, symptomatology, substance use, and service usage. At other assessments, the independent assessors will perform semi-structured interviews, collect questionnaire data, and administer cognitive and performance tests.**

2.1.3. exact location where data will be collected, **In a pre-arranged 2nd floor MIRECC interview room (B228).**

2.1.4. exact location where data entry will take place. **In the pre-arranged 2nd floor MIRECC interview room (B228) and the research coordinator's and independent assessors' cubicles in the 2nd floor MIRECC (B228).**

2.1.5. the "title" of individual(s) collecting the data and analyzing the data, e.g. principal investigator, research coordinator. **Principal Investigator, Co-Investigators, Research Coordinator, Independent Assessors.**

2.2. Provide a time line for each aspect of the study. **Assessment sessions will occur at baseline, and at 6, 12, and 18 months after treatment groups begin. Check-ins will occur at baseline, and then every 3 months after treatment groups begin.**

Subjects in the iCBT condition will receive weekly or twice weekly group sessions for 12 months. It incorporates cognitive remediation strategies, and a specific computerized cognitive remediation 4-month block (see below). Subjects assigned to usual care will continue to receive usual care for 12 months. Subjects in both conditions will participate in the existing SE program at CMCVAMC. All participants will continue to receive any services (medical, psychiatric, case management) they were already receiving. The primary outcome measure will be the indices of workforce participation (jobs attained, hours per week, average days worked while employed, weeks employed, total income for the reporting period) . Secondary outcomes measures will be the total score on the Work

Behavior Inventory (WBI) and the total score on the Specific Levels of Functioning inventory (SLOF) measured at 6 months, 12 months, and 18 month post-treatment follow-up.

2.3. Chart/Records/Data Review (retrospective and/or prospective)

2.3.1. Provide the planned or approximate number of charts/records/data to be accessed

2.3.1.1. CMCVAMC **Phase I – 192; Phase II – 96**

2.3.1.2. Other site

2.3.2. Does this protocol employ an Honest Broker? ☐YES ☒NO

2.3.2.1. If yes, provide name of individual.

2.3.2.2. If no, explain who will access the charts/records. **Research coordinator, PI, Co-I.**

2.3.2.3. Describe from what database charts/records/data will be accessed. **CPRS**

3. **Future Use of Data and Re-Contact**, if applicable. **Not Applicable**

3.1. If any of the participant's data are going to be retained after the study for future research, the following information must be provided to the participant:

3.1.1. Where will the data be stored?

3.1.2. Who will have access to the data?

3.2. If the subject is going to be re-contacted in the future about participating in future research, this must be specified. Describe the circumstances under which the participant would be re-contacted whether within the VA or outside the VA. **Not Applicable**

3.2.1. If subjects will receive aggregate study results at the end of the study, the informed consent document must contain this information.

4. **Specimen Collection**

4.1. Give the source of all specimens and whether they were collected for research, treatment or diagnosis. **Not Applicable.**

4.2. State where specimens will be stored, secured and when discarded. **Not Applicable.**

4.3. Explain how destruction of samples will be substantiated. **Not Applicable.**

P. **Genetic Testing, if applicable**

1. Explain if the study is looking for an association between a genetic marker and a specific disease or condition, but at this point it is not clear if the genetic marker has predictive value. **Not Applicable.**

1.1. The uncertainty regarding the predictive value of the genetic marker is such that studies in this category will not involve participant counseling.

1.2. Describe if the study is based on the premise that a link between a genetic marker and a specific disease or condition is such that the marker is clinically useful in predicting the development of that specific disease or condition.

1.3. Will the subject be notified of the results and the provision for genetic counseling?
☐ Yes ☐ No ☒ N/A

1.3.1. If yes, explain further.

1.4. If biological specimens are used in this protocol, please respond to the following questions by checking the appropriate box:

	YES	NO	N/A
a. Does the project involve genetic testing?	☐	☐	☒
b. Will specimens be kept for future, unspecified use?	☐	☐	☒
c. Will samples be made anonymous to maintain confidentiality? *(Instructions: Note: If there is a link, it is not anonymous. Coding is not anonymous.*	☐	☐	☒
d. Will specimens be destroyed after the project-specific use is completed?	☐	☐	☒

e. Will specimens be sold in the future?	☐	☐	☒
f. Will subjects be paid for their specimens now or in the future?	☐	☐	☒
g. Will subjects be informed of the results of the specimen testing?	☐	☐	☒
h. Are there any implications for family members based on specimen testing results? (If yes, they may be participants.)	☐	☐	☒
i. Will subjects be informed of results obtained from their DNA?	☐	☐	☒

1.5. Will specimens be de-identified? ☐YES ☐NO ☒ N/A
  1.5.1. If yes, please describe the procedures to be used.
  1.5.2. Include at what point in the process the specimens will be de-identified.

1.6. Describe what measures will be taken to minimize the following risks from breaches of confidentiality and privacy resulting from participating in **THIS aspect** of the research project:
  1.6.1. physical
  1.6.2. psychological
  1.6.3. financial
  1.6.4. social
  1.6.5. legal harm

Q. **Banking of Collected Specimens**

1. **Will collected specimens be banked**? ☐YES ☐NO ☒N/A
  1.1. *IF BANKING SPECIMENS, IT MUST BE AT AN APPROVED VA REPOSITORY*. (*For additional information, refer to VHA Handbook 1200.12, Use of Data and Data Repositories in VHA Research - March 9, 2009.)*
  1.2. If yes, specify the location where specimens will be banked.
  1.3. Explain how destruction of banked samples will be substantiated.

R. **Subject Recruitment** (characteristics of the study population)

1. **Provide the planned or targeted enrollment at**:
  1.1. CMCVAMC - **Phase I: 192; Phase II**: **96**
  1.2. Other sites - **0**
  1.3. Not applicable; chart review or use of previously collected data - ☐

2. **Screening and/or Eligibility Requirements**
  2.1. Describe and provide justification for:
    2.1.1. Inclusion criteria

The study inclusion criteria are as follows:

- **i. Diagnosis of DSM-IV schizophrenia or schizoaffective disorder (SCID)**
- **ii. Severe/extreme functional disability [World Heath Organization Disability Assessment Scale (WHODAS) score ≥ 50]**
- **iii. Clinical stability (as per primary mental health provider)**
- **iv. Receiving treatment at the Veterans Administration**
- **v. Minimal engagement in psychiatric rehabilitation services (just psychiatrist and therapist/case management in the last 6 months)**
- **vi. Eligible and willing to be enrolled in Supported Employment program**
- **vii. Age 18 to 65**
- **viii. Proficient in English**
- **ix. Able to give informed consent**

    2.1.2. Exclusion criteria

- **i. Neurologic disease or damage that would make the diagnosis of schizophrenia questionable**
- **ii. Current opioid or stimulant dependence (SCID).**

iii. **Not appropriate due to safety concerns (based on risk assessment)**

2.2. List all screening and/or eligibility requirements. **The Study Research Coordinator will gather the appropriate records relevant to inclusion. The study team will recruit research participants from the Compensated Work Therapy (CWT) program, the outpatient psychiatric clinic, and the inpatient psychiatric unit at the CMCVAMC. At the time of baseline assessment, subjects will be told that the study staff will query the subject's psychiatrist regarding symptoms, psychosocial functioning, and medications.**

2.3. Explain any special test or evaluations potential subjects may have to undergo before they are actually determined to be eligible for the study. **Based upon all available information (records and the clinical interview), a best-estimate diagnosis will be determined on consensus basis by the PI and Co-Investigator (Dr. Grant). The PI will then determine if eligibility criteria are met.**

2.4. Not Applicable; subjects not recruited; chart review. ☐

3. **If applicable, indicate what populations will be targeted for recruitment as participants. Check all that apply.**

Males	☒
Females	☒
Inpatients	☒
Outpatients	☒
VA Employees	☐
Non-English Speaking**	☐
Veteran Family members***	☐
Non-Veterans***	☐
Other (Specify)	☐
Not Applicable, chart review	☐

3.1. **For non-English speaking subjects - If an investigator proposes to use a participant population that does not speak or read English, a copy of the translated document, as well as the English version, needs to be forwarded to the IRB for approval. Translator certification is also required. **Not Applicable.**

3.2. ***If non-veterans will be recruited for this study, explain why sufficient veterans are not available to participate in the project [VHA Handbook 1200.5, paragraph 16a]. Veteran's spouses/partners, caregivers, etc. are considered non-veterans for the purposes of this study. **Not Applicable.**

3.3. ***Has approval to recruit non-veterans been received from the ACOS/R&D and Medical Center Director?

3.3.1. ☒ Not Applicable

3.3.2. ☐ Pending *(Non-veteran forms should be used. IRB office will obtain approval from ACOS/R&D and Medical Center Director.)*

4. **Does this project target a specific race or ethnic group as participants?** ☐YES ☒ NO
If yes, check all that apply.

Race	
American Indian or Alaskan Native	☐
Asian	☐
Black or African American	☐
Native Hawaiian or other Pacific Islander	☐
Black, not of Hispanic origin	☐
White, not of Hispanic origin	☐
Other	☐

Ethnicity	
Hispanic or Latino	☐
Not Hispanic or Latino	☐
Other	☐

4.1. Provide justification why this/these group(s) was/were chosen.

5. **What is the age range of participants?** Check all that apply.

Children (Under 18) Requires Waiver from CRADO (VHA Directive 2001-028, Research Involving Children)	☐
Young Adults (18-21)	☒
Adults (22-65)	☒
Seniors (Over 65)	☐
Over 89	☐
Not Applicable, chart review	☐

6. **Are there specific reasons why certain populations (i.e., age, gender or ethnic groups) are excluded as participants?** ☒YES ☐NO ☐N/A

6.1. If yes, specify reasons. **Because of the supported employment (difficult to find competitive employment after age 65) and cognitive remediation (possible confound of age-related declines in older populations) portions of the protocol, veterans over the age of 65 are excluded.**

7. **Does the project require enrollment of the following classes of participants?**

	YES	NO
a. Employees	☐	☒
b. Individuals with impaired decision making capability	☐	☒
c. Pregnant women	☐	☒
d. Economically and/or educationally disadvantaged persons	☐	☒
e. Prisoners	☐	☒
f. Illiterate, limited, or no English language proficiency	☐	☒
g. Terminally ill patients	☐	☒

7.1. If applicable, what is the justification for including any of the above classes of participants in the project? **Not Applicable.**

7.2. If the project requires enrolling any of the above classes of participants describe any project-specific measures or special considerations, steps, or safeguards to ensure that these individuals are adequately protected. **Not Applicable.**

8. **Describe the exact plan how subjects will be identified and recruited for the study.**

8.1. Discuss methods, e.g., referrals from physician offices, clinics, programs, or through advertisements and brochures. **Potential participants will be identified through the outpatient mental health clinic, the inpatient psychiatric unit, and the Compensated Work Therapy (CWT) program at the CMCVAMC. Identification of potential research participants will be two-fold: (1) the research team will conduct a review of the caseloads of the treating psychiatrists in the CMCVAMC outpatient mental health clinic and the inpatient psychiatric unit via CPRS review under a Waiver of Individual Authorization for Disclosure of Protected Health Information. The research team will communicate securely (e.g., via CPRS, encrypted email, secure server) regarding patients who may be eligible for the research study, and confer on the appropriateness of research participation; (2) treating psychiatrists in the outpatient mental health clinic and inpatient psychiatric unit will identify potentially eligible participants based on interest in SE and interest in learning about research. In either case, treating psychiatrists at the outpatient mental health clinic will refer individuals with SMI as per CMCVAMC standard protocol to the CWT program. (This referral would be made regardless of eligibility in the research study.) Providers who refer potentially appropriate Veterans will ask them if they would consider participating in the research study. The study team will remind the clinician that they should document this referral in the patient's chart. Those who agree will be approached by the research staff (the PI, RC, independent assessors, and/or the SE**

specialists) after they are referred to the CWT program through a CPRS consult created specifically for study referrals (i.e., SE Research Consult – Vocational Rehab Outpt). The consult note will remind providers that they can only refer patients who want to hear more about the study. The study team will receive an alert in the CPRS system once a study consult has been placed. The study team will regularly check for consults in the CPRS system. All consults will be received and resolved by the study team within 24 business hours, per CMCVAMC standard of care. Providers and the research team may also collaborate to identify potentially eligible participants with whom the provider has not yet discussed SE or study participation to receive a "recruitment opt-in letter" describing study participation and requesting that Veterans contact their treating providers and/or the study team to learn more about the study. Study referrals will follow guidelines outlined above and below if the Veteran reaches out to their provider and/or the research team to learn more about participation.

If meeting in person, Research staff will provide the potential participant with information about the study (e.g., the research flyer, informational letter) and be given the option to consider participation in research. Research staff will also call potential subjects who have expressed interest in hearing more about the research study (See phone script). Individuals who are interested in participating in the research will be invited to participate in the baseline assessment portion of the research study to determine eligibility for the treatment phase of the study. Potential participants may speak directly with a research team member or contact the research team via the telephone number listed on the recruitment materials (e.g., research flyer, informational letter). Potential subjects who we cannot reach by phone and who the research team are unable to meet with during visits to the VA, will be mailed an informational letter (See Recruitment letter).

Amendment August 15, 2016: The research team has interacted with a number of Veterans who disagree with their psychiatric diagnosis, or feel uncomfortable labeling themselves as someone with a diagnosis of schizophrenia/schizoaffective disorder, however still very much meet study inclusion criteria and otherwise express desire to participate in the study. To be sensitive to this issue, we have modified our consent documents – Veterans will be given the option of disagreeing with their psychiatric diagnosis while agreeing to study participation during the informed consent process.

Mental Health Providers will learn about this research study through direct contact with research staff (i.e., PI, RC, SES), research flyers/brochures, and also through the CMCVAMC Mental Health services informational materials (e.g., the MIRECC's Research Opportunities – Mental Health Provider Informational Sheet - a document distributed to CMCVAMC mental health providers, advertising CMCVAMC research studies, the Resource Center desktop icon).

Research consult note is based on the current Supported Employment consult note and will include the following information. The consult is for Veterans who are interested in Supported Employment services, and who are also open to hearing about the research study. Veterans who decline participation in the research study components, but who are still interested in Supported Employment, will be referred to the CWT Supported Employment Program Manager for follow-up.:

Current PC Provider:
Current PC Team:
Current Pat. Status:
Primary Eligibility:

Patient Type:
OEF/OIF:

Service Connection/Rated Disabilities
SC Percent:
Rated Disabilities:

Order Information
To Service: SE RESEARCH CONSULT - VOCATIONAL REHAB OUTPT
From Service:
Requesting Provider:
Service is to be rendered on an OUTPATIENT basis
Place: Consultant's choice
Urgency: Routine
Earliest Appr. Date:
Orderable Item: SEE RESEARCH CONSULT - VOCATIONAL REHAB OUTPT
Consult: Consult Request
Provisional Diagnosis: (Schizophrenia/Schizoaffective Disorder)
Reason For Request:
ERA:
Service Connected:

COMBAT SERVICE - Yes/No

_____
Service Connected Condition?

Is the reason for this consult because of a Service Connected condition: (Yes/No)
****
All patients must have a diagnosis of schizophrenia or schizoaffective disorder. (Schizophrenia or Schizoaffective Disorder)

Reason for Request:
(e.g., Patient is interested in finding employment. Patient is also interested in hearing about research study).

Inter-facility Information
This is not an inter-facility consult request.

Status:
Last Action:

8.2. If using a clinic, be specific about who will identify the potential subject and how that information will be transmitted to the research staff. **The PI, RC, independent assessors, and/or the SE specialists will meet with all mental health clinicians in the outpatient clinic, the inpatient psychiatric unit, and the CWT program to discuss the study with providers. They will give them recruitment materials (e.g., flyers) to hand out to patients they feel might be interested in this study.**

8.3. If snowball method will be used, discuss the process and how the first individuals will be recruited. **Providers can then give their patients a copy of the IRB-approved flyer.**

8.4. Describe how information will be disseminated to subjects, e.g. handouts, brochures, flyers and advertisements *(include all recruitment materials with this submission)*. **Providers can give their patients a copy of the IRB-approved flyer.**

8.5. **Non-Veteran participants will be given a copy of the Notice of Privacy Practices.**

9. **Informed Consent**

9.1. Informed Consent will not be sought. ☐

9.2. Written informed consent from participants. ☒

9.3. Written informed consent from participants' legally authorized representative (LAR) as required by VA policy and/or applicable state laws. ☐

9.4. Request Waiver of Documentation of Informed Consent ☐

9.5. List the **title** of the key personnel involved in the following activities:

9.5.1. **Person Obtaining Consent**

9.5.1.1. Provide the title(s) of individual(s) **Principal Investigator, Co-Investigator, Research Coordinator, Supported Employment Specialists, Independent Assessors**

9.5.1.2. Type of training received to perform this process: All Staff: **HIPAA, GCP, and Human Subjects Protection Training. The research coordinator will attend the Research Coordinator training class offered by the Research Compliance Officer prior to engaging in research activities.**

9.5.2. **Pre-Recruitment Screening** (the use of medical records and other data bases to determine populations and individuals eligible for the study), **Not Applicable**

9.5.3. **Recruitment Process** (the process in which individuals are contacted and first introduced to the study and to the possibility of participating as subjects), **Principal Investigator, Co-Investigators, Research Coordinator, Supported Employment Specialists, Independent Assessors**

9.5.4. **Informed Consent Process** (the process by which recruited subjects are fully informed about participating in the study and then formally give their voluntary consent for participating), **Principal Investigator, Co-Investigator, Research Coordinator, Supported Employment Specialists, Independent Assessors**

9.5.5. **Screening of Recruited Subjects** (those activities in the protocol in which a final determination of eligibility of prospective subjects is made during the early phases of the study, using laboratory data, inclusion and exclusion criteria, and other person-specific information), **Principal Investigator, Co-Investigator, Research Coordinator**

9.5.6. Include the breakdown of each individual's responsibilities:

9.5.6.1. Principal Investigator, **Oversee the entire study design, implementation, and data collection. He will also provide clinical and diagnostic guidance.**

9.5.6.2. Co-Investigator, **Dr. Grant will provide all the CBT trainings and monitor for fidelity and reliability. He will oversee training on structured interviews, questionnaires and oversee reliability. He will provide clinical and diagnostic guidance. Our TBD biostatistician will analyze all the data. S/he will also maintain the randomization key.**

9.5.6.3. Research Coordinator, **The Research Coordinator (RC) will perform the baseline clinical interviews and assessments to determine eligibility for the treatment portion of this study. She will perform quality assurance checks on all research data; therefore she will not be blinded to treatment condition. The RC will obtain informed consent for all assessment procedures and will write the Research Consent Note. She will scan the informed Consent Documents and HIPAA Authorization forms into CPRS. She will call subjects to remind them of research assessment visits.**

9.5.6.4. Additional research staff by title: **Supported employment specialists/therapists (SES) will assist in recruitment, may**

obtain informed consent, conduct integrated cognitive behavioral therapy and cognitive remediation sessions, and log on to the Brain HQ site. They may call subjects to remind them of group sessions. The SES will gather Check-In information at 3-, 9-, and 15-months. He or she will engage in all SE activities as usual (these activities are not part of the research study). The SES will collect information from the WBI and data on employment (i.e., job obtainment, number of hours worked per week, compensation per hour) in the course of SE activities, as standard of care measures. Independent Assessors will perform the follow-up assessments for this study (at 6-months, 12-months, and 18-months) and assist in conducting check-ins. They may obtain informed consent and assist in recruitment activities. Independent Assessors will be blinded to treatment condition. The Counseling Psychologist Supervisor (Dr. Aaron Brinen) will provide ongoing supervision to the SES regarding integrated cognitive behavior therapy. He will review videotaped therapy sessions. The SES Consultant (Richard Toscano) will provide ongoing consultation services regarding Supported Employment activities. He will conduct SE fidelity measurements throughout the study, which will include contact with research participants. The DMU Administrators (Christopher Petro and Ming Li) will provide ongoing support related to the VA DMU server. In this role they will have access to coded study data. This data will include visit date, which is the only identifying information stored on the DMU server. The co-investigator (Virginia "Jennie" Keleher) will provide hands-on supervision and guidance regarding Supported Employment activities. She will interact with research participants during evaluations of our Supported Employment Specialists.

9.6. Will informed consent be obtained from potential subjects prior to determining eligibility?
☒YES ☐NO ☐N/A

9.6.1. If no, provide justification and a HIPAA Waiver of Individual Authorization for Disclosure of Protected Health Information.

9.7. Define when a subject is enrolled into the study, e.g. after the subject signs the informed consent or after randomized to treatment. **After all eligibility requirements have been verified and informed consent and HIPAA authorization has been provided, the patient will be considered enrolled into the study.**

9.8. Describe:

9.8.1. The process when informed consent will be obtained and protecting patients' privacy. **After subjects are referred to the research study team, they will be scheduled for a baseline assessment, to determine eligibility for the treatment phase of the research study. At this appointment, which will be conducted in a private room, informed consent will be obtained and documented by the research coordinator. Consenting patients will be administered a baseline assessment battery (diagnostic, work outcomes, functional outcomes, symptom, neurocognitive, and attitude measures) to determine eligibility. Subjects will be told of their eligibility status for the treatment portion of the research study by phone within 2 weeks of their baseline assessment. Eligible and willing subjects will be scheduled for a consenting appointment for the treatment portion of the study, which will be conducted and documented by the research coordinator. Eligible subjects who give a second informed consent will**

be randomly assigned to receive either iCBT or to receive usual care. It may take several weeks to accumulate enough eligible and willing subjects to form a treatment group (i.e., 6-8 participants); participants will be contacted by phone to inform them of the start of the treatment groups. Subjects will be invited to participate in follow-up assessment procedures, as documented in the informed consent documents, at 6-months, 12-months, and 18-months after treatment groups begin. The research coordinator will review informed consent documents at these follow-up assessment appointments. A 15-minute check-in will occur at baseline by the Research Coordinator, then at 3-, 9-, and 15- months after treatment groups begin by the SES, and at 6-, 12-, and 18-months after treatment groups begin by an Independent Assessor.

9.8.2. Any waiting period between informing the prospective participant and obtaining consent. **Not Applicable.**

9.8.3. Steps taken to minimize the possibility of coercion or undue influence. **Consent will be sought only under circumstances that provide the prospective participant sufficient opportunity to consider whether or not to participate. The information that is given to the participant shall be in language understandable to the participant. The informed consent does not include any exculpatory language through which the participant is made to waive or appear to waive any of the participant's legal rights. The informed consent does not release or appear to release the investigator, the sponsor, the institution, or its agents from liability for negligence.**

9.9. Provide the language

9.9.1. used by those obtaining consent **English; we will use simple language at no higher than a 5th grade level to minimize misunderstandings with participants.**

9.9.2 understood by the prospective participant or the legally authorized representative **English, we will use simple language at no higher than a 5th grade level to minimize misunderstandings with participants.**

9.10. Provide location where informed consent will be obtained. **In the PI's office or in a private office within the Mental Illness, Research, Education, and Clinical Center (MIRECC).**

10. **Waiver or Alteration of Informed Consent Requirements/Waiver of Requirement to Obtain Documentation of Informed Consent**

10.1. Are you requesting a waiver or alteration of informed consent? *(Check all that apply)*

10.1.1. No ☐

10.1.2. Yes; provide justification. ☐

10.1.3. Yes; for recruitment purposes only. ☒

10.2. **Are you requesting a waiver to obtain documentation of informed consent?**

10.2.1. No ☒

10.2.2. Yes; provide justification. ☐

S. **Compensation** *(The amount of compensation may not constitute an undue inducement to participate in the research.)*

1. Summarize any financial compensation that will be offered to subjects. **Subjects will receive $40.00 for each assessment visit completed.**

2. Provide the schedule for compensation. **Subjects will receive compensation at each assessment, including the initial assessment, and at the 6, 12, and 18 month follow-up assessments. Subjects will not receive compensation for participation in the CBT, usual care, or SE treatment components of the study, or for check-ins.**

2.1. Per study visit or session. **See above, $40.00 per assessment completed**

2.2. Total amount for entire participation. **$160 over the 2 year study.**

3. Explain how compensation will be provided via cash, voucher, gift card, etc. **The subjects will receive a VA voucher that can be redeemed at the Cashier for cash.**

4. If financial compensation will be prorated, explain the process. **N/A**

5. Not Applicable - ☒

T. **Withdrawal/Early Withdrawal**

1. Describe how and when a subject may withdrawal from the study. **Subjects may withdraw from the study at any time without consequences by contacting the PI in writing. Subjects may also inform any research staff member of their desire to discontinue their participation in the research study at any time. Staff members will then inform Dr. Sayers.**

2. Provide procedures for the orderly termination of participation by the participant and if any consequences would result from early withdrawal from the study. **Subjects may withdraw from the study at any time without consequences. Subjects who terminate from study treatment, but who are willing to remain active in the assessment portion of the research, will be followed by phone and encouraged to attend assessment visits at 6-months, 12-months, and 18-months after treatment groups begin, and check-ins at 3-, 6-, 9-, 12-, 15-, and 18-months after treatment groups begin. They will be referred back to their treatment team who will have been following them during their participation and kept informed of any study related matters.**

3. Explain if survival data is required. If so, clarify how data will be obtained. **Not Applicable.**

4. Not Applicable; subjects not recruited; chart review. ☐

U. **Risk/Benefit Assessment**

1. **Potential Study Risks**

1.1. Describe and assess all of the following risks that may be associated with the research:

1.1.1. Physical**– Assessment procedures at baseline are expected to take approximately 4-5 hours, while follow-up assessment sessions are expected to take approximately 3-4 hours. Check-ins will take approximately 15-minutes.Therapy sessions will take approximately 1 hour. Subjects may become uncomfortable during periods of prolonged sitting, and will be encouraged to requests breaks whenever necessary. Research staff will frequently check-in with subjects to determine if a break is necessary, and will be encouraged to supply breaks if they feel this is in the best interest of the subject.**

1.1.2. Psychological - **Subjects may experience anxiety while completing the assessments or during iCBT sessions. They may feel uncomfortable answering questions, and may refuse any such questions. They may also feel tired or frustrated during the computerized training. They may be frustrated or stressed by the demands of looking for and maintaining employment in the SE setting. Subjects may become frustrated or angry with each other in the group setting.**

1.1.3. Social **- NA**

1.1.4. Economic -***NA***

1.1.5. Monetary **- NA**

1.1.6. Legal - NA

1.1.7. Loss of confidentiality **There is a risk for breaches of confidentiality, especially in the setting of group treatment. All efforts will be taken to**

minimize this risk (i.e., secure storage of research documents, reviewing confidentiality in the therapy groups).

1.1.8. Assess the likelihood and seriousness of such risks. – **The likelihood of physical and psychological risks occurring is high, however the seriousness of these risks is considered minimal. The likelihood of a loss of confidentiality is moderate (given the group therapy session); the seriousness of this risk is considered moderate.**

1.1.9. Other**– There may be other unforeseen risks. Subjects and the IRB will be notified in a timely manner if additional risks are discovered.**

1.2. Specify what steps will be taken to minimize these risks. **Subjects will be counseled by their supported employment specialist/therapist if they are experiencing stress or agitation. They will be allowed to leave a group at any time if they feel it is necessary. As is part of the supported employment program, employment specialists will advocate for subjects with the employer should the subject be experiencing extra stress. This will be routinely done as part of the supported employment paradigm and not because the subject is involved in a research trial. If a subject becomes severely agitated, he or she will be brought to the emergency room for psychiatric evaluation by study staff and VA police.**

1.3. If methods of research create potential risks, describe other methods, if any, that were considered and why they will not be used. **Group interventions incur more risks than individual interventions, such as breaches of confidentiality and friction between group members. However, the benefits of a group approach to CBT and cognitive remediation outweigh the risks. The benefits relate to the additional learning subjects do in the group setting.**

1.4. If chart review, breach of confidentiality is always a concern. Specify what steps will be taken to minimize these risks. **Not Applicable.**

2. **Potential Study Benefits**

2.1. Assess the potential benefits to be gained by the individual subject, as well as benefits that may accrue to society in general as a result of the planned work. **Although antipsychotic medications have been readily available for more than half a century, the impact of these agents on functional outcomes has been modest, even when medication regimes have been optimized. By contrast, psychiatric rehabilitation programs have been shown to improve psychosocial functioning. Vocational rehabilitation services, in particular supported employment (SE), have the best evidence base. As compared to those patients not participating in such services, subjects successfully engaged in SE are more likely to be working competitive jobs, working full time, earning higher wages, and reporting a higher quality of life. Furthermore, steady employment has been shown to generate significant savings in the use of mental health services use compared to subjects who are minimally employed.**

2.2. If the subject does not receive any direct benefit, then it must be stated here and in the consent form. **Not Applicable.**

3. **Alternate Procedures**

3.1 Describe the alternatives available to the subject outside the research context. **The alternative for subjects is not to participate in the study and to continue treatment as usual with their clinical team receiving medications, supported employment, and therapy as prescribed routinely.**

3.2 If none, state that the alternative is not to take part in this research study at all. **Not Applicable.**

V. **Data and Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC) (**<u>All Phase III studies are required to have a DSMB. *However, the IRB has the right to require a DSMB with any study.)*</u>

1. **Will an independent DSMB or DMC oversee the project?** ☐YES ☒NO ☐N/A
   1.1. If yes, please provide contact information for the DSMB or DMC or Coordinating Center Representative and attach a copy of the charter.
   Name: Phone Number:
   Title: E-mail**:**

2. **If a DSMB or DMC will not monitor this study, who will monitor this study? Check all that apply.**
   ☒ Principal Investigator
   ☐ Sponsor
   ☐ VA Cooperative Studies Program
   ☐ Safety monitoring committee

W. **Data Monitoring** (*Monitoring plans describe how a monitor, independent of the study team, regularly inspects study records to ensure the study is adhering to the study protocol and applicable research regulations and CMCVAMC requirements. Monitoring plans do not necessarily require the use of an independent Data and Safety Monitoring Board (DSMB). Such independent boards are usually reserved for high-risk phase I studies, or large, multi-center phase III trials. Federally funded studies may require the use of an independent DSMB.)*

1. **Describe the data monitoring plan** (All protocols must have a data monitoring plan appropriate for the potential risks and the complexity of the study.) **The PI and the rest of the study team will perform regular data monitoring to inspect study records to ensure the study is adhering to the study protocol and applicable research regulations and CMCVAMC requirements. This data monitoring will occur monthly and be overseen by the PI.**

2. **Describe how protocol deviations, adverse events, serious adverse events, breaches of confidentiality, unanticipated adverse device effect (UADE), and unanticipated or unexpected problems will be reported to the CMCVAMC IRB and sponsor** *(Refer to the CMCVAMC IRB Standard Operating Procedure (SOP) Manual for reporting guidelines.)*
   Protocol deviations, serious adverse events, unanticipated or unexpected problems and breaches of confidentiality will be reported to the CMCVAMC IRB via email using the appropriate CMCVAMC forms in a timely manner (no more than 5 days) after learning of the event. Adverse events that are not considered serious will be reported to the IRB at the time of continuing review.
   2.1. Describe the management of information obtained that might be relevant to participant protections such as:
      2.1.1. Unanticipated problems involving risks to subjects or others: **We will update the informed consent form and make existing subjects aware of the new information through a revised informed consent procedure.**
      2.1.2. Interim results: **We will update the informed consent form and make existing subjects aware of the new information through a revised informed consent procedure.**
      2.1.3. Protocol modifications: **We will update the informed consent form and make existing subjects aware of the new information through a revised informed consent procedure.**

3. **If applicable, define the plan for subjects if research shows results such as:**
   3.1. Unanticipated problems involving risks to subjects or others – **Subjects and the IRB will be informed in a timely manner (as above) should any unanticipated risks to subjects be identified**.
   3.2. Interim results- **The IRB will be notified of interim results at the time of continuing review.**
   3.3. Protocol modifications **The IRB will be notified of requests for protocol modification prior to the institution of any modified procedures, either at the time of continuing review or in a stand-alone amendment request. Subjects will be notified in a**

timely manner about any protocol modifications that have a direct impact on research subjects (e.g., changes to consent form). If necessary, informed consent will be re-obtained.

To ensure the safety of participants, review of all collected information in the form of surveys and interview data will be conducted by study staff. If any current evidence of major depression, suicidal ideation, or homicidal ideation with no intent is present, this information will be discussed with the participant by a psychiatrist or doctoral level psychologist. The information will be provided to their mental health care provider for follow-up. In the case that a subject does not have a mental health care provider (e.g., they have left care against advice and/or after enrollment in the research study) they will be referred appropriately for treatment. If indicated, assistance will be provided in making this contact. If suicidal ideation or homicidal ideation with intent is present or there are reports of abuse of a child or elder, the participant will be referred for evaluation in the nearest emergency room and the treating mental health care provider will be notified. In emergent situations, emergency assistance will be sought from hospital security and/or by contacting 911 emergency services. Subjects may be withdrawn from the study if they are considered a risk to themselves or others. Subjects may continue with the study if they are psychologically stable, even if they do not have a current treating psychiatrist. However, they will be encouraged to reestablish clinical care.

4. **Statistical Analysis**

4.1. Include statistical power calculations and the assumptions made in making these calculations.

Power analysis

For the primary outcome variable (composite index of workforce participation), and secondary outcome, Work Behavior Inventory (WBI), we used an uncorrected alpha level (Type 1 error rate) of 0.05 in designing our study. There are many different perspectives on adjusting for multiple comparisons in general, and randomized trials in particular. A number of researchers believe that with a primary outcome and all other outcomes treated as secondary (i.e., exploratory) there is no need for multiple comparisons.

This study is powered to detect a clinically significant difference between iCBT and the usual care conditions. Meta-analysis of medical and behavioral outcomes indicates that a medium effect-size between conditions will have a significant impact on quality of life. In a previous study we observed an average effect of about d=0.55 SD. To allow for a somewhat smaller effect in this proposed study, we design our study to have 80% power to detect clinically significant effect of d=0.5 SD. In the pilot data, we found a within-subject correlation structure consistent with a stationary autoregressive process with correlation parameter 0.4. We also assume a dropout rate of 20% for these power calculations. With these assumptions on effect size, covariance structure, and dropout rates, and with a two-sided alpha level of 0.05, the methods of Hedeker et al.86 estimate that a sample size of 48 subjects per group will provide 80% power for the test of our primary hypothesis.

We believe that this is a conservative estimate, based on the larger effect size observed in our prior study, and the higher than expected dropout rate used in the calculation, In addition, our analyses will use the baseline measure of Psychosocial Functioning as a covariate, which should reduce the standard errors in our test, and therefore increase the smallest detectable effect size.

4.2. Define plans for data and statistical analysis, including key elements of the statistical plan, stopping rules and endpoints.

Planned Analyses

(i) Overview

Logistic, log-linear and linear random effects models (hierarchical regression models) will be implemented with random intercepts and slopes for longitudinal binary, count, and continuous outcomes, respectively. These models will contain separate main effects for change from baseline to each follow-up visit at 6, 12, and 18 months, main effect for the treatment, and interactions between the visit and treatment indicator variables. For each of the primary (workforce participation indices) and the secondary (Work Behavior Inventory, Specific Levels of Function) outcomes, separate intent-to-treat (ITT) tests and estimates (with 95% confidence intervals) of randomized group contrasts at 6, 12, and 18 months will be obtained from the estimates of the respective time-treatment interactions.

We will assess residuals in the longitudinal linear random effects model with normal QQ plots and estimation of the skewness and kurtosis coefficients. If these are coefficients exceed their classical cut-offs of 3 and the QQ plots confirm skewness and/or kurtosis, we will then perform a longitudinal analysis based on a random effects generalized linear model with a gamma error distribution (with SAS Proc GLIMMIX) that handles skewed and kurtotic distributions. We will fit such a model with identity link function (linear mean model), such that the resulting estimates and tests are comparable to those of the normal error random effects model. We will compare the estimates and p-values. If the two approaches agree with respect to significance at the specified alpha level, then we will use the results from the linear random effects model with normal error. If they disagree we will base results on the gamma error distribution model.

Prior to each hierarchical analysis, baseline outcomes, pre-treatment assessment scores, and demographics (except gender which by definition is balanced due to be a stratification factor in the randomization) will be compared between the two treatments at the two-sided alpha = .05 level. Any significant baseline variables will be included as covariates in the hierarchical regression models. We will also perform as a sensitivity analysis based on an adjustment of the ITT models for post-randomization confounding due to differences in medication patterns between the randomized groups. Such adjustments will be based on a causal modeling approach that distinguishes between direct effects of the iCBT intervention, on the one hand, and differences in medication patterns, on the other, using randomization and its products with baseline covariates as the instrumental variables to control for unmeasured confounding due to choice of medication.

While the present study is designed to minimize lost observations, the proposed random effects or hierarchical regression approach is superior to last observation carried forward in minimizing bias and Type 1 error and inferentially equivalent to multiple imputation.79 To assess the sensitivity of treatment effect estimates to missing data, we will compare the results under the above hierarchical regression models with those based on shared parameter models that account for informative missingness that is dependent on unobserved outcomes through a latent variable.80 If the results between the two approaches are similar then we will present the proposed hierarchical regression models as robust to informative missing data; otherwise we will note that the results may be

sensitive to informative missing data and augment them with those based on the shared parameter model.

(ii) Work outcome. The primary trial outcome measure, workforce participation (composite index) at 6, 12 and 18 months analyzed in the manner described above. A significant ITT difference on the total WBI score across 6 and 12 months would support the hypothesis that iCBT is more efficacious than usual care at improving work outcomes by the end of treatment (Primary Aim 1). Similarly, WBI score at 18 months is a secondary outcome, and a separate ITT effect on work outcomes at 18 months with the respective month-treatment interaction in favor of iCBT would support the hypothesis that it promotes better work outcomes than usual care during the 6 months after the completion of treatment (Secondary Aim 2).

(iii) Functional outcome. The second trial outcome measures include the Work Behavior Inventory and the total score on the Specific Levels of Functioning Inventory (SLOF) at 12 months A significant ITT difference on the WBI and the total SLOF score across 6, 12 months would support the hypothesis that ICBT is more efficacious than usual care at improving functioning by the end of treatment (Secondary Aim 1). Similarly, WBI and SLOF total score at 18 months is a secondary outcome, and the separate ITT effects on functioning at 18 months with the respective month-treatment interaction in favor of iCBT would support the hypothesis that it promotes better functioning than usual care during the 6 months after the completion of treatment (Secondary Aim 3).

(iv) Neurocognitive performance. Following previously established procedures, accuracy scores of the neurocognitive domain scores most closely related to functioning (attention, verbal memory, and executive function) will be averaged to form the variable, neurocognitive performance (NP). The ITT analysis will be the same as for WBI. (Exploratory Aim 1).

(v) Negative symptoms. The sum of the 13 items of the Brief Negative Symptom Scale (BNSS) will serve as the index of negative symptoms. The ITT analysis will be the same as for work outcomes. (Exploratory Aim 2).

(vi) Mediation and moderation. We will follow the MacArthur model of identifying mediating and moderating variables by adding two terms to the above hierarchical regression models: main effects of the putative mediator on outcome, as well as interactive effects of the potential mediator by treatment condition (moderation) on outcome. With randomization and its products with baseline factors as instrumental variables, we also will test causally the effect of the intervention on outcome to see if there is full mediation (main effect of treatment is not significant) or partial mediation (main effect of treatment is still significant). Additionally, mediation analysis requires appropriate temporal ordering such that the mediator changes prior to the change in outcome that it putatively causes.83 Four classes of model will be tested: (a) whether change in symptoms (mediators = SAPS total and BNSS total) mediates subsequent change in work outcomes or functional outcome (DVs = Workforce participation compositive, WBI total, SLOF total) [Exploratory Aim 3], (b) whether change in neurocognition (mediator = composite score) mediates subsequent change in work outcome or psychosocial functioning (DVs = Workforce participation compositive, WBI total, SLOF total) [Exploratory Aim 4], (c) whether change in dysfunctional attitudes (mediators = defeatist beliefs, asocial beliefs) mediates subsequent change in work outcomes and psychosocial functioning or symptoms (DVs = Workforce participation compositive, WBI total, SLOF total)

[Exploratory Aim 5], (d) whether baseline prognostic variables predict treatment response independent of treatment condition and whether prescriptive factors predict differential treatment response (prognostic/moderator variables = illness duration, neurocognition, emotion recognition, cognitive insight, defeatist beliefs; DVs = Workforce participation compositive, WBI total, SLOF total) [Exploratory Aim 6].

X. **Privacy and Confidentiality** *(Privacy refers to persons and to their interest in controlling the access of others to themselves.) (Confidentiality refers to protecting information from unauthorized disclosure or intelligible interception.) (Investigator should contact the Privacy Officer for additional details.)*

1. **Indicate the type of data that will be received by the Principal Investigator. Check all that apply.**
   - 1.1. ☐ De-identified – Without any identifiers that could link the data to a specific participant. (Contact Privacy Officer for assistance. *If data is coded, it is not considered de-identified.)*
   - 1.2. ☒ Identified – Linked to a specific participant by identifiers sufficient to identify participants. (See HIPAA and Common Rule Criteria for list of identifiers.)
   - 1.3. ☒ Coded – Linked to a specific subject by a code rather than a direct identifier. If coded is checked, specify:
     - 1.3.1 Explain who will maintain the link or code. **The code key will be maintained by the principal investigator and research coordinator on a mapped network drive on a secure VA server (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work).**
     - 1.3.2 Describe who will have access to the link or code. **The study staff will have access to and maintain the code.**
     - 1.3.3 Provide exact details for how the data is coded. **Data will be coded by assigning subjects a study number based on consent order upon entrance into the study. The code will be kept separate from the rest of the data. In addition, when subjects who are in the CBT treatment arm are logged on to the Brain HQ server by their SES, they will be assigned a separate coded number, which will be maintained by the CMCVAMC study staff and not accessible by Posit Science at any time. CNB data are uploaded automatically to the VA MIRECC secure server using PGP encryption and reviewed for validity (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work).**

2. **Does the project require the use of existing Protected Health Information (PHI) from a database, medical records, or research records?** ☒YES ☐NO ☐N/A
   - 2.1. If yes,
     - 2.1.1. Specify the source of the existing PHI **CPRS**
     - 2.1.2. Indicate the specific data elements/identifiers (e.g., name, address, phone numbers, etc.) on the below table.
   - 2.2. If the study uses an existing database/data warehouse,
     - 2.2.1. Provide a description of the database/data warehouse. **Not Applicable**
     - 2.2.2. Make clear who is responsible for maintaining it. **Not Applicable**
     - 2.2.3. Cite any relevant Standard Operating Procedures (SOP) for the database/data warehouse. **Not Applicable**
     - 2.2.4. Provide a copy of the SOP.

3. **Will PHI be collected prior to obtaining informed consent?** ☒YES ☐NO ☐N/A
   - 3.1. If yes, complete and provide a HIPAA Waiver of Individual Authorization for Disclosure of Protected Health Information with this submission.

4. **HIPAA Identifiers** - Indicate the PHI that will be collected from project participants directly or indirectly.

4.1. ☒ Name
4.2. ☒ All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of the Census
4.3. ☒ All elements of dates (except year) for dates directly related to an individual, and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.
4.3.1. ☒ Birth Date ☐ Date of Death
4.3.2. ☒ Discharge date ☒ Admission date
4.3.3. ☒ Appointment Dates ☐ Other Dates (e.g. lab tests, x-rays, MRI, etc.)
4.4. ☒ Telephone numbers
4.5. ☐ Fax numbers
4.6. ☐ Electronic mail addresses
4.7. ☒ Social Security/Medical Record Number
4.8. ☐ Health plan beneficiary numbers
4.9. ☐ Account Numbers
4.10. ☐ Certificate/license numbers
4.11. ☐ Vehicle identifiers and serial numbers, including license plate numbers
4.12. ☐ Device identifiers and serial numbers
4.13. ☐ Web universal resource locators (URLS)
4.14. ☐ Internet protocol (IP) address numbers
4.15. ☒ Biometric identifiers, including fingerprints, voiceprints, audio recordings
4.16. ☒ Full-face photographic images and any comparable images
4.17. ☐ Any other unique identifying number, characteristic, or code
4.18. ☒ Personal and Family History
4.19. ☒ History and Physical Examination ☒ Progress Notes
4.20. ☒ Discharge Summary(ies) ☒ Photographs, videotapes, other images
4.21. ☐ X-Ray ☐ HIV (testing or infectious disease) records
4.22. ☐ Diagnostic/Laboratory tests ☐ Sickle cell anemia
4.23. ☒ Drug Abuse Information ☒ Behavioral Health notes
4.24. ☒ Alcoholism or Alcohol Use ☐ Operative Reports
4.25. ☐ Billing records ☒ Medication List
4.26. ☐ Health Summary Reports ☐ Anatomic Pathology Report
4.27. ☒ Other Records: Supported Employment records

5. **Will participants be contacted from existing PHI?** ☒YES ☐NO ☐N/A
5.1. If yes, clearly explain how participants will be contacted (NOTE: this would be the same information as listed under section R.8 identification and recruitment of subjects).
Potential participants will be identified through the outpatient mental health clinic, the inpatient psychiatric unit, and the Compensated Work Therapy (CWT) program at the CMCVAMC. Identification of potential research participants will be two-fold: (1) the research team will conduct a review of the caseloads of the treating psychiatrists in the CMCVAMC outpatient mental health clinic and inpatient psychiatric unit via CPRS review under a Waiver of Individual Authorization for Disclosure of Protected Health Information. The research team will communicate securely (e.g., via CPRS, encrypted email, secure server) regarding patients who may be eligible for the research study, and confer on the appropriateness of research participation; (2) treating psychiatrists in the outpatient mental health clinic and inpatient psychiatric unit will identify potentially eligible participants based on interest in SE and interest in learning about research. In either case, treating psychiatrists at the outpatient mental health clinic and inpatient psychiatric unit will refer individuals with SMI as per CMCVAMC standard protocol to the CWT program. (This referral would be made

regardless of eligibility in the research study.) Providers who refer potentially appropriate Veterans will ask them if they would consider participating in the research study. The study team will remind the clinician that they should document this referral in the patient's chart. Those who agree will be approached by the research staff (the PI, RC, independent assessors, and/or the SE specialists) after they are referred to the CWT program through a CPRS consult created specifically for study referrals (i.e., SE Research Consult – Vocational Rehab Outpt). The consult note will remind providers that they can only refer patients who want to hear more about the study. The study team will receive an alert in the CPRS system once a study consult has been placed. The study team will regularly check for consults in the CPRS system. All consults will be received and resolved by the study team within 24 business hours, per CMCVAMC standard of care. Providers and the research team may also collaborate to identify potentially eligible participants with whom the provider has not yet discussed SE or study participation to receive a "recruitment opt-in letter" describing study participation and requesting that Veterans contact their treating providers and/or the study team to learn more about the study. Study referrals will follow guidelines outlined above and below should the Veteran reach out to their provider and/or the research team to learn more about participation.

6. Provide the titles of the exact individuals who will have access to the collected data. **The following members will have access to the data: The PI, the Research Coordinator, the Independent Assessors, the Supported Employment Specialists, the Co-investigator, the Counseling Psychotherapist Supervisor, the Supported Employment Consultant, the co-investigator, the study biostatistician and the DMU administrators. Our study consultant, Irene Hurford, MD, will not have access to any study data. Dr. Hurford will assist in the interpretation of the results of analyzed data.**
   6.1. Explain why these individual will have access to this data. **This is because these are the study staff that will be involved in collecting and entering the PHI into the database, or supervising the collection of PHI.**

Y. **Information Security** (*Contact the Information Security Officer for additional assistance regarding confidentiality (storage/security) of research data.)*
1. Provide the precise plan how data is to be collected or acquired (repeat the same information as listed under "Data Collection" section of this form. **At the baseline assessment interview, a member of the research team (PI, Co-I, or research coordinator) will administer a comprehensive, face-to-face interview that allows for a reliable diagnosis of schizophrenia and queries subject psychosocial functioning levels, symptomatology, substance use, service usage, and check-in. At other assessments, the independent assessor will perform semi-structured interviews, collect questionnaire data, administer cognitive and performance tests, and complete the check-in. The Supported Employment Specialists will complete the check-ins after treatment groups begin, which are not tied to an assessment (i.e., at 3-months, 9-months, and 15-months). They will collect data from the WBI at baseline, and at 6-months, 12-months, and 18-months after treatment groups begin (obtained in the course of standard SE care).**

   Some data (e.g., demographics, diagnosis, study enrollment and tracking) will be stored on the centralized VA server and uploaded daily (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work). Research data from the questionnaires and some study scales (e.g., SAPS, BSES-SF) will be collected electronically via web interface, a password protected website run within the CMCVAMC firewall and stored on the VHAPHIFOCMIRECC direct-entry data server. The server is maintained by CMCVAMC FITS. Interview data and self-report data are entered directly onto computers at the research site, by research technicians and study subjects respectively. The technician will be present with the subject through the entire

assessment, and will review each instrument as it is completed. CNB data are uploaded automatically to the VA MIRECC secure server using PGP encryption and reviewed for validity (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work).

Data from the cognitive remediation program will also be stored on the Posit Science server for quality assurance/quality improvement analysis of the program by the Posit Science Company. All data sent to Posit Science will be coded and the code will not be available to them. The participants will be logged on to the Brain HQ server (by their SE specialist) using a coded number, separate from their study ID number. The Posit Science/Brain HQ Company will have no access to the study ID number at any time and will not be able to de-code the data in any way. No identifying information will be included with the data stored on the Posit Science server (https://portal.brainhq.com/?study=best_vet). Data will be saved on the VA server (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work).

Media recordings of the therapy sessions will be stored on the centralized VA server and uploaded daily (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work). Recordings will include the subjects' faces, bodies, and voices.

<u>December 2015 amendment to change data storage location</u>: Due to a system failure of the DMU at the VA, which was the main interface for entering research data for clinical studies for Behavioral health / MIRECC, an amendment to this ongoing protocol was made to change where data was stored (as detailed above and in below sections that describe data storage). This is being done with the input from the ISO and PO, and under the current PENN-VA MOU on data storage (even though there is a separate PENN component to our study). The need to use the DMU at Penn is critical because the use of is pen/paper has many problems related to privacy and errors and storage.

Data from the 2 subjects enrolled, but not randomized, will not go to Penn. Data from the 2 subjects randomized, but not active, will not go to Penn. We will re-consent all active subjects (n=6); data for these subjects will only be entered in to the Penn DMU server after re-consent/agreement from participants.

We also note that there was no data loss due to the VA DMU failure.

<u>April 2016 Amendment to change data storage location from Penn's Data Management Unit (DMU) back to VA DMU</u>. NOTE: VA DMU server issues were fixed prior to finalization of UPenn DMU server for this study; no participant data was entered in the UPenn DMU server.

2. Provide a listing of the exact research data that will be stored, including but not limited to signed, original informed consent and HIPAA authorization forms, case report forms, etc. **Informed Consent Forms, HIPAA authorizations, tests, recorded sessions, and questionnaires/surveys.**

3. Indicate how project's research data (original and all copies) will be stored and provide corresponding security systems. **The participant's research records containing any personal health information will never leave the VA grounds. Hard copies of consents, HIPAA authorizations, tests, and surveys, and recorded sessions, will be stored inside of a locked cabinet in the principal investigator's locked office at the VA in the MIRECC of the CMCVAMC. Some electronic data, including overall study tracking files, will be maintained on the CMCVAMC secure server (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work). The data will be coded and the code will be maintained separate from the rest of the data, locked in a cabinet in the MIRECC.**

CNB data are uploaded automatically to the VA MIRECC secure server using PGP encryption and reviewed for validity (i.e., vhaphiwebcnp2.v04.med.va.gov/). Data from the cognitive remediation program will also be stored on the Posit Science server for quality assurance/quality improvement analysis of the program by the Posit Science Company. All data sent to Posit Science will be coded and the code will not be available to them. The Posit Science/Brain HQ Company will have no access to the study ID number at any time and will not be able to de-code the data in any way. No identifying information will be included with the data stored on the Posit Science server(https://portal.brainhq.com/?study=best_vet). Data will be saved on the VA server (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work). Research assessment data (including questionnaire data, clinical assessment data – including use of alcohol/substances, performance measures, supported employment tracking and fidelity ratings, and treatment group tracking data) will be housed on the VA DMU server ; data will be uploaded to the secure MIRECC server at least quarterly, for long-term storage (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work). NOTE: VA DMU server issues were fixed prior to finalization of UPenn DMU server for this study; no participant data was entered in the UPenn DMU server.

4. Provide exact location where research data (original and all copies) will be stored and secured. **Physical research data will be stored in the MIRECC, CMCVAMC. Some electronic data, including overall study tracking files, will be maintained on the CMCVAMC secure server. CNB data are uploaded automatically to the VA MIRECC secure server using PGP encryption and reviewed for validity (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work). The data will be coded and the code will be maintained separate from the rest of the data, locked in a cabinet in the MIRECC. Data from the cognitive remediation program will also be stored on the Posit Science server for quality assurance/quality improvement analysis of the program by the Posit Science Company. All data sent to Posit Science will be coded and the code will not be available to them. The Posit Science/Brain HQ Company will have no access to the study ID number at any time and will not be able to de-code the data in any way. No identifying information will be included with the data stored on the Posit Science server (https://portal.brainhq.com/?study=best_vet). Data will be saved on the VA server (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work). Research assessment data (including questionnaire data, clinical assessment data – including use of alcohol/substances, performance measures, supported employment tracking and fidelity ratings, and treatment group tracking data) will be housed on the VA DMU server; data will be uploaded to the secure MIRECC server at least quarterly, for long-term storage (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work).**

5. Explain how data is to be transported or transmitted from one location to another. **Data from the cognitive remediation program will be stored on the Posit Science server for quality assurance/quality improvement analysis of the program by the Posit Science Company. All data sent to Posit Science will be coded and the code will not be available to them. The Posit Science/Brain HQ Company will have no access to the study ID number at any time and will not be able to de-code the data in any way. No identifying information will be included with the data stored on the Posit Science server (https://portal.brainhq.com/?study=best_vet). Data will be saved on the VA server (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work). Research assessment data (including questionnaire data, clinical assessment data – including use of alcohol/substances, performance measures, supported employment tracking and fidelity ratings, and treatment group tracking data) will be housed on the VA DMU server; data will be uploaded to the secure MIRECC server at least quarterly, for**

long-term storage (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work).

5.1. Informed Consent discloses PHI transported or transmitted off-site. ☐YES ☐NO ☒ N/A

5.2. HIPAA Authorization discloses entities to whom PHI will be transported or transmitted. ☐YES ☐NO ☒N/A

5.2.1. List all entities or individuals outside CMCVAMC to whom data is to be disclosed, and the justification for such disclosure and the authority:

5.3. If yes, list the exact data that will be transmitted:

5.4. If yes, explain how data will be protected during transmission outside of CMCVAMC:

5.5. Off-site, provide exact location (If off-site, attach at least one of the following.)

5.1.1. Data Use/Transfer Agreement ☐YES ☐NO ☒N/A

5.1.2. Off-Site Storage/Transfer of Research Data ☐YES ☐NO ☒N/A

5.1.3. Memorandum of Understanding ☐YES ☐NO ☒N/A

5.1.4. (Note: VA data disclosed to a non-VA investigator at an academic affiliate for research purposes needs to be approved by the Under Secretary of Health or designee.)

6. List who is to have access to the data and how they are to access it (anyone who has access to the data is responsible for its security). **The following members will have access to the data: The PI (Dr. Sayers), the RC, the Co-investigator (Dr. Grant), the SES, the Independent Assessors, the Counseling Psychotherapist Supervisor (Dr. Brinen), the SE Consultant (Richard Toscano), the co-investigator (Virginia "Jennie" Keheler) and the study biostatistician (TBD). They can access the hard copies kept in the MIRECC, as well as the electronic copies on the secure server. Our study consultant, Irene Hurford, MD, will not have access to any study data.**

7. Describe who is to have access and be responsible for the security of the information (e.g., the Coordinating Center, the statistician, and PI who has ultimate responsibility). **The following members are responsible for the security of the data: The PI (Dr. Sayers), the RC, the independent assessors, the supported employment specialists, the Co-investigator (Dr. Grant), the Counseling Psychotherapist Supervisor, the SE Consultant, the co-investigator, and the study biostatistician (TBD).**

8. Provide mechanisms used to account for the information. **Only the above-named study staff will have access to the information.**

9. Give security measures that must be in place to protect individually identifiable information if collected or used. **The participant's research records containing any personal health information will never leave the VA grounds. Hard copies of consents, HIPAA authorizations, tests, and surveys will be stored inside of a locked cabinet in the principal investigator's locked office at the MIRECC, CMCVAMC. Some electronic data, including overall study tracking files, will be maintained on the CMCVAMC secure server. Research assessment data (including questionnaire data, clinical assessment data – including use of alcohol/substances, performance measures, supported employment tracking and fidelity ratings, and treatment group tracking data) will be housed on VA DMU server ; data will be uploaded to the secure MIRECC server at least quarterly, for long-term storage (i.e., \\VHAPHIFPCMIRECC \Research Studies\Sayers - Integrated CBT to Improve Work).The data will be coded and the code will be maintained separate from the rest of the data, locked in a cabinet in the MIRECC.**

10. How and to whom a suspected or confirmed loss of VA information is to be reported. **The Investigator will notify the Information Security Officer, Privacy Officer, IRB, Associate Chief of Staff for Research and Research Compliance Officer within one hour of a suspected or confirmed loss of VA information.**

11. Identify any circumstances that may warrant special safeguards to protect the rights and welfare of subjects who are likely to be vulnerable including, but not limited to, those subjects who may be susceptible to coercion or undue influence, and describe appropriate actions to provide such safeguards. **Not Applicable**

12. Electronic PHI will be stored on the following:
    - 12.1. CMCVAMC desktop computer with password protection and/or encryption. ☐YES ☒ NO ☐N/A
      - 12.1.1. If yes, identify where the desktop is located.
    - 12.2. CMCVAMC secure server. ☒YES ☐NO ☐N/A
      - 12.2.1. If yes, identify the CMCVAMC server. **\\VHAPHIFPCMIRECC \Research Studies\Sayers -Integrated CBT to Improve Work.**
      - 12.2.2. External drive that is password protected and/or encrypted. ☐YES ☐NO ☒N/A
        - 12.2.2.1. If yes, identify the external drive.
    - 12.3. Off-Site server ☐YES ☐NO ☒N/A (If off-site, attach at least one of the following.)
      - 12.3.1. Provide exact location and the name of the off-site server:
      - 12.3.2. Data Use/Transfer Agreement ☐YES ☐NO ☒N/A
      - 12.3.3. Off-Site Storage/Transfer of Research Data ☐YES ☐NO ☒N/A
      - 12.3.4. Memorandum of Understanding ☐YES ☐NO ☒N/A

13. Explain how data is to be transported or transmitted from one location to another**.**

14. Informed Consent discloses PHI transported or transmitted off-site. ☐YES ☐NO ☒N/A

15. HIPAA Authorization discloses entities to whom PHI will be transported or transmitted. ☐YES ☐NO ☒N/A

16. List all entities or individuals outside CMCVAMC to whom data is to be disclosed, and the justification for such disclosure and the authority**: Not applicable.**

17. Clarify what protection exists for a database. **PHI will be housed on secured CMCVAMC servers that reside behind the VA firewall.**
    - 17.1. Data is stored:
      - 17.1.1. With identifiers - ☒YES ☐NO
      - 17.1.2. Coded - ☒YES ☐NO
      - 17.1.3. De-Identified - ☐YES ☒NO
      - 17.1.4. Provide the exact list of identifiers that will be stored. **The list of identifiers that will be stored is as follows: Name; address; telephone number; date of birth; social security/medical record number; date of administration**

18. Describe the plan for protecting research data from improper use or disclosure. **Research data will only be accessible to research staff.**
    - 18.1. **The Investigator must notify the Information Security Officer, Privacy Officer, IRB, Associate Chief of Staff for Research and Research Compliance Officer within one hour of the improper use or disclosure.**

19. Is there a plan to apply for a Certificate of Confidentiality? ☐YES ☒NO ☐N/A
    - 19.1. If yes, provide a copy of the certificate with this application or to the IRB Office as soon as received.

20. **Record Retention**:
    - 20.1. The required records, including the investigator's research records, must be retained until disposition instructions are approved by the National Archives and Records

Administration and are published in VHA's Records Control Schedule (RCS 10-1). VHA Handbook 1200.05 §26.h

20.2. Until a schedule for local research records is published, ALL records including identifiers must be retained." ORO/ORD Guidance on Informed Consent Form Modifications Addressing VA Record Retention Requirements (July 23, 2009)

20.3. If there are additional procedures for record retention, explain further. **N/A**

Z. **Qualification of the Investigators**

1. Provide a description of the qualifications of each investigator/co-investigator and their specific role in the study. **Principal Investigator, Steven Sayers Ph.D. Dr. Sayers is the Director of the Advanced Fellowship Program in Mental Illness Research and Treatment, and investigator and Co-Associate Director of Education for VISN4.**

   Co-Investigators:

   - **Dr. Grant developed the iCBT model. He has a long track record of research into CBT for psychosis with Dr. Aaron Beck. He will provide all the CBT trainings and monitor for fidelity and reliability. He will oversee training on structured interviews, questionnaires and oversee reliability. He will provide clinical and diagnostic guidance.**
   - **Ms. Keheler is an expert in the field of Supported Employment. She will provide supervision and evaluations for our Supported Employment Specialists/Program.**

2. If applicable, the Principal Investigator must identify a qualified clinician to be responsible for all study related healthcare decisions. **Not Applicable**

3. PI should submit a current, dated CV with each new initial review.

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