# Understanding Social Situations (USS): Training to improve social function in people with psychosis

NCT04557124

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## PROJECT DESCRIPTION

**1. Principal Investigator:** Joanna Fiszdon, Ph.D.

**Project Title:** Understanding Social Situations (USS): Training to improve social function in people with psychosis

**2. Purpose:** We propose to evaluate the efficacy of Understanding Social Situations (USS), a behavioral training targeting social cognitive skills. The current proposal is to conduct a fully powered, rigorous randomized controlled trial to test the efficacy of USS versus an active control condition. One hundred twenty Veterans with psychotic spectrum disorders (PSD) will be randomized to 2 months of USS or an active control (AC) intervention matched for duration, therapist contact, and mode of delivery. Key social functioning outcomes will be measured using a multi-method approach of self-report, role-play, and experience sampling, conducted pre-intervention, post-intervention, and at 2 month follow-up, with an additional limited assessment at treatment mid-point.

**Primary Aim:**

**Aim 1: Examine the efficacy of USS in improving social functioning.**

H1.1: Compared to AC, USS will be associated with greater improvements on the Social Functioning Scale.

**Secondary Aims:**

**Aim 2: Examine the efficacy of USS in changing real-world social behaviors.**

H.2.1: Compared to AC, USS will be associated with greater improvements in real-world social behaviors, as measured by ecological momentary assessment (EMA).

**Aim 3: Examine efficacy of USS in improving social interaction skills.**

H.3.1: Compared to AC, USS will be associated with greater improvements on the UCSD Social Skills Performance Assessment, a performance-based measure of social skills.

**Aim 4: Examine durability of USS effects on clinician and self-rated social functioning, real-world social behaviors, and social skills.**

H 4.1 Above group differences will be maintained at 2-month follow-up.

**Exploratory Aims: Examine mechanisms of USS effects.**

A. Target engagement and validation: examine impact of USS on a measure of USS content learning (USS Skills Test) and relationship between content learning and improvement in social functioning.
B. Personalization: explore baseline cognitive, treatment dose, symptom clusters and demographic variables as potential moderators of USS efficacy.

**Additional Aims:** collect normative (psychiatric control) information about social function in non-psychotic psychiatric sample in order to better characterize the nature of social function and factors impacting social interactions in Veterans with versus without psychosis.

**3. Background:**

Functional disability is a core, defining feature of psychotic spectrum disorders (PSD), and persists even when psychotic symptoms are in remission[4]. A majority of people with schizophrenia are not competitively employed, have never been married, have some difficulty with self-care, and have poor community integration[5-8]. Impairments in social function are also prominent, leading to significant social isolation and impeding recovery[9]. Social function deficits are present prior to illness onset[10], persist throughout different phases of the illness[11], and are more severe in PSD than in other serious mental illnesses[12]. Pharmacotherapy and other existing treatments fall short of significantly improving social and community functioning, and social re-

integration is among the top treatment needs both consumers and clinicians feel are not adequately addressed by existing interventions[13, 14].

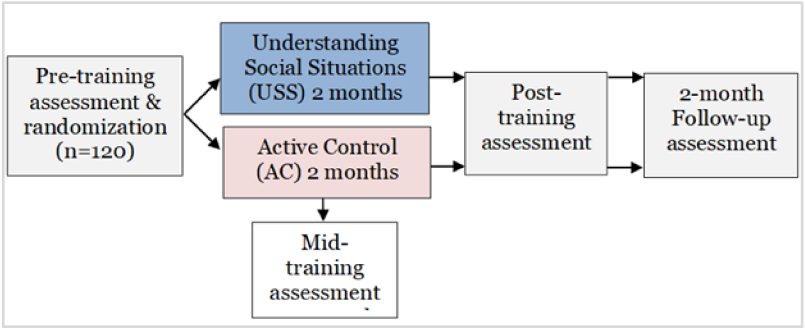
Poor social function in people with psychotic spectrum disorders (PSD) has been linked to significant impairments in social cognition, or how a person processes, interprets and responds to uniquely social information, including complex inferences a person makes about other people's thoughts, feelings and actions. In an effort to improve social functioning, a number of interventions targeting complex social cognitive skills have been developed in recent years. These treatments show some promise, but many of the trials have had significant methodological weaknesses, there is limited data about effects on everyday social functioning outcomes, and nearly all of the work has been conducted in non-Veteran samples. The only group that did examine social cognitive training in Veterans did not find effects on social functioning. Needed now are additional rigorous social cognitive treatment efficacy trials, specifically in Veteran samples, and with an emphasis on everyday social functioning outcomes.

Impairments in concentration, memory, and problem solving are also common in PSD and can make it challenging to learn complex social cognitive skills. With this in mind, we developed a social cognitive training that leverages successful methods from bottom-up cognitive remediation to reduce cognitive load and aid with acquisition of social cognitive skills. The training was developed under an NIMH R34 grant and is called Understanding Social Situations (USS). To date, we have developed and refined USS training content, created a treatment manual, conducted a single-arm pilot of the intervention, and collected preliminary data on the effects of USS when incorporated into a psychosocial rehabilitation program. The current proposal is to conduct a fully powered, rigorous randomized controlled trial to test the efficacy of USS versus an active control condition.

**4. Significance:**

Schizophrenia and other psychotic disorders are among the top 10 causes of disability in the world[2], with an economic burden of over $150 billion[3]. Psychotic disorders are characterized by significant functional disability, including severe impairments in social and community function. Existing treatments fall short of significantly improving social and community functioning, and social re-integration is among the top treatment needs consumers feel are not adequately addressed by existing interventions. If effective, the proposed intervention has the potential to promote rehabilitation and recovery efforts by meaningfully impacting the social lives and wellbeing of Veterans with psychosis.

**5. Research Plan:**




Overview**:** We propose a randomized, controlled trial investigating the efficacy of Understanding Social Situations (USS) in improving social functioning in participants with psychotic disorders. We will examine the efficacy of USS on social functioning (primary outcome), real-world social interactions, and social skills. We will also explore moderators and mediators of treatment effects, specifically the impact of baseline variables on treatment efficacy and the relationship between USS content knowledge test and social functioning change. One hundred twenty participants will be randomized to two months of individually administered USS or a matched active control training. Comprehensive assessments will occur at baseline, end of training phase, and two-month follow-up, with an additional assessment of the primary outcome and of USS content-related skill (treatment target) at training mid-point. We will additionally obtain baseline-only social function information for a normative (non-psychotic) psychiatric sample, in order to better understand and characterize the patterns of social interactions in our primary psychotic spectrum sample.

**Participants:**

**Psychosis sample:** Participants will be Veterans with a psychotic spectrum diagnosis (PSD). Specific inclusion/exclusion criteria will be as follows: diagnosis of psychotic disorder (e.g. schizophrenia, schizoaffective disorder, delusional disorder, psychosis NOS); no prior exposure to USS training, age 18 and

over; not meeting criteria for substance use disorder in past 30 days; psychiatric stability as evidenced by minimum of 30 days since last psychiatric hospitalization and since last change in psychiatric medications; no evidence of developmental disability in chart or on baseline assessment; no severe, uncorrected auditory/visual impairment; no diagnosis of medical or neurological illness known to impair brain function including dementia, presence of seizures, history of head trauma with loss of consciousness > 1hr, or clear cognitive sequelae from other illness or injury, per medical chart review; fluency in English; ability to provide legal written informed consent (i.e. the participant does not have a conservator); not currently enrolled in another treatment study targeting, or expected to impact, functioning. We hope to randomize approximately 120 Veterans into the study conditions.

**Psychiatric control sample:** Specific Inclusion/exclusion criteria for the psychiatric control group: age 18 and over; currently receiving mental health treatment; no lifetime diagnosis of psychotic disorder (e.g. schizophrenia, schizoaffective disorder, delusional disorder, psychosis NOS) based on clinical interview; not meeting criteria for PTSD in the past 30 days based on clinical interview; not meeting criteria for substance use disorder in past 30 days based on clinical interview; not meeting criteria for a major depressive or manic episode in the last 30 days based on clinical interview; psychiatric stability as evidenced by minimum of 30 days since last psychiatric hospitalization, no current high risk for suicide flag on their chart, and no active suicidal or homicidal ideation in that past 30 days; no evidence of developmental disability in chart or on baseline assessment; no severe, uncorrected auditory/visual impairment; no diagnosis of medical or neurological illness known to impair brain function including dementia, presence of seizures, history of head trauma with loss of consciousness > 1hr, or clear cognitive sequelae from other illness or injury, per medical chart review; fluency in English; access to a smartphone to which they are willing to receive surveys via text message; ability to provide legal written informed consent (i.e. the participant does not have a conservator); We hope to have approximately 20 participants complete study procedures.

**Measures for primary psychotic-spectrum sample:**

Baseline assessments will consist of demographic, intelligence, psychiatric, cognitive, social function and knowledge of USS training content measures. Post-training and 2-month follow-up assessments will mirror baseline assessments, with the exception of diagnostic interviews and IQ estimate, which will only be administered at baseline. An additional assessment of the primary outcome, SFS, and of the proposed mediator of treatment effects, USS Skills Test, will occur at treatment mid-point. Please refer to Assessment Timeline below. The baseline assessment will be split into a screening assessment to confirm study eligibility (demographics, WASI, SCID, SFS), and a subsequent baseline assessment for those who pass the screening (PANSS, PHQ-9, QLS, MCCB, SSPA, USS Skills Test)

*Intelligence*: The Wechsler Abbreviated Scale of Intelligence (WASI[68], 2-subtest estimate) will be used to obtain estimates of current intelligence (IQ Estimate score). The WASI 2-subtest IQ estimate correlates highly (r=.87) with the Wechsler Adult Intelligence Test [69], the most commonly used and accepted measure of intellectual function. It also has high internal consistency reliability (r=.93 for adult sample), and 2-12 week test-retest stability (r=.85). The WASI will be used to characterize the study sample and screen for intellectual disability (IQ < 70) at baseline.

*Diagnostic and Symptom*: The Structured Clinical Interview for DSM-V (SCID[70]) will be used to confirm psychotic spectrum diagnoses. The SCID is the most commonly used semi-structured interview for obtaining DSM-V diagnoses. Modules A through E will be used to determine presence of psychotic and mood syndromes, substance use history, and differential diagnosis. The Positive and Negative Syndrome Scale (PANSS[71]) will be used to characterize participants by assessing the presence and severity of psychiatric symptoms. The PANSS is an interviewer-rated scale indexing the core symptoms of psychosis as well as a broad range of general psychiatric symptoms *including depression and anxiety*. Each symptom is rated on a Likert-type scale ranging from 1-7, for total score range of 30 to 120. Initial reports using this scale provide evidence of good internal reliability for the three subscales (alpha =.73 to .83), with adequate test-retest reliability over 3-6 month inpatient phase (r=.60 to .80) and good interrater reliability (r=.83 to.87). Within our research group, ICC's against gold standard, study PI, range from .85-.97 for PANSS components. For initial exploratory analyses of symptom severity as a potential moderator of treatment effects, PANSS Total Score will be used. As warranted, subsequent analyses may examine the Positive, Negative, and General symptom

subscales, *as well as Depression and Anxiety scores.* The Patient Health Questionnaire (PHQ-9) will also be used to assess depression. The PHQ-9 is a commonly used, 9-item, likert-style, self-report measure (Kroenke, Spitzer & Wiilliams, 2001). The Quality of Life Scale (QLS[95]) will be used to assess interviewer-rated functioning. In addition to providing a total score, this well known measure of functioning can be subdivided into four separate domains; intrapsychic foundations, interpersonal relations, instrumental role functioning, and common objects and activities.

| **Assessments**<br>**Timeline** | **Duration** | **Measure type** | **Pre** | **Mid** | **Post** | **FU** |
|---|---|---|---|---|---|---|
| Demographics/Psychosocial | 10 min | sample characteristics, potential moderators | X | | | |
| Wechsler Abbreviated Scale of Intelligence (WASI, 2 subtest) | 20 min | IQ estimate, sample characteristics, potential moderator | X | | | |
| Structured Clinical Interview for DSM (SCID) | 60 min | diagnostic, sample characteristics | X | | | |
| Quality of Life Scale (QLS) | 30 min | social functioning, sample characteristics, potential moderator | X | | X | X |
| Positive and Negative Syndrome Scale (PANSS) | 30 min | symptom severity, sample characteristics, potential moderator | X | | *X* | *X* |
| Patient Health Questionnaire-9 | 2 min | Depression symptoms | X | | X | X |
| Matrics Consensus Cognitive Battery (MCCB) | 60 min | cognition, sample characteristics, potential moderator | X | | X | X |
| Social Functioning Scale (SFS) | 15 min | social function primary outcome, potential moderator | X | X | X | X |
| 7-day EMA assessment | 3min/each assessment (total 12 min/day) | social function secondary outcome | X | | X | X |
| Social Skills Performance Assessment (SSPA) | 10 min | social function secondary outcome | X | | X | X |
| USS Skills Test | 5 min | social cognition training target, potential moderator | X | X | X | X |

*Cognitive*: Cognition will be assessed using the MATRICS Consensus Cognitive Battery (MCCB[72]). The MCCB was developed by an expert panel of researchers, under NIMH contract, as a broad yet sensitive measure to assess cognitive change in treatment studies. The MCCB includes assessment of 7 domains: speed of processing, attention/vigilance, working memory, verbal learning, visual learning, reasoning and problem solving, and social cognition. While an overall composite score is available, in recognition of differences between neurocognitive and social cognitive impairments, it is becoming more and more common in studies of neurocognitive function in psychosis to calculate a 6-domain composite score, omitting the social cognitive domain. This composite score will be used for initial exploratory analyses of cognition as a potential moderator of treatment effects.

*Social Functioning primary outcome*: Social functioning will be measured using the interviewer-administered Social Functioning Scale (SFS[73]), which assesses social functioning across seven domains: social engagement/withdrawal, interpersonal behavior/communication, prosocial activities, recreation, independence—competence, independence—performance, and employment/occupation. The SFS is one of the best known measures of social functioning in schizophrenia, and was one of two social function measures nominated by experts and selected by a RAND panel for a large-scale investigation of measures to assess real-world outcomes[74] based on its psychometric properties, sensitivity to change, relationship to symptoms,

and comprehensiveness. Importantly, our pilot data indicates that the SFS is sensitive to the effects of the USS intervention. Total score will be used as our primary outcome.

*Social Functioning secondary outcomes*: Social Skills Performance Assessment (SSPA[75]) is a role-play measure of social skill ability. It consists of two, 3-minute, structured role plays (tenant meeting a new neighbor; tenant calling landlord to request repair). The role plays are audio-taped and rated on a number of characteristics including interest/disinterest, clarity, social appropriateness, negotiation ability, and overall conversation, among others. For our analyses, scores from the two role-plays will be summed into a single total score. Smartphone-delivered Ecological Momentary Assessment (EMA), an experience sampling method, will be used to capture information about the extent and type of social interactions, along with participants' dispositions toward and subjective appraisals of these interactions. Questions were mostly adapted from earlier EMA work with similar populations[76-79], and include prompts about the frequency and nature of social interactions, enjoyment level, perceived clarity of communication and confidence in understanding the other person's intent, and anticipation of future social interactions. EMA methodology has the advantage of reducing memory demands and/or recall bias and providing an ecologically valid measure of day-to-day experiences. EMA has been successfully used to assess real-world interactions in Veterans with psychotic disorders, with reports of excellent adherence (85% of surveys), high test-retest reliability (r=.83), and modest correlations to in-lab self-report measures of functioning (E. Granholm, May 2019 personal communication, manuscript under review[77]). EMA questions will be administered via smartphone 4 times per day for a 7-day period at baseline, immediately after the end of the 2-month active phase, and at a follow-up two months following end of the active phase. Please refer to Appendix for additional details of EMA administration protocol, along with preliminary EMA questions.

*Training target*: Consistent with the experimental therapeutics approach, we will not only evaluate outcomes of interest, but also the potential impact of the intervention on the hypothesized treatment mechanism. In this case, we hypothesize the mechanism to be social cognitive skill, indexed by learning of content taught during USS. Hence, we will use the USS Skills Test to index target engagement. The USS Skills Test is a 22-item measure assessing knowledge of principles and skills taught during the training[54]. Items on the USS Skills Test are similar to (though not identical) to those used in the USS training stimuli, and as such, should provide a proximal measure of training effects. Our pilot data indicates that the USS Skills Test is sensitive to training effects.

**Measures for normative psychiatric (non-psychotic) sample:**

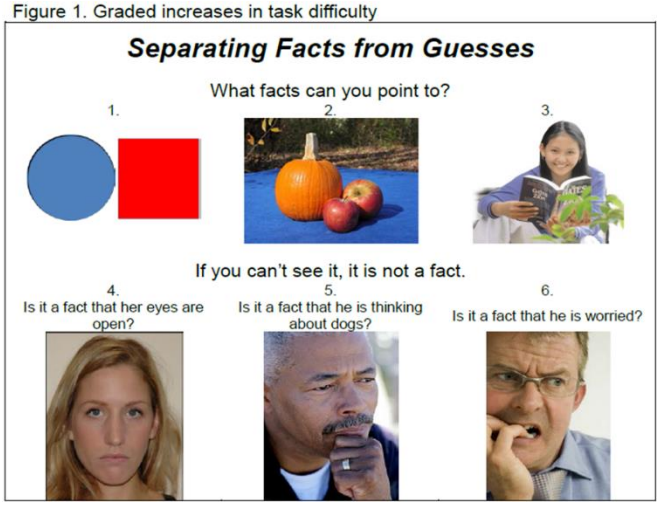
Veterans in the psychiatric subgroup will be asked to complete a subset of measures administered to the psychosis sample and described above, specifically: background/demographic information, Social Functioning Scale (SFS), Patient Health Questionnaire-9 (PHQ-9), the Social Skills Performance Assessment (SSPA), and a baseline Ecological Momentary Assessment (EMA). Psychiatric diagnosis will be confirmed via psychiatric interview, using the Structured Clinical Interview (SCID) as needed.

## ***Interventions (only administered to psychotic-spectrum sample):***

*Experimental intervention, Understanding Social Situations (USS):*

USS was developed by the PI and collaborator Roberts under an NIMH R34 grant. It was developed to train higher-order social cognitive skills. Training content was largely adapted from successful lab-based experimental interventions targeting theory of mind and attributional bias. Given that significant cognitive impairments in people with psychosis can limit skill acquisition, USS was uniquely developed to lessen cognitive load by relying on delivery techniques that have previously been successfully used in cognitive remediation including scaffolding, hierarchical training, massed drill and practice, performance-based increases in task difficulty, and verbal mediation. Additional techniques include motivational enhancement and use of homework to promote bridging to real-world situations. Complex skills are trained by first practicing their individual components. There are four training modules (see below) that are administered over 8-10, individual, hour-long sessions. Training stimuli consist of photos, videos, cartoons, written vignettes, and audio clips of mostly social situations. Once participants complete the four USS modules, all training content will again be reviewed. This approach mirrors many real-world clinical setting where Veterans undergo multiple cycles of an intervention, is intended to further compensate for cognitive impairments, and is intended to assure that training content is learned and consolidated. In total, participants will be asked to undergo 16-20 USS sessions over 2 months.

Figure 1. Graded increases in task difficulty




| **UNDERSTANDING SOCIAL SITUATIONS (USS) TRAINING** |
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| Techniques employed throughout USS content include hierarchical training, massed drill and practice, breaking skills into subcomponents, graded increases in task difficulty, scaffolding, errorless learning, verbal mediation, modeling, minimizing memory load via visual cues, and use of homework to promote bridging to real-world situations. The first three USS modules contain hierarchical difficulty levels, with task difficulty manipulated by adjusting response format, plausibility of foils, stimulus ambiguity, valence, self-relevance, etc. Progress through the training is tailored to individual performance in order to provide an optimal level of challenge while minimizing frustration. Sessions are highly structured and include homework, review of prior session's content, modeling and practice of new skills, and assignment of new homework. |
| **Psychoeducation and motivation enhancement:** The trainee is provided with a rationale for engaging in the ensuing training (to better understand social situations which will help in getting along well with others). Brief video vignettes of social problems are reviewed and the trainee's own experiences with situations where s/he had difficulty figuring out what the other person was thinking or feeling are discussed. The trainee identifies a specific goal pertaining to his or her social life. An overview of the skills to be trained is provided. |
| **Module 1 Separating Facts from Guesses**: Training focuses on distinguishing between observable behavior and inferences about thoughts, feelings and social meanings. Training progresses from identifying what are tangible facts, and distinguishing them from guesses, particularly about others' mental states. Training further progresses to distinguishing between good, fact-based guesses versus bad guesses that have little or no support. (Techniques adapted from Social Cognition Interaction Training, SCIT; Roberts & Penn[55, 56]). |
| **Module 2 Probability Judgments and Not Jumping to Conclusions**: Training focuses on developing skills to evaluate the quality of guesses based on how much information is available to support guesses. Training progresses from rating guesses as good or bad, to rating the relative likelihood of multiple guesses about a single situation, to re-rating quality of different guesses as more information is provided about the situation (techniques adapted from Moritz & Woodward[57]). |

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| **Module 3 Determining Others' Mental States and Intentions**: Training focuses on using verbal mediation to process temporal sequences of social events and identify information in support of various guesses about a character's current or future intentions. Training progresses from evaluating individual stimuli to integrating information from multiple stimuli to making guesses about characters' mental and emotional states and intentions (techniques adapted from Sarfati and colleagues[58, 59]). |
| **Module 4. Inducing Positive Interpretive Bias:** Cognitive bias modification training. Goal of this module is for trainees to develop an automatic bias toward interpreting ambiguous social events in a positive manner. Trainees practice by completing very brief written stories about themselves in social situations, with each story resolving in a favorable way. Unlike other modules, there are no difficulty levels (techniques adapted from Constans and colleagues[60, 61]). |

*Matched Active Control intervention (AC):*
The active control (AC) intervention was selected to match USS on interaction with study staff, treatment duration and intensity, and delivery format. "Moving Forward: Overcoming Life's Challenges" is a free, web-delivered training developed by the VA as part of the Integrated Mental Health Strategy initiative to expand access, ensure quality of care, promote resilience and build better behavioral health systems. The training is based on Problem Solving Therapy[80], an evidence-based cognitive-behavioral approach to developing problem solving skills to effectively cope with stressors[81]. It consists of 8 modules focused on what the training is, how it may be helpful, how to solve problems under stress, steps of problem solving, and how to apply what was learned to daily life. In preparation for the current grant submission, we thoroughly reviewed and timed module content, developed procedures for how this normally self-administered program can be delivered by a study trainer in 45-60 minute sessions, and created a training manual (see Appendix). Similarly to those in the USS condition, participants in AC condition will be asked to attend two cycles of the training, for a total of approximately 16-20 sessions over two months.

**Procedures for psychotic spectrum sample:** Please refer to the study design and the assessments timeline (above) for detailed schematics of study procedures and assessments. Following written informed consent and baseline assessment, Veterans will be randomized (1:1) into one of two training conditions: Understanding Social Situations (USS) or a matched Active Control (AC). Training sessions will occur approximately twice per week for two months (16-20 sessions, given some expected variability in individual time to complete the training content). Training sessions will be video recorded for later fidelity ratings by research staff. Comprehensive assessments will be conducted at baseline and repeated at two months (end of active phase), and four months (two-month follow-up from end of active phase). An additional assessment for the primary outcome (SFS) and hypothesized moderator (USS Skills Test) will occur at one month (midpoint through the active phase). Participants will be oriented to the EMA procedures during the baseline assessment. This will include practice with receiving EMA survey links, navigating the questionnaires, and a comprehension check of survey questions and responses. Smartphones will be given to participants so that they can complete these EMA surveys. In addition to the smartphones, a data plan will be provided for 6-months or until study completion. Participants will then be provided with instructions for how to transfer the phone service into their name if they wish to keep the phone. For participants who are terminated for cause or decide to withdraw from the study, the dataplan will be terminated and the phone will be locked to prevent it being used to obtain a new wireless service plan. Orientation, including basic use and charging of the smartphone will be provided when the phones are given out. We anticipate that length of study participation for individual participants will be approximately 5 months.

**Procedures for normative psychiatric (non psychotic) sample:** Following written informed consent and baseline screening assessment using measures described above (approximately 90 min session), participants who continue to meet all eligibility criteria will be oriented to the EMA procedures. This will include practice with receiving EMA survey links, navigating the questionnaires, and a comprehension check of survey questions and responses. Participants will be asked to save to their contacts the telephone number from which the surveys originate. Next, over the course of 7 days they will receive 4x/day brief surveys about their social interactions. Survey questions are the same as for the psychosis spectrum sample. Length of study participation for the normative sample is approximately 7 days (baseline screening assessment plus 7 days of EMA assessments).

**COVID-19 Pandemic Procedures**: As long as COVID-19 remains a significant concern, this study will conduct the majority of research procedures remotely, via VA-approved telehealth platforms, for all participants recruited during the pandemic. Conducting as many procedures remotely as possible will help to reduce the length of time that in-person interactions are taking place and thus increase staff and participant safety during this pandemic.

*Remote procedures*: In the setting of the novel coronavirus pandemic, the consent form will be mailed to subjects after participating in a phone screening to determine initial eligibility. Upon receipt of the consent form, the consent form will be reviewed with the subject during a telehealth visit, signed and returned to the research team when the participant comes in for their in-person visit. The majority of the study assessments will be conducted using VA-approved video conference platform. Appointments conducted via video will not be recorded, with the exception of the USS/active control sessions, which are also recorded during in-person sessions, to allow for fidelity ratings to be conducted later.

Any virtual sessions will follow safety guidelines that are used in routine VA telehealth care, including the following:

1. Communicating to the participant the importance of having private space to ensure their confidentiality during study sessions
2. Determining an emergency contact, and the location/address of participant at the time of the study session
3. Using available elements of the video platform to ensure confidentiality (e.g., "locking" the virtual meeting room)

When administering assessments that measure depression or SI (PANSS, PHQ-9, or SCID) remotely, in addition to the safety precautions above, we will ensure that the PI is readily available. If the subject expresses SI, whoever is doing the assessment will contact the PI who will do a more detailed imminent risk assessment over the phone. If the PI believes there is risk and is concerned for the study participant's safety, 911 will be called for a welfare check.

In order to allow for remote administration and to limit in-person visits, some changes to the MCCB cognitive assessments have been made including:

- Eliminating spatial span, BVMT and mazes subtests
- Replacing the MCCB Symbol Coding with an oral version of the Symbol Digit Modalities Test,
- Using the oral version of Trails A and B instead of the standard version of the Trails A

In-person study visits conducted at baseline, post-training and follow-up time points will kept as brief as possible, and include the following safety guidelines:

- For any in-person visits that take place, one day prior to the visit and/or at time of visit, participants will be asked the standard COVID-10 screening questions in place at VACHS, and be asked to use a hand sanitizer upon entering the office.
- Participants will be required to wear a 2-ply face mask when in the room with research staff, and if they do not have one, one will be provided for them.
- Staff will utilize masks, gloves, face shields and social distancing during study visits, and will sanitize the office between each in-person visit and at the end of the day.

Recruitment: Veterans with and without psychotic spectrum diagnoses will be recruited from VACHS outpatient clinics via flyers, presentations of study to treatment teams, other research groups, and MH clinicians. The study will also be presented to Veterans during community meetings of the VACHS Psychosocial Rehabilitation and Recovery Center, which serves Veterans with serious mental illness. Recruitment will also

occur through our re-contact repository (those who have participated in our group's prior studies and agreed to be re-contacted with information about additional research opportunities), with the exception of those who participated in the initial USS treatment development trial. We may also pull MH clinic appointment lists, screen upcoming appointments for potential eligibility, alert providers to upcoming appointments with potentially eligible participants, and ask that they refer those who are interested in learning more about the study. We will also offer a small incentive to past/current participants who refer other eligible Veterans. For Veterans with psychotic spectrum diagnoses only, we may also send out study solicitation letters (with opt-out cards), as has previously been approved by the HSS.

Randomization for psychotic spectrum sample: Veterans who meet eligibility criteria and consent to study participation will be randomized to receive either USS or AC in a 1:1 ratio. Randomization will be stratified by baseline SFS score, using a permuted block design with variable block size. The randomization scheme will be computer-generated by the statistician and the allocation sequence will be concealed.

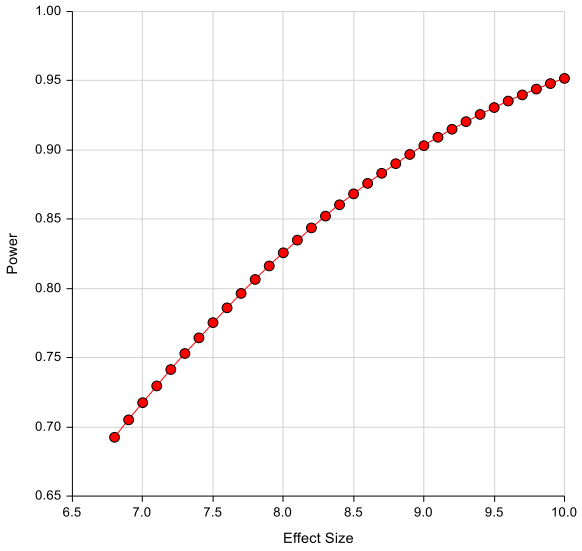
Payment for psychotic spectrum sample: $50/each for baseline ($25 for initial screening plus $25 for subsequent baseline assessment), post-training and 2-month follow-up assessments; $10 midpoint assessment; $1/each EMA survey assessment ($4/day); $10/training session. Smartphones will be provided to all participants with 6-month data plans and the option to keep the phone at the conclusion of the study and transfer service into their name.
Payment for normative psychiatric control sample: $25 for baseline screening assessment; $1/each EMA survey assessment done within 1 hour of survey receipt ($4/day over 7 days, for $28 EMA maximum). Total study participation payment up to $53.

Fidelity: In the full study, we will promote equipoise between the USS and AC conditions by describing the project to potential participants as evaluating the efficacy of two different trainings in improving quality of life. The success of this will be assessed at end of study participation, when participants will be asked to indicate whether they thought they received the experimental or control condition (dichotomous ratings). As detailed below, we are using an active intervention (with different treatment targets) for the control condition, hence expect that most participants will indicate they received an active, potentially efficacious treatment.

Data integrity and management: Data integrity is a process that begins with appropriate administration, scoring, and recording of results. All study staff will be trained on any new procedures. Data flow will be reviewed during weekly lab meetings. We will use VA RedCAP (Research Electronic Data Capture) for data collection and management for all but the EMA assessments. VA RedCAP is a web-based application, accessible only on VA network, and housed on the VA Informatics and Computing Infrastructure (VINCI) server. It was specifically designed for human subjects research, and includes multiple features to enhance data quality control, ease data entry, and assure data security. Because VA RedCAP survey links can only be accessed on VA intranet, to which study participants do not have access, we will use our Qualtrics to capture EMA data. Procedures for using Qualtrics for EMA data are in place, and have previously been approved by the VACHS IRB, Information Security Officer and Privacy Officer.

**Statistical Analysis Plan:**

Justification of Sample Size: The primary hypothesis is that USS will result in greater total SFS scores immediately following training (i.e. 'post' assessment) compared to control. We have powered our study to detect what we consider a clinically meaningful, moderate effect on this measure. Given the following: 1) power of 90%, 2) a two-sided 0.05 significance level, 3) a standard deviation for total SFS score of 13.1 (from our preliminary data), and 4) a 1:1 intervention allocation, a sample size of 46 subjects per group will be required to detect a 9 point difference (i.e. moderate effect size d=0.69) between USS and control in total SFS score at the post assessment. Please refer to Figure, showing the power to detect different effect sizes in total SFS given this sample size. A total of 120 participants will be enrolled and randomized to accommodate up to 20% dropout.




While inherently difficult to define as it varies by perspective (e.g. researcher, consumer, insurance company)[82], we settled on moderate ES on SFS as clinically meaningful based on past social cognitive studies that used the SFS and noted that improvement in social relationships (more friends, less time spent alone, higher quality of social communication) were observed with small-medium effect sizes[83]. Small-medium effects on the SFS have also been related to greater social acceptability by peers, better overall social skills ability, and higher medication compliance, with effects greater than 0.50 on social cognitive measures distinguishing between patients with psychosis and higher functioning patients with bipolar disorder[84]. Perhaps the most striking example of the real-world significance of change on the SFS comes from the original SFS validation study, wherein 11 point difference separated those who were employed from those who were not[73].

General Approach: Nominal and ordinal categorical variables will be summarized using frequencies and percentages. Continuous variables will be summarized with the following descriptive statistics: N, mean, standard deviation, median, minimum, maximum, interquartile range, and range. No imputation of missing data will be performed in the primary and secondary analyses. Diagnostic tests and sensitivity analyses will be performed. Parametric distributional assumptions will be checked. If assumptions fail, other distributions will be considered prior to transformations and non-parametric methods. For all analyses, two-sided significance tests will be implemented and will be performed using SAS v9.4 (Cary, NC).

Comparability of Baseline Characteristics: Distributions of baseline demographic and clinical characteristics will be summarized. Comparability for continuous variables will be examined graphically and by summary statistics (means, medians, quartiles, etc.). Categorical variables will be examined by frequency distributions.

Analysis of Primary Outcome SFS (Aim 1): The primary objective of the analysis is to demonstrate that USS will improve social functioning at the end of training more than active control in participants with PSD and impaired social functioning. The primary outcome (total scores on the SFS) will be assessed prior to initiation of intervention (pre), the training mid-point (mid), the end of training (post) and 2 months following the end of training (FU). Likelihood-based ignorable analysis using a linear mixed model will be used to compare social functioning between groups[85, 86]. The primary advantage of the repeated measures linear mixed model when compared to commonly used methods such as complete case analysis and single imputation (e.g. last observation carried forward) is its flexibility in handling missing data. This analysis will assume that missing data occurs at random (i.e. MAR, not informative). The inclusion of pre, mid and FU outcome data in the model will assist in meeting this assumption. Furthermore, we will evaluate patterns of missing data as well as determine baseline characteristics that are predictive of dropout. If identified, these characteristics will be included in the model to meet the MAR assumption. The mixed model will include fixed effects for intervention (USS vs. active control), time (mid, post, FU), and the interaction of intervention with time. An additional fixed effect will be included for baseline SFS at pre. An unstructured covariance pattern will be used to accommodate correlation from repeated measures. A linear contrast will be used to estimate intervention group differences and 95% confidence intervals at the post assessment.

Analysis of Real World Social Behaviors (Aim 2): Ecological momentary assessment (EMA) analyses will be conducted using a multilevel modeling approach[87]. Analyses handle data estimation with a restricted maximum likelihood approach. Data will be organized hierarchically, with within-person/random EMA prompts across the study period nested within people. Random (within-person) coefficients will be estimated for each person at Level 1, while fixed (between-person) coefficients will be estimated at Level 2. Within-person variables will be centered at Level-1 and between-person variables will be grand mean centered at Level-2 [88-90]. We will examine associations between [e.g., attributions] and [e.g., number of interactions] at Level 1, and fit models with fixed [e.g. group, age, gender] main effects at Level 2. We will also examine [L1] and [L2] cross-level interactions.

Analysis of Social Interaction Skills (Aim 3) and Durability (Aim 4): The secondary outcome social interaction skills, assessed by SSPA, will be compared between USS and control using a repeated measures linear mixed model similar to that described in the analysis of the primary outcome. Durability will also be compared between USS and control using the mixed model. For primary and secondary outcomes, linear contrasts will be used to estimate intervention group differences and 95% confidence intervals at the 2-month FU assessment.

Analysis of Mediation (Exploratory Aim A): We will explore content learning (USS Skills Test) as a potential mediator of the relation between intervention and changes in social functioning. Direct and indirect effects will be estimated using a structural equation model. Mediation (i.e. indirect effects) will be tested using the bootstrapping approach[91].

Analysis of Moderation (Exploratory Aim B): Heterogeneity of treatment effects (HTE) for the primary outcomes will be explored in subgroups of participants based on baseline characteristics including cognition, symptom clusters, illness characteristics, medication dose (chlorpromazine equivalents) and demographic variables. These subgroup analyses are aimed at determining whether there is differential effectiveness of the interventions among participant subgroups. Evidence of HTE will be based on tests of interaction within the longitudinal model structure described above.

Interim Monitoring: Interim monitoring will focus on safety, recruitment, adherence to protocol, baseline comparability of intervention groups, completeness of data retrieval, and uptake of the assigned intervention. A set of monitoring tables will be generated for this purpose. No interim monitoring for efficacy or futility is being proposed.

Analysis of social function between the psychotic spectrum and normative psychiatric sample: Multilevel modeling will be used to examine the predictive ability of social rewards on later social motivation and compared between the psychosis spectrum and normative samples. To examine the frequency of negative appraisals of social interactions and their predictive ability, and to compare this information between psychotic and normative samples, two models will test the effect of group (PSD/control) on social rewards (model 1) and negative social appraisals (model 2). Additional multi-level models will examine desire for socialization and initiation of future social activity. In each model, group, social reward, and the group-by-social-reward interaction will be included as predictor variables. Similar models predicting desire for socialization and initiation of future social activity will be computed with group, negative social appraisal, and their interaction as the predictor variables.

Plan for Missing Data: Several strategies will be imposed to accommodate the likelihood that missing data will occur during this study. Prevention is the most obvious and effective manner to control bias and loss of power from missing data[92]. Prior to the trial we will pilot data collection procedures. Variables with large proportions of missing data will be excluded from collection. We will follow the intent to treat principle, requiring follow-up of all participants randomized regardless of the treatment received[93]. Regular data entry into case report forms (CRFs) combined with monitoring and missing data reports will trigger protocols for tracking and obtaining missing data. Despite these prevention efforts it is reasonable to assume missing data will occur. Our proposed primary and secondary analyses make use of all available data and are valid under the assumption that missing data will be missing at random (MAR)[86, 94]. We will evaluate the plausibility of this assumption by determining the extent of missing data and use logistic regression to identify factors associated with missing data. We will conduct sensitivity analysis using a pattern-mixture approach implemented using multiple

imputation under missing not at random (MNAR) assumptions to examine the robustness of conclusions of the primary analysis to missing data[86, 92].

## 6. References:


1. World Health Organization. Schizophrenia: Fact sheet No 397.; Sept 2015.
2. National Institutes of Mental Health. [Archive Material] Translating behavioral science into action: report of the national advisory mental health council behavioral science workgroup; 1999.
3. Cloutier M, Aigbogun M, Guerin A, et al. The economic burden of schizoprenia in the United States in 2013. Journal of Clinical Psychiatry 2016;77(6):764-771.
4. American Psychiatric Association TFoD-V. Diagnostic and statistical manual of mental disorders, fifth edition. Arlington, VA: American Psychiatric Association; 2013.
5. Bellack AS, Green MF, Cook JA, et al. Assessment of community functioning in people with schizophrenia and other severe mental illnesses: a white paper based on an NIMH-sponsored workshop. Schizophr Bull May 2007;33(3):805-822.
6. Mueser KT, Bellack AS, Douglas MS, Morrison RL. Prevalence and stability of social skill deficits in schizophrenia. Schizophrenia Research Sep 1991;5(2):167-176.
7. Melle I, Friis S, Hauff E, Vaglum P. Social functioning of patients with schizophrenia in high-income welfare societies. Psychiatric Services Feb 2000;51(2):223-228.
8. Penn DL, Mueser KT, Tarrier N, Gloege A, Cather C, Serrano D, Otto MW. Supportive therapy for schizophrenia: possible mechanisms and implications for adjunctive psychosocial treatments. Schizophr Bull 2004;30(1):101-112.
9. Green MF, Horan WP, Lee J. Social cognition in schizophrenia. Nature Reviews Neuroscience 2015;16(10):620-631.
10. Neumann CS, Walker EF. Developmental origins of interpersonal deficits in schizophrenia. In: Mueser KT, Tarrier N, eds. Handbook of social functioning in schizophrenia. Boston: Allyn and Bacon; 1998.
11. Robinson DG, Woerner MG, McMeniman M, Mendelowitz A, Bilder RM. Symptomatic and functional recovery from a first episode of schizophrenia or schizoaffective disorder. American Journal of Psychiatry Mar 2004;161(3):473-479.
12. Walkup J, Gallagher SK. Schizophrenia and the life course: national findings on gender differences in disability and service use. International Journal of Aging & Human Development 1999;49(2):79-105.
13. Bengtsson-Tops A, Hansson L. Clinical and social needs of schizophrenic outpatients living in the community: the relationship between needs and subjective quality of life. Social Psychiatry & Psychiatric Epidemiology Oct 1999;34(10):513-518.
14. Middelboe T, Mackeprang T, Hansson L, et al. The Nordic Study on schizophrenic patients living in the community. Subjective needs and perceived help. European Psychiatry: the Journal of the Association of European Psychiatrists Jun 2001;16(4):207-214.
15. Green MF. What are the functional consequences of neurocognitive deficits in schizophrenia?[see comment]. American Journal of Psychiatry Mar 1996;153(3):321-330.
16. Green MF. Impact of cognitive and social cognitive impairment on functional outcomes in patients with schizophrenia. Journal of Clinical Psychiatry 2017;77 Suppl 2:8-11.
17. Green MF, Kern RS, Braff DL, Mintz J. Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the "right stuff"? Schizophr Bull 2000;26(1):119-136.
18. Fett AK, Viechtbauer W, Dominguez MD, Penn DL, van Os J, Krabbendam L. The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: a meta-analysis. Neuroscience & Biobehavioral Reviews 2011;35(3):573-588.
19. Fiszdon JM, Fanning JR, Johannesen JK, Bell MD. Social cognitive deficits in schizophrenia and their relationship to clinical and functional status. Psychiatry Research 2013;205(1-2):25-29.
20. Fiszdon JM, Johannesen JK. Functional significance of preserved affect recognition in schizophrenia. Psychiatry Research 2010;176(2-3):120-125.
21. Savla GN, Vella L, Armstrong CC, Penn DL, Twamley EW. Deficits in domains of social cognition in schizophrenia: a meta-analysis of the empirical evidence. Schizophr Bull 2013;39(5):979-992.
22. Brekke J, Kay DD, Lee KS, Green MF. Biosocial pathways to functional outcome in schizophrenia. Schizophrenia Research Dec 15 2005;80(2-3):213-225.

23. Fanning JR, Bell MD, Fiszdon JM. Is it possible to have impaired neurocognition but good social cognition in schizophrenia? Schizophrenia Research 2012;135(1-3):68-71.
24. Fiszdon JM, Richardson R, Greig T, Bell MD. A comparison of basic and social cognition between schizophrenia and schizoaffective disorder. Schizophrenia Research Mar 2007;91(1-3):117-121.
25. Pinkham AE, Penn DL, Perkins DO, Lieberman J. Implications for the neural basis of social cognition for the study of schizophrenia. American Journal of Psychiatry May 2003;160(5):815-824.
26. Adolphs R, Tranel D, Adolphs R, Tranel D. Amygdala damage impairs emotion recognition from scenes only when they contain facial expressions. Neuropsychologia 2003;41(10):1281-1289.
27. Pinkham AE, Gur RE, Gur RC. Affect recognition deficits in schizophrenia: neural substrates and psychopharmacological implications. Expert Review of Neurotherapeutics Jul 2007;7(7):807-816.
28. Couture SM, Penn DL, Roberts DL. The functional significance of social cognition in schizophrenia: a review. Schizophr Bull Oct 2006;32 Suppl 1:S44-63.
29. Schmidt SJ, Mueller DR, Roder V. Social cognition as a mediator variable between neurocognition and functional outcome in schizophrenia: empirical review and new results by structural equation modeling. Schizophr Bull 2011;37 Suppl 2:S41-54.
30. Meyer MB, Kurtz MM. Elementary neurocognitive function, facial affect recognition and social-skills in schizophrenia. Schizophrenia Research May 2009;110(1-3):173-179.
31. Horton HK, Silverstein SM. Social cognition as a mediator of cognition and outcome among deaf and hearing people with schizophrenia. Schizophrenia Research Oct 2008;105(1-3):125-137.
32. Cohen AS, Forbes CB, Mann MC, Blanchard JJ. Specific cognitive deficits and differential domains of social functioning impairment in schizophrenia. Schizophrenia Research Jan 31 2006;81(2-3):227-238.
33. Addington J, Saeedi H, Addington D. Facial affect recognition: a mediator between cognitive and social functioning in psychosis? Schizophrenia Research Jul 2006;85(1-3):142-150.
34. Addington J, Saeedi H, Addington D. Influence of social perception and social knowledge on cognitive and social functioning in early psychosis. British Journal of Psychiatry Oct 2006;189:373-378.
35. Dickinson D, Bellack AS, Gold JM. Social/communication skills, cognition, and vocational functioning in schizophrenia. Schizophr Bull Sep 2007;33(5):1213-1220.
36. Horan WP, Kern RS, Green MF, Penn DL. Social cognition training for individuals with schizophrenia: Emerging evidence. American Journal of Psychiatric Rehabilitation 2008;11(3):205-252.
37. Kurtz MM, Richardson CL. Social cognitive training for schizophrenia: A meta-analytic investigation of controlled research. Schizophr Bull 2012;38(5):1092-1104.
38. Fiszdon JM, Reddy LF. Review of social cognitive treatments for psychosis. Clinical Psychology Review 2012;32(8):724-740.
39. Fiszdon JM, Davidson CA. Social cognitive interventions. In: Lewandowski KE, Moustafa AA, eds. Social Cognition in Psychosis. San Diego, CA: Academic Press, imprint of Esevier, Inc.; 2019.
40. Grant N, Lawrence M, Preti A, Wykes T, Cella M. Social cognition interventions for people with schizophrenia: a systematic review focussing on methodological quality and intervention modality. Clinical Psychology Review 2017;56:55-64.
41. Tan BL, Lee SA, Lee J. Social cognitive interventions for people with schizophrenia: A systematic review. Asian Journal of Psychiatry 2018;35:115-131.
42. Green MF, Horan WP, Lee J. Nonsocial and social cognition in schizophrenia: current evidence and future directions. World Psychiatry 2019;18(2):146-161.
43. Horan WP, Green MF. Treatment of social cognition in schizophrenia: Current status and future directions. Schizophrenia Research 2019;203:3-11.
44. Horan WP, Dolinsky M, Lee J, Kern RS, Hellemann G, Sugar CA, Glynn SM, Green MF. Social Cognitive Skills Training for Psychosis With Community-Based Training Exercises: A Randomized Controlled Trial. Schizophr Bull 2018;44(6):1254-1266.
45. Horan WP, Kern RS, Shokat-Fadai K, Sergi MJ, Wynn JK, Green MF. Social cognitive skills training in schizophrenia: an initial efficacy study of stabilized outpatients. Schizophrenia Research Jan 2009;107(1):47-54.
46. Thorp SR, Sones HM, Glorioso D, Thompson W, Light GA, Golshan S, Jeste DV. Older patients with schizophrenia: does military veteran status matter? American Journal of Geriatric Psychiatry 2012;20(3):248-256.
47. Harvey PD, Jacobsen H, Mancini D, Parrella M, White L, Haroutunian V, Davis KL. Clinical, cognitive

and functional characteristics of long-stay patients with schizophrenia: a comparison of VA and state hospital patients. Schizophrenia Research 2000;43(1):3-9.
48. Firmin R, Luther L, Lysaker P, Salyers M. Veteran identity as a protective factor: a grounded theory comparison of perceptions of self, illness, and treatment among veterans and non-veterans with schizophrenia. American Journal of Psychiatric Rehabilitation 2016;19(4):294-314.
49. Smith TE, Hull JW, Goodman M, Hedayat-Harris A, Willson DF, Israel LM, Munich RL. The relative influences of symptoms, insight, and neurocognition on social adjustment in schizophrenia and schizoaffective disorder. Journal of Nervous & Mental Disease Feb 1999;187(2):102-108.
50. Roberts DL, Velligan DI. Can Social Functioning in Schizophrenia Be Improved through Targeted Social Cognitive Intervention? Rehabilitation Research & Practice Print 2012;2012:742106.
51. Spaulding WD, Fleming SK, Reed D, Sullivan M, Storzbach D, Lam M. Cognitive functioning in schizophrenia: implications for psychiatric rehabilitation. Schizophr Bull 1999;25(2):275-289.
52. Harvey PD. Combining training leads to better results: Implications for clinical delivery of computerized cognitive and social cognitive training. Schizophrenia Research 2018;202:48-49.
53. Barch DM. Nonsocial and social cognitive function in psychosis: interrelationships, specificity and innovative approaches. World Psychiatry 2019;18(2):117-118.
54. Fiszdon JM, Roberts DL, Penn DL, Choi KH, Tek C, Choi J, Bell MD. Understanding Social Situations (USS): A proof-of-concept social-cognitive intervention targeting theory of mind and attributional bias in individuals with psychosis. Psychiatric Rehabilitation Journal 2017;40(1):12-20.
55. Roberts DL, Penn DL. Social cognition and interaction training (SCIT) for outpatients with schizophrenia: A preliminary study. Psychiatry Research Apr 30 2009;166(2-3):141-147.
56. Roberts DL, Penn DL, Combs DR. Social Cognition and Interaction Training (SCIT). Treatment Manual 2007.
57. Moritz S, Woodward TS. A generalized bias against disconfirmatory evidence in schizophrenia. Psychiatry Research Jun 15 2006;142(2-3):157-165.
58. Sarfati Y, Hardy-Bayle MC. How do people with schizophrenia explain the behaviour of others? A study of theory of mind and its relationship to thought and speech disorganization in schizophrenia. Psychological Medicine May 1999;29(3):613-620.
59. Sarfati Y, Hardy-Bayle MC, Besche C, Widlocher D. Attribution of intentions to others in people with schizophrenia: a non-verbal exploration with comic strips. Schizophrenia Research Jun 20 1997;25(3):199-209.
60. Constans JI, Penn DL, Ihen GH, Hope DA. Interpretive biases for ambiguous stimuli in social anxiety. Behaviour Research & Therapy Jul 1999;37(7):643-651.
61. Yiend J, Mackintosh B, Mathews A. Enduring consequences of experimentally induced biases in interpretation. Behaviour Research & Therapy Jun 2005;43(6):779-797.
62. Fett A-KJ, Maat A, Investigators G. Social Cognitive Impairments and Psychotic Symptoms: What is the Nature of Their Association? Schizophr Bull 2013;39(1):77-85.
63. Brune M, Abdel-Hamid M, Lehmkamper C, Sonntag C. Mental state attribution, neurocognitive functioning, and psychopathology: what predicts poor social competence in schizophrenia best? Schizophrenia Research May 2007;92(1-3):151-159.
64. Green MF, Penn DL, Bentall R, et al. Social Cognition in Schizophrenia: An NIMH Workshop on Definitions, Assessment, and Research Opportunities. Schizophr Bull 2008;34(6):1211-1220.
65. Duff K. Evidence-based indicators of neuropsychological change in the individual patient: relevant concepts and methods. Archives of Clinical Neuropsychology 2012;27(3):248-261.
66. Leon AC, Davis LL, Kraemer HC. The role and interpretation of pilot studies in clinical research. Journal of Psychiatric Research 2011;45(5):626-629.
67. Rounsaville BJ, Carroll KM, Onken LS. A stage model of behavioral therapies research: getting started and moving on from Stage 1. Clinical Psychology: Science and practice 2001;8(2):133-142.
68. Wechsler D. Wechsler Abbreviated Scale of Intelligence (WASI) Manual. San Antonio, TX: Psychological Corporation; 1999.
69. Wechsler D. WAIS-III Manual: Wechsler Adult Intelligence Scale-III. San Antonio, TX.: Psychological Corporation; 1997.
70. First MB, Williams JB, Karg RS, Spitzer RL. Structured Clinical Interview for DSM-5—Research Version (SCID-5 for DSM-5, Research Version; SCID-5-RV). . Arlington, VA: American Psychiatric Association;

2015.
71. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull 1987;13(2):261-276.
72. Nuechterlein KH, Green MF. Matrics Consensus Cognitive Battery Manual. Los Angeles, CA: The Regents of the University of California; 2006.
73. Birchwood M, Smith J, Cochrane R, Wetton S, Copestake S. The Social Functioning Scale. The development and validation of a new scale of social adjustment for use in family intervention programmes with schizophrenic patients. British Journal of Psychiatry 1990;157:853-859.
74. Leifker FR, Patterson TL, Heaton RK, Harvey PD. Validating measures of real-world outcome: the results of the VALERO expert survey and RAND panel. Schizophr Bull 2011;37(2):334-343.
75. Patterson TL, Moscona S, McKibbin CL, Davidson K, Jeste DV. Social skills performance assessment among older patients with schizophrenia. Schizophrenia Research Mar 30 2001;48(2-3):351-360.
76. Depp CA, Moore RC, Perivoliotis D, Holden JL, Swendsen J, Granholm EL. Social behavior, interaction appraisals, and suicidal ideation in schizophrenia: The dangers of being alone. Schizophrenia Research 2016;172(1-3):195-200.
77. Granholm E. personal communication; 2019.
78. Granholm E, Ben-Zeev D, Fulford D, Swendsen J. Ecological Momentary Assessment of social functioning in schizophrenia: impact of performance appraisals and affect on social interactions. Schizophrenia Research 2013;145(1-3):120-124.
79. Granholm E, Loh C, Swendsen J. Feasibility and validity of computerized ecological momentary assessment in schizophrenia. Schizophr Bull 2008;34(3):507-514.
80. D'Zurilla TJ, Nezu AM. Problem-Solving Therapy. In: Dobson KS, ed. Handbook of Cognitive Behavioral Therapies, 3rd edition. New York, NY: Guilford Press; 2010.
81. Kropf N, Cummings S. Evidence-Based Treatment and Practice with Older Adults: Theory, Practice, and Research: Published to Oxford Scholarship Online: May 2017; 2017.
82. Keefe RS, Kraemer HC, Epstein RS, et al. Defining a clinically meaningful effect for the design and interpretation of randomized controlled trials. Innovations in Clinical Neuroscience 2013;10(5-6 Supp A):4S-19S.
83. Combs DR, Adams SD, Penn DL, Roberts D, Tiegreen J, Stem P. Social Cognition and Interaction Training (SCIT) for inpatients with schizophrenia spectrum disorders: preliminary findings. Schizophrenia Research Mar 2007;91(1-3):112-116.
84. Dickerson FB, Sommerville J, Origoni AE, Ringer NB, Parente F. Outpatients with schizophrenia and bipolar I disorder: do they differ in their cognitive and social functioning? Psychiatry Research 2001;102(1):21-27.
85. Dmitrienko A, Molenberghs G, Chuang-Stein C, Offen W. Analysis of clinical trials using SAS: A practical guide. Cary, NC: SAS Institute, Inc.; 2005.
86. Molenberghs G, Thijs H, Jansen I, Beunckens C, Kenward MG, Mallinckrodt C, Carroll RJ. Analyzing incomplete longitudinal clinical trial data. Biostatistics 2004;5(3):445-464.
87. HLM 7 for Windows [computer program]. Version. Skokie, IL: Scientific Software International Inc.; 2011.
88. Kreft IG, de Leeuw J, Aiken LS. The Effect of Different Forms of Centering in Hierarchical Linear Models. Multivariate Behavioral Research 1995;30(1):1-21.
89. Schwartz JE, Stone AA. Strategies for analyzing ecological momentary assessment data. Health Psychology 1998;17:6-16.
90. Schwartz JE, Stone AA. The analysis of real-time momentary data: A practical Guide. In: Stone AA, Shiffman S, Atienza AA, Nebeling L, eds. The science of real-time data capture. New York: Oxford University Press; 2007.
91. Shrout PE, Bolger N. Mediation in experimental and nonexperimental studies: new procedures and recommendations. Psychological Methods 2002;7(4):422-445.
92. Council NR. The Prevention and Treatment of Missing Data in Clinical Trials. Panel on Handling Missing Data in Clinical Trials. Committee on National Statistics, Division of Behavioral and Social Sciences and Education. Washington, DC: The National Academies Press; 2010.
93. Lachin JM. Statistical considerations in the intent-to-treat principle. 2000.
94. Diggle PJ, Heagerty P, Liang K-Y, Zeger S. Analysis of Longitudinal Data, 2nd edition. Oxford, UK:

Oxford University Press; 2002.
95. Heinrichs DW, Hanlon TE, Carpenter Jr. WT (1984). The Quality of Life Scale: an instrument for rating the schizophrenic deficit syndrome. Schizophrenia Bulletin 10, 388–398.

Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16:606-13.

Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. 1998;59 Suppl 20:22-33;quiz 34-57. PMID: 9881538