Intervention to Change Attributions that are Negative (ICAN): a New Approach to Reducing Anger and Aggression after Brain Injury

Study Protocol and Statistical Analyses Plan

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STUDY PROTOCOL

Study Design. We will conduct a small, randomized waitlist controlled trial of the ICAN intervention to examine feasibility and acceptability (Aim 1); effect size estimates on perspective taking and hostile attributions (Aim 2); and anger and aggression (Aim 3) in participants with TBI.

Inclusion/Exclusion Criteria.

Inclusion Criteria

- History of complicated mild to severe TBI (injury due to an external physical force), with injury severity being defined *either by*[1] Glasgow Coma Score at time of injury (≤12), or post-traumatic amnesia (≥1 day), or loss of consciousness (≥30 minutes), or positive head CT scan consistent with TBI.
- At least 18 years of age or older;
- ≥1 year post-injury;
- Have adequate vision, hearing, and speech/ language skills to participate in assessments and group therapy (determined based on interaction with the participant at screening)
- Have adequate reading comprehension (due to the primary assessment involving written scenarios)
- Have abnormal scores on *one or more* of the below measures of negative attributions or perspective taking (determined at T0 screening):
    - Epps Intent: >4.8, or
    - Epps Hostility: >4.2, or
    - Epps composite score: >-0.2, or
    - AIHQ Intent: >3.3, or
    - IRI Perspective Taking: < 14.5 for men and < 15.5 for women
- Have above average aggression (>49 at telephone prescreening; >55 at T0 screening) on one of the Buss Perry Subscales.
- No anticipated medication changes for emotions/ behavior during length of study participation; medications for emotions/ behavior must be stable within last 30 days prior to consent at T0 (Screening)
- Have reliable mode of transportation

Exclusion criteria:

- Pre-morbid neurological disorders that could affect mood and cognition (e.g. stroke); does not include controlled seizures
- Progressive central nervous system disorders (e.g. dementia, Parkinson's)
- Developmental disability (e.g., autism, developmental delay);
- Major psychiatric disorders (e.g. schizophrenia, Borderline Personality Disorder);
- Severe Depression and/or perceived risk to self or others (mental health resources will be provided and if suicide risk, approved suicide protocol will be utilized);
- Currently receiving active behavioral therapy for anger.
- On drug research study for irritability, anger, aggression

Note: Participants will *not* be excluded if they do not have caregiver.

Sample Size Calculation. Forty participants (20 per group) will be enrolled to allow for 20% dropout. Thirty-two participants (16 per group) are expected to finish the study. For Aim 1, feasibility and satisfaction percentages of 80%, a sample size of 30 will allow these proportions to be estimated to within 13% using one-sided 95% confidence intervals. For between group effect sizes for Aims 2 and 3, a sample size of 21 per group will detect an effect size of 0.9 standard deviations with 80% power using a two-sided t-test at a .05 level of significance. An ANCOVA model with pre/post correlation of 0.5 can reduce the sample size needed by 25% or to 16 per group. For within group effect sizes for Aims 2 and 3, 16 subjects will provide 80% power to detect a difference in means of .78 standard deviations using a two-sided paired t-test at the .05 level of significance.

Recruitment. The Rehabilitation Hospital of Indiana (RHI), an affiliate of Indiana University (where the PI and Co-I's have offices), will be a primary source of recruitment (see Hammond LOS). IU/RHI is one of 16 nationally recognized Traumatic Brain Injury Model Systems (TBIMS) sites in the United States, making it a strong site for recruitment of this population. On average, RHI admits around 120 individuals with TBI annually; >1,000

individuals with TBI are seen in the RHI outpatient clinics. We will use 1) past RHI inpatients, 2) RHI Outpatient Clinic, 3) RHI Research Registry (n=295), and 4) IU/RHI TBIMS Database (>230 enrolled to date). We will recruit through letters sent by physicians to their patients, pre-clinic chart screening, clinician discussions with patients, flyers posted in RHI, recruitment videos shown around the facility, researchmatch.com and through The Rehabilitation Hospital of Indiana's Facebook page. Flyers will be distributed at TBI support groups and the Brain Injury Association of Indiana. RHI patient letters will be followed with a phone call to confirm receipt of the letter and inquire about interest in the study. See Pre-screen below.

Outcome Measures.

Perspective Taking and Empathic Concern. The Interpersonal Reactivity Index (IRI),[2,3] is a subjective questionnaire that measures perspective-taking, empathic concern, fantasy, and personal distress. Participants use a scale to rate how well statements describe them. Only questions from the perspective-taking and empathic concern subtests will be administered. The IRI has good test-retest reliability and internal reliability.[2,3] It was used in the PI's previous studies on attributions. To determine the subjects' global sense of change in his/ her perspective taking and empathy, the Patient Global Impression of Change (PGIC) regarding these outcomes will be administered. To determine global behavioral changes in perspective taking and empathy as perceived by others, the Caregiver Global Impression of Change (CaGIC)[4,5] will be administered to participant caregivers. Using a 7-point Likert scale, caregivers will be asked to rate the degree of change (1=no change; 7=a great deal better) in the participant's perspective taking and empathy. The PGIC and CaGIC for perspective taking and empathy are considered secondary outcome measures for the study.

Table 1 **Outcome Measure**	**Aim**
IRI Perspective Taking	2
**PGIC and CaGIC perspective taking & empathy	2
Intent and Hostile attributions to scenarios	2
Anger Ratings to scenarios	3
**PROMIS Anger-SF	3
***Aggression Questionnaire**	3
**PGIC and CaGIC aggression	3
CSQ-8	1
*Primary Outcome; **Secondary Outcome	

Attributions of hostility, intent, blame and anger responses to hypothetical scenarios.

Epps Scenarios are 21 brief and standardized hypothetical scenarios, portraying benign, ambiguous, and hostile behaviors.[6] Scenarios have a 7th grade reading level and were sensitive enough to detect hostility bias in our previous studies.[7] On a 9-point scale, participants will first rate how angry they would be if the scenario happened to them, then how hostile, how intentional, and how much to blame they think the character's behavior was. They will then be asked, "what would you do about it?". Participants' responses will be audio recorded to assure we accurately capture their responses. Participants will be alerted before the audio recording begins.

Ambiguous Intentions Hostility Questionnaire: This questionnaire consists of 15 written vignettes describing actions/ situations that were intentional (5), ambiguous (5) and accidental (5). After participants read each vignette and imagine the scenario happening to her or him, they are asked five questions: 1) why the other person (or persons) acted that way toward you (open-ended response later rated by two independent raters; score indicates ''hostility bias''); 2) Whether the other person (or persons) performed the action on purpose (1 ''definitely no'' to 6 ''definitely yes'') using a Likert Scale (Intent score); 3) how angry it would make them feel (1 ''not at all angry'' to 5 ''very angry'') using a Likert scale (anger score); 4) how much they would blame the other person (or persons) (1 ''not at all'' to 5 ''very much'') using a Likert scale (blame score); and 5) how she or he would respond to the situation, (open-ended response).

General Anger and Aggression: Changes in anger and aggression will be evaluated with several different measures. General anger will be measured with the Anger-Affect Scale from the NIH Toolbox Emotion Battery (also known as the Patient Reported Outcomes Measurement Information System; PROMIS) Anger Short Form), and will be a secondary outcome measure.[8] This 5 item subjective questionnaire requires participants to indicate the frequency with which they have been bothered by anger symptoms in the past week using a 5 point Likert scale. Scores are converted to standard scores, and can be used to classify anger severity. Developed as part of NIH's initiatives for better outcomes measurement, this tool has good validity and reliability.[8] Aggression will be measured with the Buss-Perry Aggression Questionnaire (AQ) and the AQ will be the primary outcome measure.[9] The AQ is a standardized measure comprised of 34 statements to assess anger, hostile thoughts, and physical and verbal aggression. Participants rate statements using a 5-point scale. Raw

and scaled scores (adjusted by age and gender) are provided for aggression subcomponents and total aggression. Total aggression will be used for our analyses. The AQ is a widely used and accepted aggression measure, including for TBI studies.[10-14] It has good test-retest reliability (.72-.80), and good internal consistency (.76-.94).[9] To determine the subjects' global sense of change in anger and aggression, the Patient Global Impression of Change (PGIC) regarding these outcomes will be administered. To determine global behavioral changes in anger and aggression as perceived by others, the Caregiver Global Impression of Change (CaGIC)[4,5] will be administered to participant caregivers. Using a 7-point Likert scale, caregivers will be asked to rate the degree of change (1=no change; 7=a great deal better) in the participant's anger and aggression. The PGIC and CaGIC are considered secondary outcome measures.

Emotion Regulation: The Difficulty with Emotion Regulation Scale (DERS)[61] is a 5-point Likert scale that participants use to rate the frequency they *utilize self-regulation behaviors* in response to *general* emotional distress. There are 6 subscales: Lack of Emotional Awareness, Lack of Emotional Clarity, Difficulties Controlling Impulsive Behaviors When Distressed, Difficulties Engaging in Goal-Directed Behavior When Distressed, Non-acceptance of Negative Emotional Responses, and Limited Access to Effective Emotion Regulation Strategies. Items are summed to provide a Total Emotion Dysregulation score. The DERS has high internal consistency, test-retest reliability, and good construct validity.[61] Importantly, because this measure assesses difficulties regulating all types of emotions, it captures different information than that provided by measures specific to anxiety, anger, or depression which can miss more general, yet common, self-regulation problems.

Social Inference/Theory of Mind: The Awareness of Social Inference Test (TASIT)[15] uses short one minute video vignettes to assess emotion and social inferences. There are three subtests that comprise the TASIT: Emotional Evaluation Test (EET); the Social Inference-Minimal (SI-M); and Social Inference-Enriched (SI-E). In the EET subtest, actors portray six different emotions with dynamic facial movements, tone of voice, postures and gestures through short vignettes. These emotions include happy, sad, angry, disgust, fearful, surprised and neutral. In the SI-M test, actors depict social exchanges that are either sincere (text and context are consistent) or sarcastic (text and context are inconsistent). In the SI-E test, the actors perform social skits that depict either sarcasm or lies. Participants must make inferences about what the characters are thinking or believing and their intentions. We will use data from the EET, SI-M, and SI-E subtests for our analyses (3 variables). The TASIT was tested for construct validity and was determined to be able to distinguish the social perceptual abilities of persons with and without brain injury on overall performance.[15]

Depression: Patient Health Questionnaire 9 (PHQ-9):[64] This self-report depression assessment uses a 3-point Likert scale (maximum score 27), with established validity and reliability, including in the TBI population.[64,65] Participants rate the frequency of specified problems during the past 2 weeks.

Anxiety: Generalized Anxiety Disorder Assessment (GAD-7)[16] is a self-report 7-item questionnaire that assesses frequency of seven anxiety symptoms linked to the DSM-IV criteria for GAD.

Alexithymia: The Toronto Alexithymia Scale-20 (TAS-20)[21] is the most widely used self-report questionnaire to measure alexithymia (52-60=moderate alexithymia; ≥61=high alexithymia), and has good test-retest reliability.[21] The TAS-20 is comprised of 3 factors: 1) ability to identify emotions (e.g., I am often confused about what emotion I am feeling); 2) ability to describe emotions (e.g., It is difficult for me to find the right words for my feelings); and 3) externally-oriented thinking (e.g., I prefer to just let things happen rather than understand why they turned out that way).

Satisfaction: We will use the Client Satisfaction Questionnaire (CSQ-8)[17] which is an 8 item instrument with a 4-point Likert scale that participants use to answer questions about perceived satisfaction with the program (e.g., To what extent has our program met your needs?; Have the services you received helped you to deal more effectively with your problems? In an overall, general sense, how satisfied are you with the service you have received?). Scores are summed (8-32) with higher scores indicating greater satisfaction. Normed scores based on 8000 clients are available. The test has good reliability and validity.[17]

Post-Treatment Qualitative Interview: After participants receive the ICAN treatment (Time 2 for ICAN Subjects and Time 3 for WLC subjects), the unblinded RA will Interview the subjects with the following questions. A) Have you noticed any changes in yourself since going through the group therapy? (yes/no); B) What changes

have you noticed (if any)?; and c) What parts of the therapy do you think were the most helpful?

Subsidiary Measures

Discourse Comprehension Test (DCT): Test of reading comprehension for explicit and implicit main idea and details of short passages. There are two versions of the test. One version examines reading comprehension for information the participants read themselves (self-read). The other version tests auditory comprehension. Participants must demonstrate sufficient comprehension in one version or the other (6/8 questions correct or 75% correct). For the auditory version, subjects will listen to the story once, and then answer the 8 yes or no questions. For the self-read version, participants will read the story on his/ her own and this will be followed by eight written yes/no questions, based on the stated (4) and implied (4) information within the story. When the subjects are answering the questions, they may refer back to the text for information, so that the test will truly assess comprehension and not memory skills. Responses are recorded in terms of number of items correct for stated versus implied main ideas and details. Participants will need to achieve 75% accuracy in either the self-read or auditory version.

Cognition/ Executive Functioning: We will assess executive functioning skills for attention, dis-inhibition and verbal fluency. The following tests were chosen based on findings from our preliminary study. Color-word interference (Stroop): Attention and dis-inhibition will be assessed with a commonly used color-word interference test that assesses skills such as basic color naming; word reading; and names of colors written in different color ink (participants must name the color of the ink, not read the words). Verbal Fluency: assesses word association fluency; we will examine letter fluency and category fluency. This test measures a person's ability to make verbal associations to letters and categories. Responses for verbal fluency will be audio recorded for data integrity.

Neurobehavioral Functioning: We will evaluate how participants' caregivers perceive the neurobehavioral functioning of our participants with TBI with the *Frontal Systems Behavior Scale* (FrSBe).[18,19] It is a 46-item subjective questionnaire that measures apathy, dis-inhibition, and executive dysfunction with a 5-point Likert scale. The FrSBe has good reliability and validity[18,19] and has been used in variety of clinical populations, including brain injury and Alzheimer's disease.[20]

Table 1a. ICAN MEASURES AND TIMELINE (Subjects with TBI)

	T0 (screen)	T1	T2	T3 (WLC only)
Consent/ HIPPA*	X			
Demographics*; TBI History*; medication infor and therapy status*	X (inc)			
Med and therapy status update only*		X	X	WLC only
Discourse Comprehension Test*	X (inc)			
Epps stories (attributions and anger to hypothetical scenarios)	X (inc)		X	WLC only
AIHQ Scenarios	X (inc)	X**	X	WLC only
IRI Perspective Taking and Empathic Concern*	X (inc)	X**	X	WLC only
Buss Perry Aggression*	X (inc)		X	WLC only
NIH Toolbox Anger Affect*		X	X	WLC only
TASIT (theory of mind)		X	X	WLC only
PHQ9 (Depression)*	X (inc)		X	WLC only
GAD7 (anxiety)*		X	X	WLC only
TAS-20 (alexithymia)*		X	X	WLC only
DERS (emotion regulation)*		X	X	WLC only
COWAT verbal fluency (cog f)*	X			
Color word interference (Stroop) (cog f)	X			

Patient Global Impression of Change in Anger and Aggression*			X	WLC only
Patient Global Impression of Change in Empathy/ Perspective Taking*			X	WLC only
Client Satisfaction Questionnaire 8 (CSQ-8)*			ICAN only	WLC only
Post-Treatment Qualitative Interview*			ICAN only	WLC only
RA opinion of group allocation			X	

*** May be administered via phone, mail, REDCap survey, video conference call and/or in person; ** These measures will be collected at T1, if participants did not complete them at prior T0 due to protocol change.**

Table 1 b. ICAN MEASURES AND TIMELINE Caregivers			
	T1	T2	T3
FrsBE*	X		
IRI PT and EC (perspective taking and empathy (Aim 1)*	X	X	WLC only
CaGIC Aggression & Empathy/ Perspective Taking*		X	WLC only

Intervention (Intervention to Change Attributions that are Negative; ICAN). In a group therapy format (approximately 5 subjects per group), ICAN will train perspective taking through role-playing and *perspective-positioning* exercises.
Each of the 6 sessions will include the core exercises outlined in Table 2. See publication for more detail.[21]

A) Role Play Video Scenario
Participants will watch video scenarios depicting situations in which a character's motives are ambiguous (e.g., some-one bumped into you). After watching the scenario, participants will be asked to generate possible motives. In other words, produce as many potential explanations for the behavior[22] After generating possible motives, they will be asked to role-play the scenario assuming a positive interpretation of the motive for the observed behavior. After the role-play, participants will be asked questions to process the experience and how the role play changed how they felt about the person's actions.

B) Perspective-Positioning Personal Experiences
Participants will be asked to produce personal examples of situations in which someone's behaviors led to an unpleasant outcome for the participant, and possibly perceived by the participant as purposeful. After introducing this scenario to the group, the participant will take part in a Perspective-positioning exercise in which participants will sit in one chair representing self-perspective (Chair A) to explore his/ her own thoughts and feelings surrounding the situation, and then move to a different Chair (Chair B) to experience the other person's perspective, eliciting their thoughts and feelings. After the Perspective-positioning activity, participants will be asked questions to help them process the experience and how it felt to "be" the other person and what they learned about the other person's feelings and motives for their actions, and how that in turn changed how they felt about the situation and the person's actions.

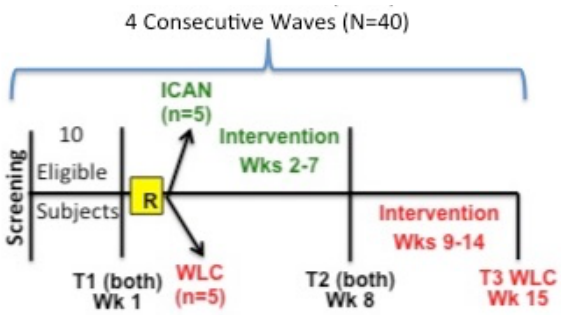
Procedures. This is a randomized waitlist controlled trial. We will recruit waves of approximately 6-10 participants, resulting in the need for 4-7 waves, depending on how large each wave is (N=40). For each wave, participants will be screened for eligibility. Once approximately 6-10 eligible participants have been identified, they will be invited to come back for baseline testing (Time 1). Once they complete Time 1 testing, they will be randomized to the ICAN group (n=3-5 / wave) or the WLC group (n=3-5/ wave). See Figure 2 for design and Tables 1 a and b schedule of events. Each Time 0-4 visit may be split up over multiple sessions in order to keep

testing time reasonable and limiting in-person interactions as a safety precaution due to the COVID-19 pandemic.

The specified weeks outlined for testing and treatment in this protocol are approximate. While specified timing is ideal, many unforeseen and uncontrollable factors will influence the ability to strictly adhere to this timeline. Thus the specified windows for assessment and treatment will fluctuate. Most important to the study integrity is that Time 2 testing for both subject groups occur within an approximately 2-3 week time period (and within approximately 1-2 weeks of ICAN subjects completing treatment). Time 3 testing for WLC should be within approximately 2 weeks of completing treatment. When applicable, video conference call via HIPAA-compliant Zoom Health may be used for testing/data collection. Video will not be recorded when this happens.

Prescreening (telephone script). Some people with TBI (RHI patients/ or former patients) will receive a patient recruitment letter. These letters will be followed by a phone call (see Telephone script) to confirm receipt of the letter and inquire about their interest in the study. Others may call us after receiving one of our recruitment materials. We will use the telephone script to provide them with more detail about the study. The Telephone script will also serve as a Pre-screener to determine if subjects meet initial inclusion criteria in order to reduce any unnecessary burden of coming in to RHI if we can determine early on, that they will not meet inclusion criteria. One of those criteria is "above average aggression" based on a standardized test. If after hearing the description of the study, participants are still interested, they will be administered an aggression questionnaire over the phone along with some inclusion / exclusion questions.

Fig 2. Study Design R=Randomization; T=Time; WLC = Waitlist Control



<u>*Screening/ enrollment (T0)*</u>**.** Participants who indicate an interest in the study and provide informed consent will be screened for meeting inclusion criteria (described above). Screening may be discontinued at any point in the visit if ineligibility is determined before the visit is over. Order of assessments may vary depending on in-person versus remote administration (e.g., over the phone, video conference call) as well as eligibility criteria met at any given point throughout screening.

- Injury criteria will be determined with a demographic and injury interview (later verified via medical report), which also includes a Substance abuse survey.
- <u>Reading comprehension (inclusion)</u>: Following procedures from our past two studies[23,24], we will use the Discourse Comprehension Test (DCT)[25] to determine adequate comprehension. If this criterion is not met, screening will discontinue.
- <u>Aggression (inclusion)</u>: Participants will also have to score higher than average on one of the Buss Perry Aggression Questionnaire subscales. If this criterion is not met, screening will discontinue.
- <u>Depression (inclusion)</u>: Severe Depression and/or perceived risk to self or others will be evaluated. If the participant is severely depressed or a perceived risk to self or others, the participant will be provided with Mental health resources, and if suicide risk, approved suicide protocol will be utilized. Additionally, this person will be excluded, and screening will discontinue.
- <u>Negative attribution and perspective taking (inclusion)</u>: Participants will be presented with two different attribution measures (Epps scenarios or AIHQ) and a perspective taking measure (IRI respective taking). Since the intervention trains perspective taking for negative attribution styles, participants must have abnormal attribution or perspective taking scores on one of these measures.
- Other measures administered at the screening visit (not inclusion criteria), are indicated in Table 1 a (Screen T0) and include COWAT and Stroop Color word interference.

**Past screen failures and re-screening: Several new inclusion criteria have been added since the study start, and it is possible the changes may have altered the eligibility of earlier screened subjects. Subjects who initially failed screening will be allowed to be re-screened. Formerly excluded subjects will be contacted to see if they are interested in being screened again. If they are interested in being screened again, they will be re-consented (explaining they have previously been screened and failed and are now being re-tested) and re-administered all assessments as outlined in the protocol with the exception of subjects who have screen failed within 8 weeks from the new inclusion criteria.

Assessment Visits T1, T2, and T3. Assessments as outlined in Tables 1 a and b (except for the CSQ8 and the Post-Treatment Qualitative Interview; see below) will be conducted by the blinded RA. For T2, the RA will be blinded to group assignment. Because T3 is only WLCs, the RA will no longer be blinded to group assignment at that point. At the end of T2, the blinded RA will complete a survey on their belief regarding group allocation.

Randomization and Stratification. Participants will be randomized to group after T1 testing by the study statistician using a random number generator. Randomization will be blocked and stratified by gender due to expected gender differences in hostility bias. For each treatment wave, ~6-10 participants will be randomly assigned to ICAN or WLC. Once ~6-10 eligible participants have been identified and completed Time 1 testing, the statistician will assign treatment allocation to ICAN or WLC. An unblinded RA will notify the subject of their group allocation. This method will allow blinded Research assistants to remain blinded to group assignment. After the 4-7 waves, 20 participants will have been randomized to ICAN and 20 to WLC (n=40).

Intervention Procedures and Treatment Fidelity. Participants randomized to ICAN will start treatment after Time1. For WLC participants, their treatment will be delayed until after Time 2 data collection. ICAN will be delivered over six sessions each lasting approximately 2 hours, once a week in a group setting (n=~5 participants/ group), for 6 weeks by 1-2 clinical facilitators. Participants will be given a notebook with information and exercises. **Treatment Fidelity**. Steps from an adapted Treatment Fidelity Checklist (NIH Behavior Change Consortium working group on treatment fidelity;[26]) will be used to ensure fidelity of Theory, Provider Training, Treatment Implementation, Treatment receipt, and Treatment Enactment. *Specific to Training:* Facilitators will have a minimum of 2 years of brain injury experience and clinical experience. Facilitators will be trained by the PI and study consultant, Dr. Winegardner (ICAN creator; see LOS), which will involve reviewing a treatment manual and role-play of the ICAN exercises. The treatment manual will consist of a power point presentation outlining treatment procedures and activities, which will also be used to guide the treatment sessions with the subjects. *Delivery*. For all sessions, the power point presentation outlining treatment procedures and activities will be followed and an implementation checklist will be completed.

Satisfaction Survey (CSQ8): To encourage honest feedback and ensure blinding of RA's, an unblinded RA will be responsible for collecting data on the CSQ-8 within approximately 1-2 weeks of completing the intervention (proximal to Time 2 for ICAN subjects and Time 3 for WLC subjects). In the case of withdrawal from treatment, the CSQ-8 may be conducted upon withdraw from treatment, if the participant is agreeable. If participants withdraw, reasons for withdraw will attempt to be collected. At the end of the CSQ-8, the participant is presented with an optional comments section regarding their feedback and thoughts about what they liked/ did not like about the program.

Post-Treatment Qualitative Interview: To encourage honest feedback and ensure blinding of RA's, an unblinded RA will be responsible for administering the post-treatment Interview with the participant over the phone, via mail, email or in person within 1-2 weeks of completing treatment (proximal to Time 2 for ICAN subjects and Time 3 for WLC subjects).

Statistical Analysis Plan.

Primary Analyses. For Aim 1, the proportion of participants who complete at least 5 out of 6 sessions, and the proportion of participants who have satisfaction ratings that are average or higher on the standardized CSQ-8 will be calculated. For between group comparisons for Aims 2 and Aim 3, the primary analysis will be ANCOVA models with T2 measures as the outcomes, treatment group as the explanatory variable, and covariates of wave and T1 outcomes (except CaGIC which will not have T1 data since it is only collected at T2). Effect sizes (ω^2) will be calculated.

Secondary Analyses. WLC control outcomes at T2 will be compared to T1 for the ICAN and WLC group. If there are no significant differences, secondary analyses combining the data from the two treatment groups (assessments before and after intervention) will include ANCOVA, paired t-tests, and estimating effect sizes.

Missing Data. We will compare all baseline variables between subjects who drop out of the study to those who don't using two-sample *t* tests, chi-square tests or their non-parametric equivalents as appropriate. Also, we will collect as much information regarding reasons for missing data as possible. If we find that the missing data appear to be not at random, this important information will be used in designing the larger trial. Because of the small sample size, we will not attempt to model the missing data mechanism in this study.

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