ClinicalTrials.gov Cover Page - Protocol

Title: Talk Therapy by Phone to Promote Treatment for Alcohol Problems
NCT number: NCT03758274
Date (of revised protocol): March 10, 2022

Kenneth R. Conner, PsyD, MPH (Principal Investigator)
Department of Emergency Medicine and Psychiatry
University of Rochester Medical Center

1. STUDY OVERVIEW – PURPOSE AND BACKGROUND

Alcohol use disorder (AUD) is a prevalent and consequential condition (Grant et al., 2015; Hasin & Grant, 2015). Unfortunately, even though obtaining alcohol-related care is associated with both improved drinking outcomes and recovery for those with AUD (Cunningham, 2005; Trim, Schuckit, & Smith, 2013), those with the disorder who end up getting help average going 18 – 20 years before doing so (Blanco et al., 2015). In fact, one of the strongest predictive factors for individuals to seek treatment is whether they have previously sought treatment (Blanco et al., 2015), making that first step all the more crucial to their lifetime prognosis. A recent treatment development study (R21 AA07143) adapted a novel and comparatively brief intervention based on Cognitive Behavioral Therapy delivered over the telephone, and found that it led to significantly increased use of alcohol-related treatment (Stecker, McGovern, & Herr, 2012).

The current study is a phase-II RCT using a two-group parallel design to further and more extensively test the efficacy of this intervention (CBT-TE) to promote use of alcohol-related care and improve drinking outcomes. Participants (n=450) will be recruited through advertisements, screened for eligibility by telephone, and those who are interested in participating and eligible will be consented, followed by administration of part one of a baseline assessment. Next, participants will be randomized to an intervention condition (45-60 minute CBT-TE intervention) or a control condition (being read a NIAAA brochure on AUD treatment). Participants are administered one of these interventions immediately following completion of part two of the baseline assessment which is to be completed within 21 days of part one of the baseline assessment. Follow-up assessments of alcohol-related treatment use and alcohol consumption will be conducted at 1,3, and 6 months after the administration of part one of the baseline assessment, with the assessors blinded to study condition. Prior to June 1, 2022, 9-month and 12-month follow-up assessments will also be conducted. On June 1, 2022 and after, follow-up assessments will be limited to 1, 3, and 6 month follow-ups.

2. CHARACTERISTICS OF THE RESEARCH POPULATION

2.1. Subject Characteristics

Participants will be adult residents of The Greater Rochester, Buffalo, and Syracuse Area with most likely being from Rochester and Buffalo specifically.

a) **Number of Subjects:** Approximately 450 participants will be recruited into the study.

   a. *What is the total (maximum) number of subjects to be enrolled (or their records/specimens accessed) at the University of Rochester (and other institutions if applicable to a multi-center study)? The total should include the number of evaluable subjects (i.e., those who meet eligibility criteria), as well* ***as the number of anticipated screen failures necessary to obtain the enrollment goal****. A subject is considered in the total count once informed consent has been obtained (as applicable). If evaluable subjects who withdraw from the study will be replaced to meet the enrollment goal, this should also be stated here.*

b) **Gender and Age of Subjects:** Participants will be age 18 and older and based on prior experience of the study team (Stecker et al., 2012), we further expect that 56% of participants will be male, 44% will be female, and the mean age will be 40 years old.

c) **Racial and Ethnic Origin:** Based on the demographics of Monroe County, it is expected that the racial composition will be approximately 65% while, 32% black, 3% Asian, and <1% American Indian/Alaskan Native. Ethnic composition is expected to be approximately 13%

Hispanic or Latino and 87% non-Hispanic.

2.2. Inclusion and Exclusion Criteria

a) **Inclusion Criteria:** 1) age 18-plus; 2) score ≥ 16 on AUDIT; 3) within the past 30 days, exceeding the limits for low-risk drinking adopted by NIAAA: >3 standard drinks on any occasion or >7 drinks per week (women); >4 drinks on any occasion or >14 drinks per week (men).

b) **Exclusion Criteria:** 1) unable to communicate with the researcher in English; 2) unable to comprehend the nature of the study; 3) history of alcohol-related care; 4) alcohol withdrawal necessitating medical evaluation; 5) residency outside of The Greater Rochester, Buffalo, and Syracuse Area; 6) Providing false information such as false name, contact information, or study responses.

3. SUBJECT IDENTIFICATION, RECRUITMENT, WITHDRAWAL AND CONSENT

3.1. Method of Subject Identification and Recruitment

Study participants for the proposed project will be recruited within the Greater Rochester, Buffalo and Syracuse Area. The Greater Rochester, Buffalo, and Syracuse area can be defined as the 17 surrounding counties: Orleans, Genesee, Wyoming, Monroe, Livingston, Ontario, Yates, Wayne, Seneca, Steuben, Niagara, Erie, Cortland, Madison, Oneida, Onondaga, and Oswego. Moreover, study participants for the proposed project will be recruited through a varied of online advertisements (e.g., Facebook, Instagram, Digital Banners, Craigslist, Reddit, Paid Search Ads, etc.) and local television, Print, and radio advertisements. Any use of digital advertisements will direct potential participants to a landing page where they can get in contact with the study team. IRB approved documents may also be used (e.g. flyers, billboards, digital signage, banners, etc.) in select targeted locations such as local bars, University affiliated healthcare clinics and hospitals, supermarkets, and other relevant locations. Advertisements will consist of an appropriately brief study description (based on the advertisement method) and contact information for interested persons to privately reach out for further information.

Recruitment for the study will also include the use of ResearchMatch, a national health volunteer registry that was created by several academic Institutions and supported by the U.S. National institutes of health as part of the Clinical Translational Science Award (CTSA) programs. ResearchMatch has a large population of volunteers who have consented to be contacted by researchers about health studies for which they may be eligible. Review and approval for this study and all procedures was obtained from the IRB.

Individuals inquiring about the study will be provided a brief overview and, if interested, screened using the 10-item AUDIT, 4-items from the National Survey of Drug Use and Health (NSDUH; Center for Behavioral Health Statistics and Quality, 2015) to determine if alcohol use within the past 30 days exceeds the limits for low-risk drinking adopted by NIAAA, and screening items on the Alcohol Use Disorders and Associated Disabilities Interview (AUDADIS; Grant et al., 2011) to determine if there is any history of professional alcohol-related treatment.

3.2. Circumstances for Withdrawal

Participants may be withdrawn from the study if they cannot keep appointments for study visits, if they cannot complete study activities, if study funding has been terminated, if alcohol withdrawal necessitating medical is required, or if subjects provide false information (false name, contact information, study responses etc.).

If a subject is withdrawn early, they will be notified of the following: No further information from them is required, they are being discontinued from the study, and that no further research session will be scheduled or take place. In addition, if the study subject is withdrawn before

treatment (a one-time phone intervention meeting), then treatment will not be provided. However, if it is discovered that the subject should be withdrawn after the treatment was provided, then the delivery of the treatment would not be affected but any subsequent follow-up assessments would be discontinued. Furthermore, no follow-up data will be continued to be collected and the information that they provided may not be used in study analysis and will be protected (see confidentiality of data and information storage). Lastly, these subjects will be replaced.

3.3. Process of Consent

Research staff will thoroughly go over the consent form with the participant by phone while clarifying any points as needed and answering all questions the subject may have. The informed consent will also be done with the aid of an interpreter for deaf/hard of hearing individuals as needed.

The informed consent form will contain a detailed description of the study procedures, along with statements regarding participants' rights to withdraw from the procedure at any time without consequences. It will be explained to participants in easy-to-understand language. The limits of confidentiality will also be explained, including the potential to break confidentiality in the acute risk of suicidal behavior or violence, or disclosures of unreported physical or sexual abuse of a child. This will occur prior to any data collection and the consent form will include text regarding the retention and use of that data.

Research staff will sign their name at the bottom of the form to show that they have explained the research, answered all questions to the subject's satisfaction, that the subject has demonstrated comprehension of the information, and provided oral consent to participate.

4. METHODS AND STUDY PROCEDURES

4.1. Study Procedures and Assessments

4.1a. Assessments: Nineteen relatively structured assessments will be used, which are described along with the schedule of administration in the table below. Each measure has been included in the online IRB application as appropriate. Supervision of the phone assessments for quality assurance (QA) will come in three forms:

1. The PI meets monthly with the IRB approved assessors to avoid drift in interviews, discuss any difficulties that arise, and answer any questions regarding the phone assessments.
2. The PI at the University of Rochester Medical Center or a Co-I at Syracuse University will act as a supervisor during select phone assessments. The purpose of this is to effectively complete a "check-in" to ensure that drift is not occurring and to provide feedback that might arise pertaining to assessment style and technique. The supervisor would be an IRB-approved Co-I or PI on the study team. The supervision of the phone assessment will occur by means of a three-way call, and when a supervisor does observes an assessment, the subject will be notified by the assessor at the start of the phone assessment (e.g. "my supervisor will be monitoring this phone call for quality assurance purposes"). At this point, the supervisor may also introduce himself/herself. Moreover, we will record in REDCap that instance for which live supervision was provided for a given follow-up assessment including the subject number, date of the follow-up assessment, the study assessor performing the assessment, and the investigator providing supervision (The co-I at Syracuse will not be receiving data, as his role pertains to provide QA). After the completion of the phone assessment (at this time the subject would have disconnected), the supervisor and the assessor would stay on the call and verbally go over the quality of the assessment (if time allows) or schedule a time to go over the feedback. The feedback to the assessor would address the following topics:

a. Opening the interview:
b. Establishing rapport:
c. Neutrality:
d. Listening:
e. Reading items verbatim:
f. Voice clarity:
g. Information recorded accurately and completely:
h. Probes used as needed:
i. Closing the interview:
j. Safety/human subjects' issues:

3. Lastly, Dr. Conner provides ongoing oversight of supervision through a weekly study conference call that he chairs and that includes all sub-investigators including sub-investigators from collaborating institutions.. During this call, the results of any supervisory observations will be discussed and any challenges that arose addressed. If there are instances that warrant further discussion, for example because an interview was problematic or an assessor requires further training, then Dr. Conner and the Co-I providing the supervision will schedule a time to talk 1:1 to make a plan for providing further training and supervision to the assessor. More specifically, Dr. Conner and Stephen Maisto, Co-I and Professor at Syracuse University, will be provide the supervision to the study assessors. Drs. Conner and Maisto are on the weekly study conference calls as a matter of course, facilitating such coordination and oversight.

Measure	*Screen*	*Baseline*	*Follow-Ups*	*Purpose*
Preliminary Demographics	✓			*Basic Information*
NSDUH	✓		✓	*Eligibility in Terms of AUG (Short-Term)*
Lifetime Treatment Use	✓			*Eligibility in Terms of Services*
Substance-related sleep problems (SUSS)	✓		✓	*Sleep QOL Assessment*
AUDIT	✓			*Eligibility in Terms of AUD (Long-Term)*
Supplemental Demographics		✓		*Describe Sample*
TLFB		✓	✓	*Substance Use*

AUDADIS-V		✓		*AUD Symptoms*
ASSIST		✓	✓	*Substance abuse in the past 30 days*
DMQ-R		✓	✓	*To assess the impacts of COVID-19 on drinking to cope with difficulties and emotion*
INDUC		✓	✓	*Substance Use*
PHQ-2 and Standardized PHQ-4 Screener		✓	✓	*Assess COVID-19 on sad mood & suicide risk screening triggered by PHQ-2*
Treatment Use Update			✓	*Utilization of AUD-Related Services*
ATOS COVID-19		✓	✓	*Assessing the impact of COVID-19 on a subject's lifestyle*
Theory of planned Behavior (TPB)		✓	✓	*Assessing the impact of COVID-19 related to telehealth*
*IMPASS**		✓	✓	*Guides Therapy Session and Examine Change in Beliefs*
WHOQOL – BREF		✓	✓	*QOL Assessment*
Insomnia Sleep Index		✓	✓	*Sleep QOL Assessment*
Debriefing Questions			✓	*Understanding a Subject's experience*

*Administered immediately prior to delivery of the intervention condition or the control condition.

4.1b. Intervention Condition: Cognitive Behavioral Therapy for Treatment Engagement (CBT-TE) is a brief, tailored on-on-one session delivered by telephone lasting 45-60 minutes (Stecker, 2010). The intervention targets a change in the beliefs that influence whether or not someone initiates behavioral health treatment. During the session, participants are given a brief introduction to CBT and informed that it is based on the theory that cognitions, feelings, and behaviors all interact with each other. Therefore, since thoughts are modifiable, changing thoughts may lead to change in behavior. Based on a 3-step process, participants will be asked to

dispute beliefs about Alcohol Use Disorder (AUD) treatment elicited by the 39-item Identifying Modifiable Perceptions of Services Scale (IMPASS; Stecker, Fortney, Hamilton, & Azjen, 2007). A maximum of three beliefs will be discussed during the session and the participant and the interventionist will mutually agree upon beliefs to be discussed. All individuals assigned to the treatment condition will be administered the same structured intervention; however, content discussed within the session will differ for each participant based on their responses and thoughts surrounding the beliefs discussed within the session. Therefore, the intervention is structured but is not scripted.

4.1c. Control Condition: Control participants will be sent a NIAAA brochure on AUD treatment, either electronically or through regular mail. They will then be read the brochure over the phone by a study staff member, which is designed to offset effects that are attributable to attention. This brochure, titled "Treatment for Alcohol Problems: Finding and Getting Help" is included in the online IRB application.

4.2. **Payment for Participation**

Participants will be paid $60 following completion of the two-part baseline assessment and will be paid additional $20 if part-two of the baseline assessment is completed within 7 days of part-one. Participants will also be paid $40 following the completion of each follow-up assessment and will be paid an additional $40 following the completion of the last follow-up assessment (whether the last follow-up occurs at 6 months, 9 months, or 12 months following the baseline assessment) if all prior follow-ups are completed. This would provide a maximum total compensation of $320 for individuals completing 1, 3, 6, 9, and 12 month follow-ups; it would provide a maximum total compensation of $280 for individuals completing 1, 3, 6, and 9 month follow-ups; and a maximum total compensation of $240 for individuals completing 1, 3, and 6 month follow-up assessments Payments will be made securely by check, gift card, cash, or electronically (Department payment cards will be used as the mechanism for purchasing e-gift cards from Amazon).

5. REPORTABLE EVENTS

5.1 **Adverse Events**

All adverse events will be identified and reported to Dr. Conner, who will be responsible for the timely reporting of adverse events to the required oversight entities. Such events will be documented in the adverse event log maintained by the study team. All adverse events will also be communicated to the IRB in the form of continuing reviews, and an annual report will be submitted to the NIAAA project officer summarizing adverse events. Adverse events that are determined to be unanticipated, study-related, and serious will be reported by Dr. Conner to the IRB, and the NIAAA Project Officer within 48 hours of discovery. All adverse events will be followed up by Dr. Conner in a timely way as to prevent any risks to participants, in coordination with the IRB.

5.2 **Suicidality**

The PHQ-2 and Standardized P4 Screener measure may result in the discovery of suicidal thoughts or behavior . Specifically, if depressed mood or lack of interest or pleasure is identified on the PHQ-2, it triggers administration of PHQ-9 item #9. If the subject endorses thoughts of self-harm on item #9, then the standardized P4 screener is administered which categorizes individuals into "minimal risk", "lower risk", and "higher risk." If a subject is determined to be at "lower risk" or "higher risk" on the P-4, following the call, the assessor conducting the assessment will contact the PI (Dr. Conner) or another qualified investigator on the research team who will review the assessment and determine if a follow-up call with the subject may be beneficial to promote safety. If this is the case, Dr. Conner or another qualified investigator will seek to follow-up with the subject as needed by telephone to obtain further assessment and assist them as necessary. Typically, subjects deemed at "higher risk" would warrant such a follow-up call, unless there are mitigating

circumstances to suggest it is not clinically indicated, whereas subjects deemed at "lower risk" would be less likely to require follow-up. There are a broad range of potential responses to address risk including further assessment by phone, making a plan to reach out for additional support or formal treatment, and, in rare circumstances, initiating an emergency intervention (e.g., calling 911).

6. RISK/BENEFIT ASSESSMENT

6.1. Risks to Subjects

Risks include that the subjects will be identified as participants in an alcohol treatment study, inadvertent breach of confidentiality concerning drinking behavior, or that assessments, the CBT-TE, or the control intervention may temporarily adversely affect an individual's well-being (e.g., experience discomfort while discussing the consequences of alcohol use).

6.2. Benefits to Subjects

Benefits to participants include the possibility of receiving an intervention, at no cost, with preliminary evidence of efficacy to promote entry into alcohol-related care.

6.3. Alternatives to Participation

The alternative to participation is not to participate.

7. CONFIDENTIALIATY OF DATA AND INFORMATION STORAGE

With respect to confidential data collection, all project data will be collected by trained research interviewers using IRB approved data collection instruments. In addition, research interviewers and interventionists will receive on-going supervision through the course of the project. All data will be stored in locked file cabinets and password protected databases and will be accessible only by appropriate research personnel. All subject data will be identified by a unique number. Subject identifiers (e.g., name, address, telephone number) will be stored separately from research data and linkable through a unique identification number. The control and treatment interventions to be used in the project have been implemented in prior research without causing serious harm (Stecker et al., 2012). All study personnel will receive mandatory education in human subjects' protection. All data will be used for research purposes only, and will not be revealed without the participants' written consent unless to protect individuals immediate safety. All paper data will be kept in locked files in a locked study office. Computerized data will be stored in databases on a secure, password protected server that is regularly backed up. As an added protection, NIH funded studies are covered by a Federal Certificate of Confidentiality.

We will share data with other researchers and use widely used measures that will facilitate harmonization with other research. However, the data sharing agreement involves sharing only de-identified data with other investigators and the use of data-sharing agreements that provide for: (1) a commitment to using the data only for research purposes and not to identify any individual participant; (2) a commitment to securing the data using appropriate computer technology; and (3) a commitment to destroying or returning the data after analyses are completed.

All research and clinical information obtained is kept confidential unless the subject is an immediate danger to him/herself or to others. Subject well-being will be monitored throughout the study. If the clinical information obtained in the course of research assessments pertains to patient safety (e.g., intent to harm one's self or others) then, to promote safety, confidentiality will not be maintained, and appropriate treating professionals will be informed. During crisis situations, this clinical information may be provided to other clinicians (or family members) in order to facilitate appropriate treatment and minimize the risks of self-harm or harm to others. This information may include the subject's medical history, financial and social resources, and history of suicidal behavior, if known.
Confidentiality is the ethical and/or legal right that information, such as research data, will be held secret and safeguarded from disclosure unless consent is provided permitting disclosure.

8. DATA ANALYSIS AND DATA MONITORING

8.1. Planned Statistical Analysis

What are the statistical/analytical methods to be used for the collected research data and to meet the goals of any specific endpoints that will be analyzed?

8.2. Data and Safety Monitoring

1. *The DSM plan must designate an experienced, qualified professional (usually the PI) who can distinguish a serious adverse event (SAE) from a non-serious adverse event (AE).*

   PI Response: Dr. Kenneth R. Conner, contact PI of this study, will review all adverse events, and decide if they are serious or non-serious adverse events. As needed, he will consult with multi-PI Dr. Tracy Stecker on these determinations. Dr. Conner has the expertise to make these judgments and will be available to make any necessary decisions within the reporting timeframe.

2. *The DSM plan must indicate that serious adverse events will be reported to the local IRB and to the NIAAA project officer within 48 hours.*

   PI Response: Any reportable serious adverse events experienced in this study (i.e., those that are serious, unanticipated, and study related) will be reported to the University of Rochester Medical Center (URMC) IRB, and to the NIAAA project officer (Dr. Roach) within 48 hours of the event.

3. *The DSM plan must indicate that an annual report will be submitted to the NIAAA Project Officer summarizing all adverse events.*
   PI Response: An annual report will be submitted to the NIAAA Project Officer summarizing all adverse events.

4. *The DSM plan must specify that female subjects who are pregnant, nursing, or not using effective methods of birth control will be excluded from studies involving the administration of alcohol and/or drugs.*

   PI Response: N/A

5. *The DSM plan must indicate that trained personnel will be present or on call when human laboratory studies of alcohol or other drug intake are conducted.*

   PI Response: N/A

6. *For studies in which alcohol is administered, the DSM plan must indicate that NIAAA guidelines for the administration of alcohol will be followed. These guidelines can be found at the following web address: http://www.niaaa.nih.gov/extramural/job22.htm*

   PI Response: N/A

7. *If the study has a follow-up phase, there must be a specific plan for referral to treatment during follow-up of any respondent requiring additional intervention due to significantly increased alcohol consumption or serious psychiatric/medical symptoms.*

   PI Response: This study will follow participants for 12 months. Any information that we

collect at any point in the study that suggests that a participant may require or could be helped by it will be referred to treatment as indicated.

8. *The DSM plan must indicate that all adverse events during follow-up will be reported (SAEs within 48 hours) to the IRB and NIAAA.*

   PI Response: All adverse events during follow-up will be reported to the URMC IRB, and to NIAAA.

9. *The DSM plan must briefly describe the procedures for data quality assurance and confidentiality.*

   PI Response: Procedures will be in place to assure data quality and participant confidentiality. The procedures for data quality are: a) Adhere to CONSORT guidelines for conducting and reporting two-group parallel RCT's (Begg et al., 1996; Moher et al., 2001; Schulz et al., 2011). b) Regular meetings of the multi-PIs and the project staff to review any concerns regarding participant data. c) All data will be entered by trained project staff and will be double checked for accuracy. d) Assessment data will be entered into REDCap (Research Electronic Data Capture), a widely software toolset and workflow methodology that was created specifically around HIPAA-Security guidelines. The procedures for confidentiality are: a) Respondent records [questionnaires, computer data] will be labeled by code number only. b) All research personnel will be trained in procedures in assuring confidentiality, and only trained personnel will have access to subject records. c) Individual data will never be presented. The data will be analyzed and reported only in terms of group outcomes. d) The project will be covered by a Federal Certificate of Confidentiality.

10. *Phase III clinical trials must have an independent data and safety monitoring board.*

    PI Response: N/A

.

9. REFERENCES

9.1. Grant BF, Goldstein RB, Saha TD, Chou SP, Jung J, Zhang H, et al. (2015). Epidemiology of *DSM-5* alcohol use disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions III. *JAMA Psychiatry, 72*, 757–766.

9.2. Hasin DS, Grant BF (2015). The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) Waves 1 and 2: Review and summary of findings. *Social Psychiatry and Psychiatric Epidemiology, 50*, 1609–1640.

9.3. Cunningham J (2005). Short-term recovery from alcohol abuse or dependence: Any evidence of a relationship with treatment use in a general population sample? *Alcohol and Alcoholism, 40*, 419–421.

9.4. Trim RS, Schuckit MA, Smith TL (2013). Predictors of initial and sustained remission from alcohol use disorders: Findings from the 30-year follow-up of the San Diego Prospective Study. *Alcoholism: Clinical and Experimental Research, 37*, 1424–1431

9.5. Blanco C, Iza M, Rodriguez-Fernandez JM, Baca-Garcia E, Wang S, Olfson M. (2015). Probability and predictors of treatment-seeking for substance use disorders in the U.S. *Drug and Alcohol Dependence, 149*, 136-144.

9.6. Stecker T, McGovern M, Herr B (2012). An intervention to increase alcohol treatment engagement: A pilot trial. *Journal of Substance Abuse Treatment, 43,* 161-167.

9.7. Center for Behavioral Health Statistics and Quality. National survey on drug use and health (NSDUH): Summary of methodological studies, 1971–2014. Retrieved May 15, 2015.

9.8. Grant BF, Goldstein RB, Chou SP, et al. (2011). *The Alcohol Use Disorder and Associated Disabilities Interview Schedule–Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition Version (AUDADIS-5).* Rockville, MD: National Institute on Alcohol Abuse and Alcoholism.

9.9. Stecker T, Fortney J, Hamilton F, Sherbourne C, Ajzen I (2010). Engagement in mental health treatment among veterans returning from Iraq. *Patient Preferences and Adherence, 4*, 45-49.

9.10. Stecker T, Fortney JC, Hamilton F, Azjen I (2007). An assessment of beliefs about mental health care among veterans who served in Iraq. *Psychiatric Services, 58*, 1358-1361