YALE UNIVERSITY
HUMAN INVESTIGATION COMMITTEE

Application to Involve Human Subjects in Biomedical Research
100 FR1 (2011-2)

Please refer to the HIC website for application instructions and information required to complete this application. The Instructions are available at http://www.yale.edu/hrpp/forms-templates/biomedical.html Submit the original application and two (2) copies of all materials including relevant sections of the grant which funds this project (if applicable) to the HIC.	**HIC OFFICE USE ONLY**	
	DATE STAMPED-RECEIVED	PROTOCOL NUMBER

SECTION I: ADMINISTRATIVE INFORMATION

Title of Research Project: Computer Based Training in CBT for Spanish-Speaking Alcohol Users			
Principal Investigator: Kathleen M. Carroll, PhD		**Yale Academic Appointment:** Professor	
Campus Address: 40 Temple Street, Suite 6C; New Haven, CT 06511			
Campus Phone: 203-737-1544	**Fax:** 203-737-1371	**Pager:**	**E-mail:** kathleen.carroll@yale.edu
Protocol Correspondent Name & Address (*if different than PI*): Joanne Corvino; 40 Temple Street, Suite 6C; New Haven, CT 06511			
Campus Phone: 203-785-2012	**Fax:** 203-737-1371	**E-mail:** Joanne.corvino@yale.edu	
Yale Cancer Center CTO Protocol Correspondent Name & Address (*if applicable*): N/A			
Campus Phone:	**Fax:**	**E-mail:**	

Faculty Advisor:(required if PI is a student, resident, fellow or other trainee) ☒ **NA**		**Yale Academic Appointment:**	
Campus Address:			
Campus Phone:	**Fax:**	**Pager:**	**E-mail:**

APPROVED BY THE YALE UNIVERSITY IRB 6/13/2019

Investigator Interests:
Does the principal investigator, co-investigator, or any other responsible research team member, or any of their family members (spouse, child, domestic partner) have an incentive or interest, financial or otherwise, that may be viewed as affecting the protection of the human subjects involved in this project, the scientific objectivity of the research or its integrity? See Disclosures and Management of Personal Interests in Human Research http://www.yale.edu/hrpp/policies/index.html#COI

√ Yes ☐ No

If yes, list names of the investigator or responsible person:

Dr. Carroll holds the copyright to CBT4CBT. Dr. Carroll has disclosed her ownership in the entity that distributes CBT4CBT to the Provost's COI committee, and has an approved COI plan in place for her other CBT4CBT-related research. A similar strategy will be used for the current project (use of Multiple PIs, quarterly DSMB reviews, a sponsor-initiated DSMP, use of an urn randomization program for allocation of participants to treatment, and transparency to the research community at large by availability of anonymized trial datasets on our website. All investigators and study staff will be informed of the conflict and the strategies used to manage it.

All Yale University and Yale New Haven Hospital individuals listed as co-investigators must have a current financial disclosure form on file with the University's Conflict of Interest Office. If this has not been done, the individual(s) should follow this link to the COI Office Website to complete the form: http://www.yale.edu/coi/

NOTE: The requirement for maintaining a current disclosure form on file with the University's Conflict of Interest Office extends primarily to Yale University and Yale-New Haven Hospital personnel. **Whether or not they are required to maintain a disclosure form with the University's Conflict of Interest Office, all investigators and individuals deemed otherwise responsible by the PI who are listed on the protocol are required to disclose to the PI any interests that are specific to this protocol.**

SECTION II: GENERAL INFORMATION

1. **Performing Organizations:** Identify the hospital, in-patient or outpatient facility, school or other agency that will serve as the location of the research. Choose all that apply:

a. Internal Location[s] of the Study:

☐ Magnetic Resonance Research Center (MR-TAC)
☐ Yale Cancer Center/Clinical Trials Office (CTO)
☐ Yale Cancer Center
☐ Yale-New Haven Hospital
☐ Specify Other Yale Location:
☐ PET Center
☐ YCCI/Church Street Research Unit (CSRU)
☐ YCCI/Hospital Research Unit (HRU)
☐ YCCI/Keck Laboratories
☐ Cancer Data Repository/Tumor Registry

b. External Location[s]:

☐ APT Foundation, Inc.
☒ Connecticut Mental Health Center
☐ Clinical Neuroscience Research Unit (CNRU)
☐ Haskins Laboratories
☐ John B. Pierce Laboratory, Inc.
☐ Veterans Affairs Hospital, West Haven

☒ Other Locations, Specify: ☐ International Research Site

Substance Abuse Treatment Unit (SATU) and Multi-Cultural Ambulatory Addiction Services (MAAS)
One Long Wharf Drive
New Haven, CT
426 East Street
New Haven, CT

c. Additional Required Documents *(check all that apply)*: ☒ N/A

☐ *YCCI-Scientific and Safety Committee (YCCI-SSC)	Approval Date:
☐ *Pediatric Protocol Review Committee (PPRC)	Approval Date:
☐ *YCC Protocol Review Committee (YRC-PRC)	Approval Date:
☐ *Dept. of Veterans Affairs, West Haven VA HSS	Approval Date:
☐ *Radioactive Drug Research Committee (RDRC)	Approval Date:
☐ YNHH-Radiation Safety Committee (YNHH-RSC)	Approval Date:
☐ Magnetic Resonance Research Center PRC (MRRC-PRC)	Approval Date:
☐ YSM/YNHH Cancer Data Repository (CaDR)	Approval Date:

☐ Dept. of Lab Medicine request for services or specimens form

Approval from these committees is required before final HIC approval is granted. See instructions for documents required for initial submission and approval of the protocol. Allow sufficient time for these requests. Check with the oversight body for their time requirements.

2. **Probable Duration of Project:** State the expected duration of the project, including all follow-up and data analysis activities.

The duration of the project in its entirety will be 5 years and consists of two phases. Phase 1 (Years 1-2) will be devoted to adapting and developing CBT4CBT for use with Spanish-speaking individuals with alcohol use disorders. In Phase 2 (Years 3-5) Spanish-speaking individuals seeking treatment for alcohol use disorders will be invited to participate in a randomized trial evaluating the feasibility, efficacy, and durability of adding CBT4CBT to standard treatment.

3. **Targeted Enrollment:** Give the number of subjects:

a. targeted for enrollment at Yale for this protocol 90 If this is a multi-site study, give the total number of subjects targeted across all sites N/A
b expected to sign the consent form 125
c. expected to complete some or all interventions for this protocol? 90
d. target enrollment for pilot: __10___

4. **Research Type/Phase: (Check all that apply)**

a. **Study Type**

☒ Single Center Study
☐ Multi-Center Study
Does the Yale PI serve as the PI of the multi-site study? Yes ☐ No ☐
☐ Coordinating Center/Data Management
☐ Other:

b. **Study Phase** ☐ **N/A**

☐ Pilot ☒ Phase I ☐ Phase II ☐ Phase III ☐ Phase IV
☐ Other (*Specify)*

c. **Area of Research: (Check all that apply)** Note that these are overlapping definitions and more than one category may apply to your research protocol. Definitions for the following can be found in the instructions section 4c:

☒ Clinical Research: Patient-Oriented
☐ Clinical Research: Epidemiologic and Behavioral
☐ Translational Research #1 ("Bench-to-Bedside")
☐ Translational Research #2 ("Bedside-to-Community")
☒ Clinical Research: Outcomes and Health Services
☐ Interdisciplinary Research
☐ Community-Based Research

5. Is this study required to be registered in a public database? Yes ☒ No ☐
If yes, where is it registered?
Clinical Trials.gov registry ☒
Other (*Specify*)

6. Will this study have a billable service as defined by the Billable Service Definition?
Yes ☐ No ☒
If you answered "yes", this study will need to be set up in Patient Protocol Manager (PPM)
http://medicine.yale.edu/ymg/systems/ppm/index.aspx

7. Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities? Yes ___ No _X__ *If Yes, please answer questions a through c and note instructions below. If No, proceed to Section III.*
a. Does your YNHH privilege delineation currently include the **specific procedure** that you will perform? N/A

b. Will you be using any new equipment or equipment that you have not used in the past for this procedure? N/A

c. Will a novel approach using existing equipment be applied? N/A

If you answered "no" to question 7a, or "yes" to question 7b or c, please contact the YNHH Department of Physician Services (688-2615) for prior approval before commencing with your research protocol.

SECTION III: FUNDING, RESEARCH TEAM AND TRAINING

1. **Funding Source:** Indicate all of the funding source(s) for this study. Check all boxes that apply. Provide information regarding the external funding source. This information should include identification of the agency/sponsor, the funding mechanism (grant or contract), and whether the award is pending or has been awarded. Provide the M/C# and Agency name (if grant-funded). If the funding source associated with a protocol is "pending" at the time of the protocol submission to the HIC (as is the case for most NIH submissions), the PI should note "Pending" in the appropriate section of the protocol application, provide the M/C# and Agency name (if grant-funded) and further note that University (departmental) funds support the research (until such time that an award is made).

PI	Title of Grant	Name of Funding Source	Funding	Funding Mechanism
Kathleen M. Carroll, Ph.D.	Computer Based Training in CBT for Spanish-Speaking Substance Users	NIAAA	☒ Federal ☐ State ☐ Non Profit ☐ Industry ☐ Other For Profit ☐ Other	☒ Grant-M# R01 AA025605 ☐ Contract# ☐ Contract Pending ☐ Investigator/Department Initiated ☐ Sponsor Initiated ☐ Other, Specify:

IRB Review fees are charged for projects funded by Industry or Other For-Profit Sponsors. Provide the Name and Address of the Sponsor Representative to whom the invoice should be sent. ***Note: the PI's home department will be billed if this information is not provided.***

Send IRB Review Fee Invoice To:

Name:
Company:
Address:

2. **Research Team:** List all members of the research team. Indicate under the affiliation column whether the investigators or study personnel are part of the Yale faculty or staff, or part of the faculty or staff from a collaborating institution, or are not formally affiliated with any institution. **ALL members of the research team MUST complete Human Subject Protection Training (HSPT) and Health Insurance Portability and Accountability Act (HIPAA) Training before they may be listed on the protocol. See NOTE below.**

	Name	Affiliation: Yale/Other Institution (Identify)	NetID
Principal Investigator	Kathleen M. Carroll, PhD	Yale	kmc3
Role: Co-Investigator	Manuel Paris, PsyD	Yale	mp267
Role: Co-Investigator	Luis Miguel Añez Nava, PsyD	Yale	lma27
Role: Project Director	Michelle Alejandra Silva, PsyD	Yale	ms664
Role: Research Associate	Melissa Gordon	Yale	mag85
Role: Research Assistant	Yudilyn Jaramillo	Yale	YJ89
Role: Data Management	Tami Frankforter	Yale	Tlf7
Role: Research Associate	Joanne Corvino	Yale	Jkc9

NOTE: The HIC will remove from the protocol any personnel who have not completed required training. A personnel protocol amendment will need to be submitted when training is completed.

SECTION IV: PRINCIPAL INVESTIGATOR/FACULTY ADVISOR/ DEPARTMENT CHAIR AGREEMENT

As the **principal investigator** of this research project, I certify that:

- The information provided in this application is complete and accurate.
- I assume full responsibility for the protection of human subjects and the proper conduct of the research.
- Subject safety will be of paramount concern, and every effort will be made to protect subjects' rights and welfare.
- The research will be performed according to ethical principles and in compliance with all federal, state and local laws, as well as institutional regulations and policies regarding the protection of human subjects.
- All members of the research team will be kept apprised of research goals.
- I will obtain approval for this research study and any subsequent revisions prior to my initiating the study or any change and I will obtain continuing approval of this study prior to the expiration date of any approval period.
- I will report to the HIC any serious injuries and/or other unanticipated problems involving risk to participants.
- I am in compliance with the requirements set by the University and qualify to serve as the principal investigator of this project or have acquired the appropriate approval from the Dean's Office or Office of the Provost, or the Human Subject Protection Administrator at Yale-New Haven Hospital, or have a faculty advisor.
- I will identify a qualified successor should I cease my role as principal investigator and facilitate a smooth transfer of investigator responsibilities.

_____ _____

PI Name (PRINT) and Signature Date

As the **faculty advisor** of this research project, I certify that:

- The information provided in this application is complete and accurate.
- This project has scientific value and merit and that the student or trainee investigator has the necessary resources to complete the project and achieve the aims.
- I will train the student investigator in matters of appropriate research compliance, protection of human subjects and proper conduct of research.
- The research will be performed according to ethical principles and in compliance with all federal, state and local laws, as well as institutional regulations and policies regarding the protection of human subjects.
- The student investigator will obtain approval for this research study and any subsequent revisions Prior to initiating the study or revision and will obtain continuing approval prior to the expiration of any approval period.
- The student investigator will report to the HIC any serious injuries and/or other unanticipated problems involving risk to participants.
- I am in compliance with the requirements set forth by the University and qualify to serve as the faculty advisor of this project.

_____ _____

Advisor Name (PRINT) and Signature Date

Department Chair's Assurance Statement

Do you know of any real or apparent institutional conflict of interest (e.g., Yale ownership of a sponsoring company, patents, licensure) associated with this research project?

☐ Yes (provide a description of that interest in a separate letter addressed to the HIC.)
☒ No

As Chair, do you have any real or apparent protocol-specific conflict of interest between yourself and the sponsor of the research project, or its competitor or any interest in any intervention and/or method tested in the project that might compromise this research project?

☐ Yes (provide a description of that interest in a separate letter addressed to the HIC)
☒ No

I assure the HIC that the principal investigator and all members of the research team are qualified by education, training, licensure and/or experience to assume participation in the conduct of this research trial. I also assure that the principal investigator has departmental support and sufficient resources to conduct this trial appropriately.

John H. Krystal, MD

_____ _____

Chair Name (PRINT) and Signature Date

Psychiatry

_____

Department

YNHH Human Subjects Protection Administrator Assurance Statement

Required when the study is conducted solely at YNHH by YNHH health care providers.

As Human Subject Protection Administrator (HSPA) for YNHH, I certify that:

- I have read a copy of the protocol and approve it being conducted at YNHH.
- I agree to notify the IRB if I am aware of any real or apparent institutional conflict of interest.
- The principal investigator of this study is qualified to serve as P.I. and has the support of the hospital for this research project.

_____ _____

YNHH HSPA Name (PRINT) and Signature Date

For HIC Use Only

_____ _____

Date Approved **Human Investigation Committee Signature**

This protocol is valid through _____

SECTION V: RESEARCH PLAN

1. **Statement of Purpose:** State the scientific aim(s) of the study, or the hypotheses to be tested.

The goal of this project is to address a major challenge in health disparities as defined by NIH and the Institute of Medicine, specifically, the need for accessible, effective, evidence-based treatments for Latino/as.

Specific aims are as follows:

- To adapt our existing CBT4CBT program for use with Spanish-speaking alcohol users in a web-based platform

- To conduct an 8-week randomized trial evaluating the feasibility and efficacy of adding CBT4CBT-Spanish to treatment as usual in a community based treatment program in a population of 90 Spanish-speaking individuals who meet current criteria for alcohol use disorder

- To evaluate the long-term durability and/or delayed emergence of treatment effects through a six month follow-up after termination of the study treatments. Given previous evidence regarding the durability of standard clinician-delivered CBT[41] and computer-assisted CBT4CBT[25], we hypothesize that CBT4CBTSpanish will be significantly more effective than standard treatment alone through the follow-up.

2. **Background:** Describe the background information that led to the plan for this project. Provide references to support the expectation of obtaining useful scientific data.

A **Health disparities among Latinos, accessibility of evidence based therapies (EBTs).**

Latinos currently represent 17% of the total U.S. population and the figure is expected to almost double by the year 2060[24] (*NB*: we use the term Latino to refer to individuals of Mexican, Puerto Rican, Cuban, Dominican, Central and South American, and Spanish descent). Although recognized as the country's largest ethnic minority group, there is ample evidence that Latinos experience circumstances that limit their access to culturally and linguistically appropriate evidence-based behavioral health treatments, compromising treatment outcomes[2, 3, 25-27]. This is highly evident in our limited ability to adequately recognize and treat substance use among Spanish-speaking Latinos and alcohol use disorders in particular[3, 28-30]. Latinos are more likely to engage in heavier drinking and binge drinking than non-Latino Whites, and when they enter treatment, they represent the ethnic minority group at highest risk for dropout [31-33]. Acculturative stressors and socioeconomic disadvantage, particularly unstable housing and limited financial resources, have been associated with poor engagement and low treatment completion rates [25, 31, 34-37].

Despite some attention to patterns of substance use among Latinos, most available data focus on prevalence and treatment outcome among Latinos as one group, with very little information on the differences in rates of disorders and treatment outcomes across subgroups[38-41]. Limited data about a growing, diverse and understudied population underscores the need for research that will shed light on the factors associated with alcohol treatment outcomes among Latinos[42, 43]. The presence and severity of risk factors such as racism, discrimination, unemployment, and migration-related stress will vary among Latino subgroups; therefore, patterns of use, vulnerability to develop an alcohol use disorder, and treatment responses can also be expected to differ [44-47]. Understanding the influence of national origin, acculturation, patterns of

consumption and alcohol-related consequences among Latino subgroups is critical to advancing the field of health disparities research and improving treatment outcomes[28, 37, 48-51].

B. Why CBT?

We focus on CBT because of its strong evidence base for addictions and other mental disorders, as well as strong evidence of effectiveness among Latinos[52-54], with literature dating back thirty years and encompassing evidence of effectiveness and efficacy with Latinos of low socioeconomic status who adhere to traditional cultural values[55-62]. CBT has been demonstrated to be effective in the treatment of depression with Latinos, and CBT adaptations with limited English proficient immigrant Latinos are promising[63-65]. Organista[62] notes that CBT is well suited for the treatment of Latinos given its: 1) focus on immediate relief of symptoms via concrete solutions and techniques, 2) didactic orientation, 3) present time orientation and problem solving, 4) active interventions, and 5) use of homework assignments and therapy manuals to structure the treatment, much of which may alleviate some of the stigma that some Latinos associate with treatment. Benuto and O'Donohue[66] reviewed the existing literature on CBT efficacy among Latinos in terms of strengths and weakness, and noted the vast majority of studies are not empirically based, and commonly theoretical and speculative in nature. Thus, there is a recognized need for rigorous research to better understand CBT's efficacy with ethnic minority populations[67-69].

Bernal, Miller and others have argued that competent delivery of appropriately adapted empirically validated therapies is of greater importance than developing completely novel approaches for multiple subsamples and groups[70-72]. For example, a meta-analysis of 76 studies that evaluated culturally adapted interventions, with the majority (84%) involving explicit integration of cultural values, suggested that interventions designed for a specific cultural group were likely to be four times more effective than those provided to a collective of clients from diverse backgrounds[73 74]. Among Latinos, several studies suggest that when culturally appropriate interventions, specifically, those delivered in Spanish and utilizing values congruent with the Latino culture, are integrated with elements of CBT, there is increased treatment effectiveness for a variety of health issues (i.e., smoking cessation, diabetes management, PTSD, HIV education)[75-80]. Level of acculturation is another variable that requires attention as to its relationship with substance use issues, as this varies across Hispanic subgroups [40, 46, 66].

C. Why computer-assisted therapy?

It has been recommended that the transfer of evidence-based treatment for ethnic minorities to real-world settings be inexpensive, accessible, and easy to apply in order to enhance successful adoption and sustainable integration[81]. Accessing health information online is a common practice, with one in three American adults reporting that they have consulted the worldwide web to better understand what medical conditions and treatment options they or someone they know might have[82]. Among U.S. Latinos, internet use has continued to rise in the past five years with nearly 78% reporting at least occasional use, up from 64% in 2009. Additionally, 65% of Spanish-dominant Latinos access the internet through handheld devices such as a cellphone or tablet computer, and 72% of Latinos report owning a laptop or desktop computer, in comparison to 83% of non-Latinos and 70% of African-Americans[83].

The rising popularity and utility of technology among Latinos offers a new method for expanding access to health interventions. Low health literacy is associated with poor health outcomes and underutilization of preventive care among Latino immigrants[84, 85]. Regardless of educational level and experience using computers, tailoring technology-based health interventions to cultural context and language preferences has resulted in improved engagement and post-intervention behavioral changes[84]. Among Latinos, internet-based health information has been

endorsed as an important source for understanding medical conditions and treatments, and accessing care[86]. Technology has thus become an important strategy for reducing barriers to care and improving health and treatment outcomes among Latinos[83, 87, 88].

D. Addressing rigor and reproducibility in evaluations of web-based therapies[11]

The efficacy data from many computerized and web-based therapies for alcohol and other substance use disorders are promising[89-96], but should be interpreted with caution due to multiple methodological problems that characterize much of the existing literature[89, 91, 97-101]. For example, our methodological analysis of 75 randomized clinical trials of computer-assisted therapies for adult psychiatric disorders indicated marked heterogeneity in study quality as no study met all 14 basic quality standards[11]. Consistent weaknesses were noted in evaluation of treatment exposure and adherence, rates of follow-up, inappropriate control and comparison conditions, and conformity to intention-to-treat principles. The uneven quality of this literature is, to a large extent, reminiscent of the early days of behavioral therapies research in mental health and addictions, where treatments were often vaguely defined, implementation was poorly monitored, and control conditions were absent or poorly conceived[11]. As described in the Preliminary Studies section below, we have sought to address each of these methodological limitations in our previous work on CBT4CBT and in the proposed study.

Although dissemination and broadening accessibility is a primary goal of our approach to developing web-based versions of CBT4CBT, another important feature of web-based therapies is that their standardization facilitates research on their mechanisms of action[102] by eliminating the key confound of variability of treatment across therapies. Once built and validated, modularized web-based therapies lend themselves well to focused research that can refine treatment packages such as CBT, for example by evaluating whether individual modules exert intended effects on theoretical outcomes (e.g., does the coping with craving module really reduce craving), or contribute meaningfully to outcome[103, 104]).

B. INNOVATION

- This project is innovative in that it adapts CBT4CBT, a highly promising computer-assisted form of CBT[13, 15, 17, 102, 105-108], to address a major challenge in health disparities highlighted by NIH and the Institute of Medicine[109]; specifically, the limited research on and scarcity of evidence-based treatments among Latinos [28, 110]. The products of the proposed study, a carefully adapted Spanish version of an effective computer-assisted therapy, as well as data on the evidence of its efficacy, is likely to have significant public health impact in improving access to an evidence-based treatment for alcohol use disorders among Latinos. Thus, this project also addresses a key NIAAA priority area; Minority Health and Health Disparities (MHHD).
- **There are no existing validated web-based therapies for Spanish-speaking individuals with alcohol use disorders**. Thus, the proposed project is also innovative in that it will develop and evaluate CBT in a highly disseminable and less expensive form[17, 94, 111]. If CBT4CBT-Spanish is demonstrated to be effective, the potential impact on reducing barriers to treatment and increasing access to effective interventions for Spanish-speaking individuals with alcohol use disorders could be of high public health significance.
- **Congruence with NIAAA's Strategic Plan to Address Health Disparities**: Despite a visible movement towards the use of evidence-based, best practice treatments and services models, study results that inform the current body of research have seriously neglected the participation of people of color when assessing treatment outcome[109]. This proposal has the potential to broaden the knowledge base on ethnic minorities; with a specific focus on monolingual Spanish speakers; a group that is significantly underrepresented in research.

Additionally, the results of this study may provide a better understanding of how acculturation and psychosocial factors contribute to treatment response.

3. **Research Plan:** Summarize the study design and research procedures using non-technical language that can be readily understood by someone outside the discipline. Be sure to distinguish between standard of care vs. research procedures when applicable, and include any flowcharts of visits specifying their individual times and lengths.

The study will be conducted in two phases:

Phase 1: Development and evaluation of CBT4CBT-Spanish-Alcohol (Years 1-2)

A. Development and evaluation of CBT4CBT-Spanish-Alcohol

The first two years of the proposed project will be devoted to developing and beta-testing the CBT4CBT-Spanish-Alcohol program. This will consist of, first, developing new alcohol-focused scenarios and translating and adapting the existing English CBT4CBT-Alcohol program for use with US Latinos whose principal/preferred language is Spanish, using a parallel approach to that described above for CBT4CBT-Spanish-Drug[165] (Appendix 1). Program content, which includes detailed scripts and storyboards for the almost 430 unique pages projected to be needed for the full program, will be developed through weekly meetings of the development team (Carroll, Paris, Silva, Añez, Gordon) in consultation with Dr. Raul Caetano. Dr. Caetano is a world-renown psychiatrist and epidemiologist who has worked in the public health field for nearly 35 years and has written extensively about alcohol problems among U.S. ethnic minorities, especially Latinos [29, 175-179], and about cultural adaptation of empirically validated treatments[180]. Our overall strategy will be to retain key features of the existing English CBT4CBT-Alcohol program and critical components of cognitive-behavioral therapy, while making appropriate cultural adaptations[4, 71, 181, 182] for use with Spanish-speaking substance users. Adaptation of the program will involve several steps as described below:

1. Generation of new content and videotaped vignettes relevant to a U.S. Latino sample

Although Latinos represent a large, heterogeneous group, the majority share Spanish as their primary language. This language, however, is also rich with complexities and variations in style and meaning[183]. As a result, language is intimately connected to both culture and the expression of emotional experience. Thus, in adapting interventions, it is imperative that providers be familiar with cultural norms such as mannerisms and verbal style, in order to make accurate interpretations of such expressions[184]. Secondary, but no less important, are cultural elements shared within the Latino culture. Though not necessarily unique to Latino populations, these cultural values are believed to play a critical role in the life of people of Latino origin[185]. Particularly important constructs include *confianza* (trust and intimacy in a relationship), *respeto* (respect; mutual and reciprocal deference), *personalismo* (personal rather than institutional relationship), and *familismo* (familial orientation). Knowledge about these values and degree of adherence among individuals served is essential in the development of effective treatments. These values carry culturally sanctioned messages that influence core elements of behavior change, decision-making, self-efficacy, and development of interpersonal relationships. Given their significance in Latino culture, researchers have emphasized the importance of understanding and incorporating these constructs in the treatment of Latino individuals[161, 162, 186-189].

We will develop 7 new sets of videotaped vignettes (one for each module, or episode, of the t*elenovela*) for CBT4CBT-Spanish-Alcohol of a linked storyline to maximize the programs' relevance to the target audience. Vignettes will take into account differing degrees of

acculturation, regional background, age, gender, education level, access to healthcare, and adherence to cultural values. In addition, we will address alcohol use within the context of immigration history, criminal justice involvement, domestic violence (with specific attention to traditional gender roles), minority status, unemployment, family intergenerational conflicts, and the stigma associated with seeking mental health and substance use services. Practice/homework assignments will be sensitive to variations in literacy level [4, 71, 181, 182].

Shooting of the narration and vignettes will be done by the Yale Center for Academic Media and Technology, using bilingual/bicultural professional actors, directors, and location shooting, as was done for the completed CBT4CBT programs. Three related vignettes (5-10 minutes each) will be developed for each of the 7 modules: The first illustrates one of the main characters dealing with a realistic, difficult, situation that illustrates the targeted concept (e.g., refusal skills, thoughts about alcohol) to highlight the importance and relevance of that concept and the skills. The beginning of the second vignette in each module is the same as the first, but the vignette has a different ending as the main character utilizes the skills taught in the module. The third vignette illustrates the character carrying out the practice exercise for that module.

Following shooting and editing of the narration, vignettes, and exercises, the program will be built and the website created through the Yale Center for Academic Media and Technology using HTML5. As in our existing versions, CBT4CBT can be used on any desktop, laptop, or tablet independent of their operating system, as it is web-based and no software needs to be downloaded. The project team works closely with the Yale Academic Media project manager to develop the beta version of the program. As with the existing CBT4CBT programs, which do not require either reading or computer skills (users are required only to push forward/backward arrows or highlighted buttons), we will make every effort to make this version even more accessible and user-friendly with additional visuals and touch-screen options.

2. Reviewing, piloting and finalizing the program

When the beta version of the CBT4CBT-Spanish-Alcohol program is completed, it will be reviewed by Dr. Caetano as well as focus groups consisting of a small group of clinicians and clients from the Hispanic Clinic. The clinicians and clients will rate ease of use, helpfulness, relevance and impact of each module, as well as any possible concerns or problems encountered. Evaluations from the clinicians and clients will be used to make corrections as needed and further improve the program. Finally, we will pilot the program with 5 clinic patients with alcohol use disorders who meet the proposed inclusion and exclusion criteria and obtain their feedback on need for clarifications and improvements. We use the 'thinking aloud' technique[190] (in which users are asked to vocalize their thoughts and reactions while using the program), which we have found very useful in refining previous versions of CBT4CBT. This feedback will be reviewed with Dr. Caetano and used to develop the final version of the program to be used in the randomized trial.

B. Randomized Clinical Trial (Years 3-5)

1. Overview

In years 3-5 of the proposed project, we will conduct a Stage 1 randomized clinical trial evaluating the program in which 90 Spanish-speaking individuals with alcohol use disorder will be randomized to (1) standard outpatient counseling at the Hispanic Clinic (ST; typically consisting of weekly individual and group supportive counseling) or (2) CBT4CBT-Spanish as an adjunct to ST. Other aspects of the trial will parallel those in our completed trial of the English version of CBT4CBT-Alcohol[16] to facilitate comparability across studies. Treatments will be delivered over an 8-week period with a 6-month follow-up to assess durability and/or delayed emergence of treatment effects. The primary outcome measure will be percent days of

abstinence (PDA) by week. Secondary outcomes include percent heavy drinking days and number of individuals with no heavy drinking days in the last 4 weeks of treatment[19].

2. Participants

Participants will be 90 individuals seeking treatment for alcohol use at the Hispanic Clinic of CMHC. The clinic treats a heterogeneous population, where 42% of those in the co-occurring treatment program report alcohol as their principal substance related issue and 43% are women. As reported above, we have demonstrated our ability to recruit, randomize, retain, and follow-up high numbers of closely related samples in this setting[191, 192].

a. Inclusion and exclusion criteria

Participants will be included who are (1) 18 years of age or older, (2) applying/referred for outpatient alcohol treatment, (3) meet current DSM-IV/DSM-5 criteria for alcohol use disorder with use in the past 30 days, (4) speak Spanish as their preferred or principal (most commonly spoken) language, (5) sufficiently stable for 8 weeks of outpatient treatment, and (6) willing to provide locator information and be contacted for follow-up for 6 months. Individuals will be excluded who (1) have an untreated/unstable bipolar or schizophrenic disorder, or (2) have a current legal case pending such that incarceration during the 8-week protocol is likely. Those physically dependent on alcohol can be rescreened following detoxification/stabilization (see Human Subjects).

b. Rationale for sample choice (also see Human Subjects section).

We are proposing broad inclusion criteria that reflect the heterogeneity of individuals seeking treatment for alcohol use disorders in this setting. Literacy is not required for using the CBT4CBT program, and, as described below, most of the assessment instruments we use are clinical interviews or can be administered by reading the questions to the participants using procedures we have worked out in our ongoing and previous trials[193-197]. We are not requiring that participants have computer access for study inclusion, as participants can access the program at the clinic.

3. Procedures

a*. Initial Screening*

All new admissions will be invited to participate in the protocol within two weeks of their clinic appointment. They will be identified by their clinicians at CMHC, the Hispanic Clinic, SATU jor MAAS, interest sheets, and clinic postings. Individuals who indicate they are interested in hearing more about the study will be offered a meeting with the research staff. An interest sheet providing a brief description of the study will be available for potential subjects to indicate their interest in learning more about the study and how to contact a member of the research team, should they be unable to speak with the research staff at the time of the clinic intake appointment. At the first interview, research staff will provide a brief overview of the protocol and obtain written informed consent. We use a multiple-choice test to assess participants' comprehension of the protocol[122, 137], with ample time to review questions to assure understanding of the protocol, consent, and treatments offered. After determination of eligibility, pretreatment assessments will be completed by the research assistant (see Table below).

b. Urn randomization

To prevent bias and increase the likelihood that treatment groups are balanced with respect to demographic variables *(gender*, *education*) and possible prognostic variables (severity of alcohol use, level of familiarity with and access to computers, level of acculturation) participants will be assigned to treatment conditions through urn randomization, using a Microsoft Access program that we have developed and implemented successfully in multiple previous trials[198-202]. In urn randomization, an algorithm modifies ongoing randomization probabilities based on prior

composition of treatment groups, maximizing multivariate equivalence of treatment groups[203], while still retaining other benefits of random assignment[204].

c. Treatment phase

Treatment conditions are described below. Study treatments will last 8 weeks. During the treatment phase, all participants will complete weekly assessments, usually at the time they come in for treatment. Weekly breath and urine sample collection will be supervised by the research assistant. The research assistant conducting weekly and follow-up assessments will be blind to the participants' treatment assignment, using procedures we have worked out in previous trials[112].

- *Clinical deterioration.* We will closely monitor participant treatment response and safety in all conditions through weekly assessment sessions. These will include breath and urine screens with assessment of psychiatric status. Although in our experience this is a very rare event in behavioral trials[119], including those of computer-assisted therapy[14, 100], participants who show significant deterioration (e.g., increased substance use or psychiatric symptoms that cannot be managed within the protocol) will be regarded as symptomatic failures, withdrawn from the treatment arm of the study, and referred appropriately, but will still be followed and included in the intent to treat analysis.
- *Strategies to minimize attrition.* In order to hold participant dropout to a minimum, we use multiple procedures recommended in our manual on enhancing compliance with substance abuse treatment[205, 206]. These include rapid assignment to study treatments, thorough explanation of study treatments and requirements and a fully bilingual staff, close monitoring of participants' clinical status, integration of the research with the clinical program, accessibility of study staff for questions and problems, and adequate compensation to participants for the time spent on completing assessment instruments.

d. Termination and posttreatment assessment

At the end of the 8-week treatment period, all participants will be re-interviewed by the 'blind' research assistant, who will complete posttreatment ratings (see Assessments, below). Access to the CBT4CBT-Spanish-Alcohol program will be terminated for participants assigned to that condition. Participants in all conditions will be strongly encouraged to continue in treatment at their primary site (Hispanic Clinic, SATU, MAAS).

e. Follow-up

Follow-up interviews will be conducted 1, 3, and 6 months after termination of treatment. Follow-up interviews will include the full posttreatment battery (see Assessments, below), including assessment of utilization of other treatments and services received. We will attempt to follow all participants in the intent to treat sample, regardless of their retention in treatment, using strategies that have been successful in multiple previous studies. These include: (a) thorough explanation at the initial consent interview to participants of the importance of follow-ups, (b) requiring that each participant provide at least 3 *verified* locators who are likely to have knowledge of their whereabouts throughout follow-up, (c) use of multiple sources and locators to track participants[207], and (d) payment to participants of $50 for each completed follow-up interview, with additional monetary incentives for completing consecutive interviews on time. Using these procedures, our current rate of follow-up approaches 90-98% across studies[16, 126]. Thus, we have been successful in conducting true intent-to-treat analyses[208, 209] in that the samples include post-treatment and follow-up data from all participants randomized, including those who have dropped out of treatment.

4. Treatments

a. Standard treatment as usual (ST)

Participants randomized to this condition will receive standard treatment at the clinic at which they participate. This typically consists of individual and group counseling in Spanish and delivered by masters-level counselors. Groups are primarily psychoeducational and individual sessions tend to use a motivational interviewing style with elements of CBT and DBT. Interventions address behavioral health, substance use, and cultural factors including migration, adherence to cultural values, language, and acculturation. All participants are offered a number of ancillary treatments and services. Drs. Añez, Paris, and Silva hold leadership positions at the Hispanic Clinic, which facilitates effective integration of the trial into the ongoing services and procedures. As an established provider of outpatient behavioral health services for the Spanish-speaking community and recognized community partner in the promotion of state-of-the-art culturally and linguistically appropriate care, the Hispanic Clinic was recently recognized for its efforts integrating mental health and addiction treatment with the SAMHSA Science to Service Award, an award designed to recognize exemplary implementation of evidence based treatments.

b. CBT4CBT + ST

At the time of randomization, participants assigned to this condition will be given a username and unique password to access the CBT4CBT-Alcohol Spanish program. The RA (Ms. Jaramillo) will work with each participant and guide them through the use of the program on-site to assure they know how to use the program and answer any questions. Participants will be asked to spend at least one hour per week working with the CBT4CBT-Spanish-Alcohol program. Participants will be asked to complete all 7 modules sequentially over the course of the 8-week study treatment period (participants can repeat who modules or any component of them at their own pace). At the start of each session, the CBT4CBT program reviews the modules that the user has completed, and directs users to either complete a module they have started or move to a new one. The program tracks, for each participant, time logged onto the program, modules accessed, completion of practice assignments, and learning of CBT principles through true/false tests at the end of each module.

c. Rationale for design: There are multiple design options for evaluating computer-assisted therapies[11, 12, 96, 210]. We chose to evaluate CBT4CBT-Spanish-Alcohol as an add-on to standard treatment for several reasons. First, current evidence suggests web-based therapies have enhanced effectiveness when delivered in conjunction with clinician involvement, including our recent trial of CBT4CBT-Alcohol[91, 92, 105]. Second, evaluation of CBT4CBT-Spanish as an 'add-on' is appropriate given that this will be the first Stage I evaluation of this novel treatment in a new language format for a new population, although it will not control for attention/ time spent. Third, participants may be exposed to some CBT or other EBTs in individual/group sessions as part of standard treatment. Thus, the proposed randomized 'add on' design maximizes the likelihood such exposure is consistent across conditions. Moreover, use of the skill acquisition measure (ARRT, see below) will allow us to evaluate change in CBT skill levels across time in both conditions[18].

Assessments:

Assessments include measures used to: 1) Describe the sample, 2) Measure primary outcomes during treatment and follow-up, and 3) Evaluate likely mediators (e.g., skills acquisition) and moderators (e.g., gender, level of acculturation) in exploratory analyses. We rely on widely used, well-validated instruments, as well as those which have validated Spanish translations (e.g., AUDIT, SCID, Timeline Follow-Back)[214, 215]; all have been used successfully in our prior studies with Spanish-speaking samples[160, 216-219]. Hence, only the less well-known instruments are described below; all assessment instruments and the schedule of their administration are listed on the Table.

Instrument name	Interview or self-report	Rater	Screen	Pre Tx	Weekly	Monthly	Post Tx (8 wks)	Follow-up 1, 3 6 mo
Informed Consent Quiz [122]	Self-report	P	x					
*PDC Screening Form	Interview	RA	x					
Inclusion/Exclusion criteria	Interview	RA	x					
*Follow-up contact & tracking sheet	Interview	RA	x				x	X
Marins	Self-report	P		x				
Patient Characteristic Form	Interview	RA	x					
Structured Clinical Interview DSM-4/5 (SCID)[222]	Interview	RA	x				x	
Urn randomization	Interview	RA		x				
Breathalyzer result	Interview	RA	x	x	x		x	x
Urine results	Interview	RA	x	x	x		x	x
CBT Website True/False Quiz	Self-report	P		x			x	x
CBT4CBT Patient Feedback Form	Self-report	P			x			
Treatment Services Utilization	Interview	RA		x		x	x	x
Latino Cultural Values Scale	Interview	RA		x				
Religious Beliefs Form	Self-report	P		x				
WHO Quality of Life Brief	Self-report	P		x				
PTSD Checklist (PCL 5)	Self-report	P		x			x	x
Perceived Stress (PSS)	Self-report	P		x			x	x
*Timeline Follow Back/ Substance Use Calendar [227] [227-229]	Interview	RA	x		x		x	X
AUDIT (Alcohol Use Dis. Ident Test) [214, 230-232]	Interview	RA		x			x	X
Drinking Consequences (SIP) [217]								
*Brief Symptom Inventory (BSI) [46, 233-235]	Self-report	P		x	x		x	x
Addiction Severity Index (ASI)[215, 236, 237]	Interview	RA		x			x	x
ARRT (Alcohol Risk Response Test) [22]	Taped role-play	RA		x		x	x	X
*Change Strategies Inventory (CSI) [240, 241]	Self-report	P		x		x	x	X
*Evaluation of treatment, endpoint[174]	Self-report	P					x	
Serious Adverse Events Reporting Form	Interview	RA						

*indicates translated and validated form available through our CTN MET-Spanish study[194] [197]

- The **Psychotherapy Development Center (PDC) Screening Form** has been used in all of our previous studies and provides general information, including demographic data, country of origin, substance use history, previous substance use and psychiatric treatment history, medical history, recent life events, family history and social support, treatment attitudes and expectations, and has been expanded to include level of experience with computers and the internet.
- The extent to which the participants can demonstrate effective coping skills will be assessed by the **Alcohol Risk Response Test (ARRT)**[22], which we adapted from the Situational Competency Test[248]. The ARRT is a role-play task that asks participants to articulate what they would do when faced with 7 problems specifically geared to the CBT4CBT modules. Hence we can evaluate the extent to which CBT4CBT is successful in imparting the specific strategies intended in comparison to ST alone. Participants' responses are audiotaped and then scored independently by 'blind' raters for number of and quality of coping plans. The ARRT has good psychometric qualities, including high interrater reliability, concurrent and predictive validity[22]. We also have used it to demonstrate treatment-specific acquisition of coping skills in CBT4CBT[108]. It will be

administered at multiple points to evaluate temporal relationships between change in this putative mediator and outcome [249, 250].

4. Genetic Testing N/A ☒

5. **Statistical Considerations:** Describe the statistical analyses that support the study design.

Outlined below is the general strategy for data analyses for the randomized clinical trial in Phase 2 (years 3-5) of the study which will address each specific aim: (1) determination of the efficacy of treatments, and (2) analysis of the follow-up data, as well as our exploratory, secondary aims (analysis of mediators).

Outlined below is the general analytic strategy for addressing the specific aims for this Stage 1 trial:

1. Determination of Treatment Outcomes

a. Data reduction: Primary outcome variables have been defined *a priori* to reduce the risk of Type I error. Preparatory analyses include evaluation of baseline equivalence of treatment groups on demographic and prognostic variables and comparability of rates of data availability across conditions.

b. Strategies for management of differential attrition: Data analyses will be conducted on the intent-to- treat sample and we will attempt to follow all participants regardless of their retention in treatment. We have established our ability to contact and follow participants who drop out of treatment and to conduct true intent-to-treat analyses [16, 208, 209], including supplemental analyses that account for whether data was collected before or after dropout/withdrawal[208]. While we anticipate that assertive efforts to locate and interview participants who drop out of treatment will result in low numbers of missing participants and minimal missing data in the final dataset, we will minimize the impact of missing data through the use of random effects regression modelling[251-253].

c. Evaluation of treatment effects at posttreatment and follow-up: The principal strategy for assessing the efficacy of the study treatments on outcome over time will be random effects regression models for continuously measured primary (e.g. percent days of abstinence by week) and secondary (e.g., acquisition of coping skills) outcome variables. The focus of the repeated measures analyses will be the 'contrast by time effects', which essentially evaluates whether the slopes, or rates of change, of one group differ from the slopes of another group. We have used these methods to evaluate main and interaction effects, with appropriate covariates (e.g., retention, compliance with treatment, time spent working with the CBT4CBT program) in multiple previous trials[14, 151, 160, 200, 201, 254]. Follow-up data will be analyzed using random-effects regression modeling [255] for our primary outcome measures across time, using the contrasts described above, with appropriate covariates (e.g., length of time in treatment, exposure to other treatment during follow-up). Random effects regression models have several advantages in follow-up data from clinical trials of substance users where participants are unlikely to attend follow-up evaluations precisely at the desired fixed points, and are less vulnerable than traditional MANOVA approaches to missing data[208, 209, 251, 252]. As in our previous trials [16, 126], we estimate that our extensive efforts to track participants will yield a 90% follow-up rate.

d. Adequacy of sample size: This Stage 1 trial is intended to provide initial pilot testing and feasibility testing of the web-based CBT4CBT program in a Spanish-speaking sample of individuals with alcohol use disorder. Based on SSize software, the proposed sample sizes will enable us to detect effect sizes of .35 or higher for either hypothesis, which will be the criterion for determining whether CBT4CBT-Spanish-Alcohol has adequate promise to justify a fully powered randomized trial[256]. This sample size was sufficient for the English-language trials of the drug and alcohol versions of CBT4CBT, which yielded effect sizes of .46-.59[13, 15, 16].

Power calculations for random effects regression	Power	Estimated effect size	Estimated ICC	# of datapoints	Sample size per cell
H1: (CBt4CBT-S + ST) v ST, main effect for active treatment phase (assessed weekly, baseline-8weeks)	.80	.35	.40	9	45
H2: (CBT4CBT-S + ST) vs ST, main effect for follow-up (assessed monthly, end of treatment-6 months)	.80	.50	.80	7	40

2. Treatment specificity and mediators

We will explore the extent to which participants improve coping skills over time using the ARRT as described above and the extent to which acquisition of coping skills may mediate outcome for CBT4CBT-Spanish-Alcohol in this sample. We have described our use of these models and strategies to evaluate treatment mediators in Preliminary Studies, above, and in several papers[13, 105, 108, 151]. Following the general analytic framework outlined by Kraemer[257], we will use the product of the coefficients method to evaluate the relationship between the mediator (e.g., acquisition of CBT-specific coping skills as measured by the ARRT), or indirect effect, and outcome[155, 156, 258]. After running a regression equation to determine (1) the effect of treatment on the mediator (provides beta weight for *a*), we will evaluate (2) the strength of the relationship between the mediator, treatment, and outcome (provides beta *b*). Using MacKinnon's software PRODCLIN[259], we will evaluate the asymmetric confidence intervals for the product of the regression estimates *(a*b)*.

SECTION VI: RESEARCH INVOLVING DRUGS, BIOLOGICS, PLACEBOS AND DEVICES

If this section (or one of its parts, A or B) is not applicable, state N/A and delete the rest of the section.

N/A

SECTION VII: HUMAN SUBJECTS

1. Subject Population: Provide a detailed description of the types of human subjects who will be recruited into this study.

Participants will be individuals seeking outpatient treatment for alcohol use at the Connecticut Mental Health Center (CMHC), where the majority of clients are male (73%), middle aged (62%), unemployed (71%), unmarried (56%), and have not completed high school (64%). Spanish-speaking participants will be recruited from two CMHC outpatient programs (The Hispanic Clinic at 34 Park Street and the Substance Abuse Treatment Unit at One Long Wharf) or Connecticut Mental Health Center clinicians. Additionally, MAAS (The Multi- Cultural Ambulatory Addiction Service at 426 East Street) has been appointed a recruitment site

2. Subject classification: Check off all classifications of subjects that will be targeted for enrollment in the research project. Will subjects who may require additional safeguards or other considerations be enrolled in the study? If so, identify the population of subjects requiring special safeguards and provide a justification for their involvement.

☐ Children	☐ Healthy	☐ Fetal material, placenta, or dead fetus
☒ Non-English Speaking	☐ Prisoners	☐ Economically disadvantaged persons
☐ Decisionally Impaired	☐ Employees	☐ Pregnant women and/or fetuses
☐ Yale Students	☐ Females of childbearing potential	

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects? ☐ Yes ☒ No (If yes, see Instructions section VII #4 for further requirements)

3. **Inclusion/Exclusion Criteria:** What are the criteria used to determine subject inclusion or exclusion?

Participants will be included who:

1. Are 18 years of age or older.
2. Are applying for outpatient alcohol treatment, with some alcohol use in the past 30 days
3. Speak Spanish as their preferred or principal (most commonly spoken) language.
4. Are sufficiently stable for 8 weeks of outpatient treatment
5. Can commit to 8 weeks of treatment and are willing to be randomized to treatment
6. Are willing to provide locator information for follow-up.

Individuals will be excluded who:

1. Have an untreated bipolar or schizophrenic disorder
2. Have a current legal case pending such that incarceration during the 8 week protocol is likely.

4. How will **eligibility** be determined, and by whom?

Individuals who indicate they are interested in hearing more about the study will be offered a meeting with research staff will provide a brief overview of the protocol and continue the informed consent process. After written informed consent has been obtained, screening assessments will be completed to determine eligibility.

5. **Indicate recruitment methods below.** Attach copies of any recruitment materials that will be used.

☒ Flyers	☐ Internet/Web Postings	☐ Radio
☐ Posters	☐ Mass E-mail Solicitation	☐ Telephone
☐ Letter	☒ Departmental/Center Website	☐ Television
☐ Medical Record Review	☐ Departmental/Center Research Boards	☐ Newspaper
☐ Departmental/Center Newsletters	☐ Web-Based Clinical Trial Registries	
☒ Other (describe):	☒ Clinicaltrials.gov Registry (do not send materials to HIC)	

Direct referral from intake clinicians; Interest Sheets, billboards

6. **Recruitment Procedures:**

a. Describe how potential subjects will be identified.

All new admissions will be invited to participate in the protocol within two weeks of their initial clinic appointment. They will be identified by their clinicians at CMHC, the Hispanic Clinic, SATU or MAAS using interest sheets, and clinic postings. Individuals who indicate they are interested in hearing more about the study will be offered a meeting with the research staff. An interest sheet providing a brief description of the study will be available for potential subjects to indicate their interest in learning more about the study, and how to contact a member of the research team, should they be unable to speak with the research staff at the time of the clinic intake appointment.

b. Describe how potential subjects are contacted.

Subjects will be introduced or referred to research staff who will have offices in the clinic. Eligibility screening may occur at this time or scheduled at a more convenient time.

c. Who is recruiting potential subjects?

Project Director and RAs

7. a. Will email or telephone correspondence be used to screen potential subjects for eligibility prior to the potential subject coming to the research office? ☐ Yes ☒ No

b. If yes, identify any health information and check off any of the following HIPAA identifiers to be collected and retained by the research team during this screening process.

HEALTH INFORMATION:

_____

HIPAA identifiers:

☐ Names

☐ All geographic subdivisions smaller than a State, including: street address, city, county, precinct, zip codes and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly-available data from the Bureau of the Census: (1) the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people, and (2) the initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.

☐ Telephone numbers

☐ Fax numbers

☐ E-mail addresses

☐ Social Security numbers

☐ Medical record numbers

☐ Health plan beneficiary numbers

☐ Account numbers

☐ All elements of dates (except year) for dates related to an individual, including: birth date, admission date, discharge date, date of death, all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older

☐ Certificate/license numbers

☐ Vehicle identifiers and serial numbers, including license plate numbers

☐ Device identifiers and serial numbers

☐ Web Universal Resource Locators (URLs)

☐ Internet Protocol (IP) address numbers

☐ Biometric identifiers, including finger and voice prints

☐ Full face photographic images and any comparable images

☐ Any other unique identifying numbers, characteristics, or codes

8. **Assessment of Current Health Provider Relationship for HIPAA Consideration:**

Does the Investigator or any member of the research team have a direct existing clinical relationship with any potential subject?

☐ Yes, all subjects

☒ Yes, some of the subjects

☐ No

If yes, describe the nature of this relationship.

Drs. Paris, Añez Nava, and Silva are licensed psychologists who provide services within the Hispanic Clinic of the Connecticut Mental Health Center.

9. Request for waiver of HIPAA authorization: (When requesting a waiver of HIPAA Authorization for either the entire study, or for recruitment purposes only. Note: if you are collecting PHI as part of a phone or email screen, you must request a HIPAA waiver for recruitment purposes.)

N/A

Choose one: For entire study: _____ For recruitment purposes only: _____

i. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data;

ii. If requesting a waiver of **signed** authorization, describe why it would be impracticable to obtain the subject's signed authorization for use/disclosure of this data;

By signing this protocol application, the investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered entity must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.

SECTION VIII: CONSENT/ ASSENT PROCEDURES

1. **Consent Personnel:** List the names of all members of the research team who will be obtaining consent/assent.
   Michelle Alejandra Silva, PsyD; Yudilyn Jaramillo, (Research Assistant),

2. **Process of Consent/Assent:** Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure subjects' independent decision-making.

   Five Spanish-speaking clinicians and clients from the clinic will be invited to review and evaluate the preliminary version of the CBT4CBT-Spanish website. The Project Director/ Research Assistant and potential subjects will discuss the basic components described in the HIC-approved translated Information Sheet in a quiet, private setting. Potential participants of Phase 1 will be provided an opportunity to ask questions and time to consider his/her decision to participate in the review and evaluation of the program. Verbal consent will be obtained by the Project Director/RA prior to engaging a client or clinician in the pilot activities. A copy of the Information Sheet will be given to the participant.

   The Project Director or Research Assistant will obtain written informed consent prior to any study related procedures of Phase 2. All study related documents will be translated into Spanish and subjects will be consented in Spanish. The informed consent process will be conducted in a private, quiet setting. The Project Director/RA and the participant will discuss the basic components described in the HIC-approved translated consent form. These include: participation is voluntary and participants may withdraw without consequences to clinic services received, purpose, procedures, randomization, visit schedule, risks and benefits, potential compensation, alternatives to study participation, and confidentiality. Potential participants will be provided an opportunity to ask questions and time to consider his/her decision to participate.

A translated comprehension quiz will be given to ensure the participant has an adequate understanding of study. A copy of the consent form will be given to the participant.

3. **Evaluation of Subject(s) Capacity to Provide Informed Consent/Assent:** Indicate how the personnel obtaining consent will assess the potential subject's ability and capacity to consent to the research being proposed.

   Study personnel will use a multiple-choice consent quiz to assess participants' comprehension of the protocol.

4. **Documentation of Consent/Assent:** Specify the documents that will be used during the consent/assent process. Copies of all documents should be appended to the protocol, in the same format that they will be given to subjects.

   Phase 1: Information Sheet (same for patients and clinicians)
   Phase 2: Compound Authorization and Consent Form

5. **Non-English Speaking Subjects:** Explain provisions in place to ensure comprehension for research involving non-English speaking subjects. Translated copies of all consent materials must be submitted for approval prior to use.

   Dr. Silva will oversee the translation of consent documents which entails initial translation and back-translation by an independent translator (Dr. Paris). A Spanish-speaking Research Assistant, Yudilyn Jaramillo will be dedicated to this project. The Research Assistant will assist with subject recruitment and the informed consent process.

6. **Waiver of Consent:** Will you request either a waiver of consent, or a waiver of signed consent, for this study? If so, please address the following:

   ☒ **This section is not applicable to this research project**

   Waiver of consent: (No consent form from subjects will be obtained.)
   a. Does the research pose greater than minimal risk to subjects? ☐ Yes ☐ No
   b. Will the waiver adversely affect subjects' rights and welfare? ☐ Yes ☐ No
   c. Why would the research be impracticable to conduct without the waiver?
   d. Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date?

   Waiver of **signed** consent: (Verbal consent from subjects will be obtained.) Phase 1 only

   ☐ **This section is not applicable to this research project**
   a. Would the signed consent form be the only record linking the subject and the research? ☐ Yes ☐ No
   b. Does a breach of confidentiality constitute the principal risk to subjects? ☐ Yes ☐ No

   OR

   c. Does the research pose greater than minimal risk? ☐ Yes ☒ No **AND**
   d. Does the research include any activities that would require signed consent in a non-research context? ☐ Yes ☒ No

7. **Required HIPAA Authorization:** If the research involves the creation, use or disclosure of protected health information (PHI), separate subject authorization is required under the HIPAA Privacy Rule. Indicate which of the following forms are being provided:

☒ Compound Consent and Authorization form
☐ HIPAA Research Authorization Form

SECTION IX: PROTECTION OF RESEARCH SUBJECTS

1. **Risks:** Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects participating in the research.
   Psychological risks are minimal and not different from those of equivalent non-study psychotherapeutic interventions.

   Computer-based interventions have been used safely in multiple investigations with a range of populations, and we are unaware of any reported risks associated with these interventions.

   The data collected from interviews and self-report forms, as well as urine and breath collection, carry no risk other than those normally associated with these procedures.

2. **Minimizing Risks:** Describe the manner in which the above-mentioned risks will be minimized.
   The Project Coordinator will supervise the participants' use and understanding of the program closely, and research and clinic staff will be available to monitor participants' reactions to the program and to answer any clinical issues. Careful training and supervision of therapists will further minimize these risks.

   The web-based intervention is highly secure (annual Security Design Review by Yale Information Technology Services is required). The program does not collect any PHI or specific information regarding recent drug use or illegal activities.

3. **Data and Safety Monitoring Plan:** Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HIC will make the final determination of the risk to subjects.) For more information, see the Instructions, page 24.
   a. What is the investigator's assessment of the overall risk level for subjects participating in this study?
   b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study?
   c. Copy, paste, and then tailor an appropriate Data and Safety Monitoring Plan from http://www.yale.edu/hrpp/forms-templates/biomedical.html for
      i. Minimal risk
      ii. Greater than minimal/moderate risk
      iii. High risk

   d. For multi-site studies for which the Yale PI serves as the lead investigator:
      i. How will adverse events and unanticipated problems involving risks to subjects or others be reported, reviewed and managed?
      ii. What provisions are in place for management of interim results?
      iii. What will the multi-site process be for protocol modifications?

   Overall level of risk for participants is minimal given the nature of this project and procedures in place for careful identification of potential subjects, informed consent process, and protection of confidentiality.

For the randomized trial phase of this study (years 3-5), a Data and Safety Monitoring Board (DSMB) will monitor this project because this population might be considered vulnerable due to their alcohol use. This board is already in place for the Yale Psychotherapy Development Center (Carroll, PI). The DSMB is composed of Yale investigators who are independent of the proposed trial and experienced in various aspects of the conduct of clinical trials for the treatment of addictive disorders. We have developed a standard DSMB report form that is used in all Center related trials that summarizes, *on a quarterly basis*:

1. Recruitment, retention, and follow-up rates for the study and compares them to target rates.
2. Rates of data completeness and availability of primary outcome data.
3. Occurrence of AEs and SAEs.
4. Report of study progress since the last report.
5. Rates of recruitment of women, minorities, and children with respect to targets.

These reports are generated by the Data Manager each quarter and signed by each study PI prior to their submission to the DSMB. DSMB comments are documented and forwarded to the Yale IRB at the time of the annual review and re-approval.

Because the projected effect sizes may not be large enough for detection during interim analyses, we are not proposing a preliminary analysis of accumulating efficacy and safety data by treatment assignment. Instead, we propose to submit a quarterly report of aggregate data to the DSMB members that contains screening data, baseline demographics, retention data, serious adverse events data, as well as accrual status including projections, times to milestones, and any other data that will help in the assessment of the clinical trial. Based on this report, each DSMB member will complete a form making one of two recommendations: 1) continue recruitment as planned; or 2) schedule formal DSMB meeting immediately. If any DSMB member recommends a meeting, this will be scheduled within one week, minutes will be kept, the report will be reviewed with the PI, and the committee will vote on whether the study should: 1) continue recruitment unchanged; 2) continue with a protocol amendment; 3) stop recruiting pending further investigation. If, after this meeting, any DSMB member votes to stop recruitment or requests a protocol modification, the Yale IRB will be informed.

Participants who experience a significant psychiatric or medical problem requiring an overnight hospitalization at an acute care facility will be considered to have experienced an SAE. In general, most SAEs will result in inpatient care and thus in transfer to the inpatient division of CMHC. All SAEs will result in the completion of an SAE Form and a verbal report within one hour to the Principal Investigator (Dr. Carroll) and the clinic directors (Drs. Añez, Paris). Within 24 hours, the following additional individuals will be informed: 1) all co-investigators; and 2) the DSMB. Adverse events that are serious and unanticipated and probably, possibly, or definitely related or adverse events occurring with greater frequency than anticipated will be reported to the Yale Human Investigation Committee within 48 hours of discovery. The procedures for SAE reporting include written documentation using the clinical notes related to the adverse event and specific forms detailing the event with a sign-off by all appropriate supervisory personnel. Communication of recommendations and decisions from all parties (DSMB, Yale Human Investigations Committee, and CMHC Administration) are made back to the investigator in a timely manner. We will report all protocol amendments or changes in the informed consent form to NIDA as well as any temporary or permanent suspension of patient accrual.

4. **Confidentiality & Security of Data:**

a. What protected health information (medical information along with the HIPAA identifiers) about subjects will be collected and used for the research?

In Phase 1, no PHI will be collected. In Phase 2, PHI that will be collected includes names, addresses, phone numbers, and email addresses for locator purposes.

Our study assessments/forms have been designed to avoid collecting identifiable information (e.g., no PHI identifiers are collected on CRFs). The only dates collected are

protocol session dates. These are changed to 'number of sessions completed' when data sets are anonymized and released to other investigators.

b. How will the research data be collected, recorded and stored?

Research data are collected on CRFs, and sent to data managers in our research offices on a closed secure network. All computers used by research staff are password protected. No identifying information is on CRFs. Only authorized individuals will have access to CRFs.

c. How will the digital data be stored? ☐ CD ☐ DVD ☐ Flash Drive ☐ Portable Hard Drive ☒ Secured Server ☒ Laptop Computer ☒ Desktop Computer ☐ Other

d. What methods and procedures will be used to safeguard the confidentiality and security of the identifiable study data and the storage media indicated above during and after the subject's participation in the study?

Do all portable devices contain encryption software? ☒ Yes ☐ No

If no, see http://hipaa.yale.edu/guidance/policy.html

Confidentiality in regards to collected materials will be maintained via a numbered reference system maintained by the Project Director. Participants' names will appear only on the consent form, HIPAA authorization form, and "key" form kept by the Project Director. The key form linking subject names to ID codes will be stored in a separate, locked file cabinet. Data are stored at our secure data management center; data sets do not include identifying information.

In addition, we have designed all of our CBT4CBT websites such that no sensitive information (i.e., information on illegal behavior) or PHI is collected or stored by the website (including IP address). Moreover, to avoid participants inadvertently revealing sensitive information, the website does not use any 'blank fills', and the program shuts down after 10 minutes of inactivity.

e. What will be done with the data when the research is completed? Are there plans to destroy the identifiable data? If yes, describe how, by whom and when identifiers will be destroyed. If no, describe how the data and/or identifiers will be secured.

Paper copies of participant records containing ID numbers will be moved to a secure archive in Temple Medical Building; 40 Temple Street, New Haven, CT. Source files with subject names will be stored in the regulatory coordinator's office separately under triple lock (building entry, office entry, separate locked file cabinet designated for name files only). The paper log linking subject names to ID codes will be stored in a separate, locked file in the regulatory coordinator's office. At the end of the required record retention period, data will be destroyed in accordance with Yale ITS policies 1609 and 1609PR.01. Source data are generally destroyed 3 years after completion of the study at a secure location by Shred-It.

f. Who will have access to the protected health information (such as the research sponsor, the investigator, the research staff, all research monitors, FDA, QUACS, SSC, etc.)? (please distinguish between PHI and de-identified data)

The Yale PI and the research staff will have access to PHI and coded data. The funding agency, NIAAA, may access the data for routine audits.

g. If appropriate, has a Certificate of Confidentiality been obtained?

Applied for.

h. Are any of the study procedures likely to yield information subject to mandatory reporting requirements? (e.g. HIV testing – reporting of communicable diseases; parent interview - incidents of child abuse, elderly abuse, etc.). Please verify to whom such instances will need to be reported.

Limits to confidentiality include only disclosure of acute suicidality, homicidality, or abuse of a minor/elder, as is standard in clinical practice and indicated in the consent form. When there is reasonable cause to suspect or believe there is a case of child abuse or elder abuse, a report will be made to the CT Department of Children and Families (DCF) or CT Department of Social Services (DSS), Protective Services for the Elderly (PSE). Designated clinic personnel will be notified as per clinic policies.

6/29/2011SECTION X: POTENTIAL BENEFITS

Potential Benefits: Identify any benefits that may be reasonably expected to result from the research, either to the subject(s) or to society at large. (Payment of subjects is not considered a benefit in this context of the risk benefit assessment.)

The major potential benefit in this study is in reduction of alcohol use via the study treatments, which may, in turn, foster improvement in participants' legal, medical, interpersonal, psychological and occupational functioning.

SECTION XI: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. **Alternatives:** What other alternatives are available to the study subjects outside of the research?

   Individuals who do not wish to participate or who are ineligible for the trial will be referred back to their clinician.

2. **Payments for Participation (Economic Considerations):** Describe any payments that will be made to subjects, the amount and schedule of payments, and the conditions for receiving this compensation.

   Phase 1 (Development of the CBT modules, Years-1-2):

   A sample of 5 clinicians will be asked to review the CBT4CBT program in Year 2; They will be paid $200 for completing all 7 modules of the program and providing evaluation and feedback. If a reviewer does not complete all of the modules they will be compensated for the modules they do complete at a rate of $28.50 per module. Their feedback will be incorporated in final modifications to the program.

   Phase 2 (Randomized trial, Years 3-5):

   Subjects will be compensated for time required to complete baseline assessment at $40, study assessments at $25 at each weekly assessment time point; $50 at post-treatment, $50 at 1-month follow-up; $75 at 3-month follow-up; and $100 at 6-month follow-up. The pilot subjects will not be participating in the follow up phase, therefore, there will be not follow up compensation.

3. **Costs for Participation (Economic Considerations):** Clearly describe the subject's costs associated with participation in the research, and the interventions or procedures of the study that will be provided at no cost to subjects.

   There will be no costs to subjects associated with participation in this study. Subjects will not be charged for study treatments or evaluations they receive at the clinic. Subjects may

be charged for treatment as usual at the clinic; but most patients receive treatment with no-out of pocket expenses or on a sliding scale.

4. **In Case of Injury:** This section is required for any research involving more than minimal risk.
   a. Will medical treatment be available if research-related injury occurs?
   b. Where and from whom may treatment be obtained?
   c. Are there any limits to the treatment being provided?
   d. Who will pay for this treatment?
   e. How will the medical treatment be accessed by subjects?

   Because we are evaluating standard behavioral approaches with strong empirical support and no known adverse consequences, study related injuries are expected to be extremely rare. There will be no compensation and/or medical treatment available if injury occurs. Participants or their insurance carrier will be expected to cover costs of any medical treatment.

LITERATURE CITED

1. U.S. CENSUS BUREAU. 2015. Profile America Facts for Features: CB15-FF.18, Vol. 2016: http://factfinder.census.gov/bkmk/table/1.0/en/PEP/2014/PEPASR2016H?slice=hisp~hisp!year~est72014.
2. GUERRERO, E. G., J. C. MARSH, T. KHACHIKIAN, H. AMARO & W. A. VEGA. 2013. Disparities in Latino substance use, service use, and treatment: implications for culturally and evidence-based interventions under health care reform. *Drug Alcohol Depend*. 133: 805-813.
3. WELLS, K., R. KLAP, A. KOIKE & C. SHERBOURNE. 2001. Ethnic disparities in unmet need for alcoholism, drug abuse, and mental health care. *American Journal of Psychiatry*. 158: 2027-2032.
4. MIRANDA, J., G. BERNAL, A. LAU, L. KOHN, W. C. HWANG & T. LAFRAMBOISE. 2005. State of the science on psychosocial interventions for ethnic minorities. *Annu Rev Clin Psychol*. 1: 113-142.
5. HUMPHREYS, K. & C. WEISNER. 2000. Use of exclusion criteria in selecting research subjects and its effect on the generalizability of alcohol treatment outcome studies. *Am J Psychiatry*. 157: 588-594.
6. WU, E., N. EL-BASSEL, S. S. WITTE, L. GILBERT, M. CHANG & P. MORSE. 2005. Enrollment of minority women and their main sexual partners in an HIV/STI prevention trial. *AIDS Education and Prevention*. 17: 41-52.
7. ZUN, L. S., T. SADOUN & L. DOWNEY. 2006. English-language competency of self-declared English-speaking Hispanic patients using written tests of health literacy. *J Natl Med Assoc*. 98: 912-917.
8. ATDJIAN, S. & W. A. VEGA. 2005. Disparities in mental health treatment in US racial and ethnic minority groups: Implications for psychiatrists. *Psychiatr Serv.* 56: 1600-1602.
9. DIAZ, E., H. PRIGERSON, R. DESAI & R. ROSENHECK. 2001. Perceived needs and service use of Spanish speaking monolingual patients followed at a Hispanic clinic. *Community Mental Health Journal*. 37: 335-346.
10. RUIZ, P. 2002. Hispanic access to health/mental health services. *Psychiatric Quarterly*. 73: 85-91.
11. KILUK, B. D., D. E. SUGARMAN, C. NICH, C. J. GIBBONS, S. MARTINO, B. J. ROUNSAVILLE & K. M. CARROLL. 2011. A methodological analysis of randomized clinical trials of computer-assisted therapies for psychiatric disorders: toward improved standards for an emerging field. *Am J Psychiatry*. 168: 790-799.
12. ROOKE, S., E. THORSTEINSSON, A. KARPIN, J. COPELAND & D. ALLSOP. 2010. Computer-delivered interventions for alcohol and tobacco use: a meta-analysis. *Addiction.* 105: 1381-1390.
13. CARROLL, K. M., S. A. BALL, S. MARTINO, C. NICH, T. BABUSCIO, M. A. GORDON, G. A. PORTNOY & B. J. ROUNSAVILLE. 2008. Computer-assisted cognitive-behavioral therapy for addiction. A randomized clinical trial of 'CBT4CBT'. *American Journal of Psychiatry.* 165: 881-888, PMCID: PMC2562873.
14. CARROLL, K. M., B. D. KILUK, C. NICH, M. A. GORDON, G. A. PORTNOY, D. R. MARINO & S. A. BALL. 2014. Computer-assisted delivery of cognitive-behavioral therapy: efficacy and durability of CBT4CBT among cocaine-dependent individuals maintained on methadone. *Am J Psychiatry*. 171: 436-444.
15. CARROLL, K. M., S. A. BALL, S. MARTINO, C. NICH, T. A. BABUSCIO & B. J. ROUNSAVILLE. 2009. Enduring effects of a computer-assisted training program for cognitive-behavioral therapy: A six-month follow-up of CBT4CBT. *Drug and Alcohol Dependence*. 100: 178-181 PMCID: PMC2742309.
16. KILUK, B. D., K. A. DEVORE, M. B. BUCK, C. NICH, B. T. YATES, D. LAPAGLIA, T. F. FRANKFORTER & C. K.M. in press. Randomized clinical trial of computer based CBT for alcohol use disorders: Efficacy as an add-on to standard treatment and as a stand alone. *Alcohol Clin Exp Res.*
17. OLMSTEAD, T. A., C. D. OSTROW & K. M. CARROLL. 2010. Cost-effectiveness of computer-assisted training in cognitive-behavioral therapy as an adjunct to standard care for addiction. *Drug Alcohol Depend*. 110: 200-207.
18. KILUK, B. D., C. NICH, T. BABUSCIO & K. M. CARROLL. 2010. Quality versus quantity: acquisition of coping skills following computerized cognitive-behavioral therapy for substance use disorders. *Addiction.* 105: 2120-2127.
19. FALK, D., X. Q. WANG, L. LIU, J. FERTIG, M. MATTSON, M. RYAN, B. JOHNSON, R. STOUT & R. Z. LITTEN. 2010. Percentage of subjects with no heavy drinking days: evaluation as an efficacy endpoint for alcohol clinical trials. *Alcohol Clin Exp Res.* 34: 2022-2034.
20. CARROLL, K. M., B. J. ROUNSAVILLE, C. NICH, L. T. GORDON, P. W. WIRTZ & F. H. GAWIN. 1994. One year follow-up of psychotherapy and pharmacotherapy for cocaine dependence: Delayed emergence of psychotherapy effects. *Archives of General Psychiatry.* 51: 989-997.

21. CARROLL, K. M., S. A. BALL, S. MARTINO, C. NICH, T. A. BABUSCIO & B. J. ROUNSAVILLE. 2009. Enduring effects of a computer-assisted training program for cognitive behavioral therapy: a 6-month follow-up of CBT4CBT. *Drug Alcohol Depend.* 100: 178-181.
22. CARROLL, K. M., C. NICH, T. L. FRANKFORTER & R. M. BISIGHINI. 1999. Do patients change in the way we intend? Treatment-specific skill acquisition in cocaine-dependent patients using the Cocaine Risk Response Test. *Psychol Assess.* 11: 77-85.
23. DEVITO, E. E., P. D. WORHUNSKY, K. M. CARROLL, B. J. ROUNSAVILLE, H. KOBER & M. N. POTENZA. 2012. A preliminary study of the neural effects of behavioral therapy for substance use disorders. *Drug Alcohol Depend.* 122: 228-235.
24. COLBY, S. L. & J. M. ORTMAN. 2014. *Projections of the Size and Composition of the US Population:* 2014-2060. Bureau, C., Ed. Washington DC.
25. ZEMORE, S. E., N. MULIA, Y. YU, G. BORGES & T. K. GREENFIELD. 2009. Gender, acculturation, and other barriers to alcohol treatment utilization among Latinos in three National Alcohol Surveys. *J Subst Abuse Treat.* 36: 446-456.
26. MANCINI, M. A., C. P. SALAS-WRIGHT & M. G. VAUGHN. 2015. Drug use and service utilization among Hispanics in the United States. *Soc Psychiatry Psychiatr Epidemiol*. 50: 1679-1689.
27. Institute of Medicine; SMEDLEY, B. D., A. Y. STITH & A. R. NELSON. 2003. *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care.* Institite of Medicine, National Academies Press. Washington, D.C.
28. ALEGRIA, M., J. B. PAGE, H. HANSEN, A. M. CAUCE, R. R. ROBLES, C. BLANCO, D. E. CORTES, H. AMARO, A. MORALES & P. PERRY. 2006. Improving drug treatment services for Hispanics: Research gaps and scientific opportunities. *Drug Alcohol Depend.* 84: S76-S84.
29. CAETANO, R. 2003. Alcohol-related health disparities and treatment related epidemiological findings among Whites, Blacks, and Hispanics in the United States. *Alcoholism: Clinical & Experimental Research*. 27: 1337-1339.
30. CHARTIER, K. & R. CAETANO. 2010. Ethnicity and health disparities in alcohol research. *Alcohol Res Health.* 33: 152-160.
31. GUERRERO, E. G., J. C. MARSH, L. DUAN, C. OH, B. PERRON & B. LEE. 2013. Disparities in completion of substance abuse treatment between and within racial and ethnic groups. *Health Serv Res*. 48: 1450-1467.
32. NIAAA. 2015. *Alcohol and the Hispanic Community,* NIH, http://pubs.niaaa.nih.gov/publications/HispanicFact/HispanicFact.htm
33. LIPSKY, S. & R. CAETANO. 2009. Epidemiology of substance abuse among Latinos. *J Ethn Subst Abuse*. 8: 242-260.
34. SALONER, B. & B. LE COOK. 2013. Blacks and Hispanics are less likely than whites to complete addiction treatment, largely due to socioeconomic factors. *Health Aff (Millwood).* 32: 135-145.
35. SAVAGE, J. E. & B. MEZUK. 2014. Psychosocial and contextual determinants of alcohol and drug use disorders in the National Latino and Asian American Study. *Drug Alcohol Depend.* 139: 71-78.
36. LEE, C. S., S. M. COLBY, D. J. ROHSENOW, S. R. LOPEZ, L. HERNANDEZ & R. CAETANO. 2013. Acculturation stress and drinking problems among urban heavy drinking Latinos in the Northeast. *J Ethn Subst Abuse.* 12: 308-320.
37. GUERRERO, E. G., A. CEPEDA, L. DUAN & T. KIM. 2012. Disparities in completion of substance abuse treatment among Latino subgroups in Los Angeles County, CA. *Addict Behav.* 37: 1162-1166.
38. RIOS-BEDOYA, C. F. & D. FREILE-SALINAS. 2014. Incidence of alcohol use disorders among Hispanic subgroups in the USA. *Alcohol Alcohol.* 49: 549-556.
39. SUBSTANCE ABUSE AND MENTAL HEALTH SERVICES ADMINISTRATION (SAMHSA). 2013. Hispanic Subgroups Differ in Rates of Substance Use Treatment Need and Receipt. SAMHSA, Ed.
40. CHARTIER, K. G., T. CARMODY, M. AKHTAR, M. B. STEBBINS, S. T. WALTERS & D. WARDEN. 2015. Hispanic Subgroups, Acculturation, and Substance Abuse Treatment Outcomes. *J Subst Abuse Treat.* 59: 74-82.
41. ALVAREZ, J., B. D. OLSON, L. A. JASON, M. I. DAVIS & J. R. FERRARI. 2004. Heterogeneity among Latinas and Latinos entering substance abuse treatment: Frindings from a national database. *J Subst Abuse Treat.* 26: 277-284.

42. SANCHEZ, M., M. DE LA ROSA, T. C. BLACKSON, F. SASTRE, P. ROJAS, T. LI & F. DILLON. 2014. Pre- to postimmigration alcohol use trajectories among recent Latino immigrants. *Psychol Addict Behav.* 28: 990-999.
43. BURLEW, K., S. LARIOS, L. SUAREZ-MORALES, B. HOLMES, K. VENNER & R. CHAVEZ. 2011. Increasing ethnic minority participation in substance abuse clinical trials: lessons learned in the National Institute on Drug Abuse's Clinical Trials Network. *Cultur Divers Ethnic Minor Psychol.* 17: 345-356.
44. VERISSIMO, A. D. O., C. E. GRELLA, H. AMARO & G. C. GEE. 2014. Disrimination and substance use disorders among Latinos: The role of gender, nativity and ethnicity. *Am J Public Health.* 104: 1421-1428.
45. ZEMORE, S. E., Y. YE, N. MULIA, P. MARTINEZ, R. JONES-WEBB & K. KARRIKER-JAFFE. 2016, in press. Poor, persecuted, young, and alone: Toward explaining the elevated risk of alcohol problems among Black and Latino men who drink. *Drug Alcohol Depend.*
46. LEE, C. S., J. ALMEIDA, S. M. COLBY, T. TAVARES & D. J. ROHSENOW. 2016. Acculturation, hazardous drinking and depressive symptomatology among Hispanics enrolled in a clinical trial. *Addict Res Theory*. 24: 69-79.
47. ALVAREZ, J., L. A. JASON, B. D. OLSON, J. R. FERRARI & M. I. DAVIS. 2007. Substance abuse prevalence and treatment among Latinos and Latinas*. J Ethn Subst Abuse*. 6: 115-141.
48. MILLS, B. A. & R. CAETANO. 2012. Decomposing associations between acculturation and drinking in Mexican Americans. *Alcohol Clin Exp Res.* 36: 1205-1211.
49. ORTEGA, A. N., R. A. ROSENHECK, M. ALEGRIA & R. A. DESAI. 2000. Acculturation and the lifetime risk of psychiatric and substance use disorders among Hispanics. *JOURNAL OF NERVOUS AND MENTAL DISEASE.* 188: 728-735.
50. VAETH, P. A., R. CAETANO & L. A. RODRIGUEZ. 2012. The Hispanic Americans Baseline Alcohol Survey (HABLAS): the association between acculturation, birthplace and alcohol consumption across Hispanic national groups. *Addict Behav.* 37: 1029-1037.
51. BURLEW, A. K., J. C. WEEKES, L. MONTGOMERY, D. J. FEASTER, M. S. ROBBINS, C. L. ROSA, L. M. RUGLASS, K. L. VENNER & L. T. WU. 2011. Conducting research with racial/ethnic minorities: methodological lessons from the NIDA Clinical Trials Network*. Am J Drug Alcohol Abuse.* 37: 324-332.
52. ARROYO, J. A., W. R. MILLER & J. S. TONIGAN. 2003. The influence of Hispanic ethnicity on long-term outcome in three alcohol-treatment modalities. *J Stud Alcohol.* 64: 98-104.
53. TRUJOLS, J., E. LUQUERO, N. SINOL, E. BANULS, A. TEJERO, F. BATLLE & J. PEREZ DE LOS COBOS. 2007. [Cognitive-behavioral therapy for the treatment of cocaine dependence]. *Actas Esp Psiquiatr*. 35: 190-198.
54. MARQUES, A. C. & M. L. FORMIGONI. 2001. Comparison of individual and group cognitive behavioral therapy for alcohol and/or drug dependent patients. *Addiction*. 96: 835-846.
55. ARAYA, R., G. ROJAS, R. FRITSCH, J. GAETE, M. ROJAS, G. SIMON & T. J. PETERS. 2003. Treating depression in primary care in low-income women in Santiago, Chile: a randomised controlled trial. *Lancet.* 361: 995-1000.
56. COMAS-DIAZ, L. 1981. Effects of cognitive and behavioral group treatment on the depressive symptomatology of Puerto Rican women. *J Consult Clin Psychol.* 49: 627-632.
57. LARA, M. A., C. NAVARRO, N. A. RUBI & L. MONDRAGON. 2003. Two levels of intervention in low-income women with depressive symptoms: compliance and programme assessment. *Int J Soc Psychiatry.* 49: 43-57.
58. MIRANDA, J., G. BERNAL, A. LAU, L. KOHN, W. C. HWANG & T. LAFROMBOISE. 2005. State of the science on psychosocial interventions for ethnic minorities. *Annu Rev Clin Psychol*. 1: 113-142.
59. MIRANDA, J., F. AZOCAR, K. C. ORGANISTA, E. DWYER & P. AREANE. 2003. Treatment of depression among impoverished primary care patients from ethnic minority groups. *Psychiatr Serv.* 54: 219-225.
60. MIRANDA, J., J. Y. CHUNG, B. L. GREEN, J. KRUPNICK, J. SIDDIQUE, D. A. REVICKI & T. BELIN. 2003. Treating depression in predominantly low-income young minority women: a randomized controlled trial. *JAMA.* 290: 57-65.
61. MIRANDA, J., N. DUAN, C. SHERBOURNE, M. SCHOENBAUM, I. LAGOMASINO, M. JACKSON-TRICHE & K. B. WELLS. 2003. Improving care for minorities: can quality improvement interventions improve care and outcomes for depressed minorities? Results of a randomized, controlled trial. *Health Serv Res*. 38: 613-630.

62. ORGANISTA, K. C. & R. F. MUNOZ. 1996. Cognitive behavioral therapy with Latinos. *Cognitive and Behavioral Practice.* 3: 255-270.
63. ROSSELLO, J., G. BERNAL & C. RIVERA-MEDINA. 2008. Individual and group CBT and IPT for Puerto Rican adolescents with depressive symptoms. *Cultur Divers Ethnic Minor Psychol.* 14: 234-245.
64. ANTONIADES, J., D. MAZZA & B. BRIJNATH. 2014. Efficacy of depression treatments for immigrant patients: results from a systematic review. *BMC Psychiatry*. 14: 176.
65. COLLADO, A., S. D. CASTILLO, F. MAERO, C. W. LEJUEZ & L. MACPHERSON. 2014. Pilot of the brief behavioral activation treatment for depression in latinos with limited english proficiency: preliminary evaluation of efficacy and acceptability. *Behav Ther.* 45: 102-115.
66. BENUTO, L. T. & W. O'DONOHUE. 2015. Is culturally sensitive cognitive-behavioral therapy an empirically supported treatment? The case for Hispanics. *International Journal of Psychological Therapy*. 15: 405-421.
67. VOSS HORRELL, S. C. 2008. Effectiveness of cognitive-behavioral therapy with adult ethnic minority clients: A review. *Professional Psychology: Research and Practice*. 39: 160-168.
68. WINDSOR, L. C., A. JEMAL & E. J. ALESSI. 2015. Cognitive behavioral therapy: a meta-analysis of race and substance use outcomes. *Cultur Divers Ethnic Minor Psychol*. 21: 300-313.
69. CARROLL, K. M. & L. S. ONKEN. 2005. Behavioral therapies for drug abuse. *Am J Psychiatry*. 162: 1452-1460.
70. MILLER, W. R., M. VILLANUEVA, J. S. TONIGAN & I. CUZMAR. 2007. Are special treatments needed for special populations? *Alcoholism Treatment Quarterly*. 25: 63-78.
71. BERNAL, G. & M. R. SHARRON DEL RIO. 2001. Are empirically supported treatment valid for ethnic minorities? Toward an alternative approach for treatment research. *Cultur Divers Ethnic Minor Psychol*. 7: 328-342.
72. SMITH, T. B., M. D. RODRIGUEZ & G. BERNAL. 2011. Culture. J Clin Psychol. 67: 166-175.
73. BERNAL, G. & E. SAEZ-SANTIAGO. 2006. Culturally centered psychosocial interventions. *Journal of Community Psychology*. 24: 121-132.
74. GRINER, D. & T. B. SMITH. 2006. Culturally adapted mental health interventions: A meta-analytic review. *Psychotherapy: Theory, Research Practice & Training*. 43: 531-548.
75. WOODRUFF, S. I., G. A. TALAVERA & J. P. ELDER. 2002. Evaluation of a culturally appropriate smoking cessation intervention for Latinos. *Tob Control.* 11: 361-367.
76. GILMER, T. P., A. PHILIS-TSIMIKAS & C. WALKER. 2005. Outcomes of Project Dulce: a culturally specific diabetes management program. *Ann Pharmacother*. 39: 817-822.
77. VILLARRUEL, A. M., L. S. JEMMOTT & J. B. JEMMOTT, 3RD. 2005. Designing a culturally based intervention to reduce HIV sexual risk for Latino adolescents. *J Assoc Nurses AIDS Care*. 16: 23-31.
78. HINTON, D. E., S. G. HOFMANN, E. RIVERA, M. W. OTTO & M. H. POLLACK. 2011. Culturally adapted CBT (CA-CBT) for Latino women with treatment-resistant PTSD: a pilot study comparing CA-CBT to applied muscle relaxation. *Behav Res Ther.* 49: 275-280.
79. BURROW-SANCHEZ, J. J., C. R. MARTINEZ, H. HOPS & M. WRONA. 2011. Cultural accommodation of substance abuse treatment for Latino adolescents. *J Ethn Subst Abuse*. 10: 202-225.
80. BENISH, S. G., S. QUINTANA & B. E. WAMPOLD. 2011. Culturally adapted psychotherapy and the legitimacy of myth: a direct-comparison meta-analysis. *J Couns Psychol.* 58: 279-289.
81. HUEY, S. J., JR., J. L. TILLEY, E. O. JONES & C. A. SMITH. 2014. The contribution of cultural competence to evidence-based care for ethnically diverse populations. *Annu Rev Clin Psychol.* 10: 305-338.
82. PEW RESEARCH CENTER. 2013. Health Online 2013. *In* Internet, Science & Tech. Fox, S., & Duggan, M., Ed. http://www.pewinternet.org/2013/01/15/health-online-2013/
83. PEW HISPANIC CENTER. 2013. *Closing the Digital Divide: Latinos and Technology Adoption*. Lopez, M. H., Ed. Pew Research Center. Washington DC. www.pewhispanic.org
84. JACOBS, R. J., J. Q. LOU, R. L. OWNBY & J. CABALLERO. 2014. A systematic review of eHealth interventions to improve health literacy. *Health Informatics J.*
85. CALVO, R. in press. Health literacy and quality of care among Latino immigrants in the United States. *Health and Social Work.*
86. PENA-PURCELL, N. 2008. Hispanics' use of Internet health information: An exploratory study. *Journal of the Medical Library Association*. 96: 101-107.

87. VICTORSON, D., J. BANAS, J. SMITH, L. LANGUIDO, E. SHEN, S. GUTIERREZ, E. CORDERO & L. FLORES. 2014. eSalud: designing and implementing culturally competent ehealth research with latino patient populations. *Am J Public Health.* 104: 2259-2265.
88. LEITE, L., M. BURESH, N. RIOS, A. CONLEY, T. FLYS & K. R. PAGE. 2014. Cell phone utilization among foreign-born Latinos: a promising tool for dissemination of health and HIV information. *J Immigr Minor Health.* 16: 661-669.
89. MARKS, I. M. & K. CAVANAGH. 2009. Computer-aided psychological treatments: Evolving issues. *Annu Rev Clin Psychol*. 5.
90. MARKS, I. M., K. CAVANAGH & L. GEGA. 2007. *Hands On Help: Computer-Aided Psychotherapy*. Psychol. Press. Hove, UK.
91. KALTENTHALER, E., G. PARRY, C. BEVERLEY & M. FERRITER. 2008. Computerized cognitive-behavioural therapy for depression: Systematic review. *The British Journal of Psychiatry.* 193: 181-184.
92. CUIJPERS, P., I. M. MARKS, A. VAN STRATEN, K. CAVANAGH, L. GEGA & G. ANDERSSON. 2009. Computer-aided psychotherapy for anxiety disorders: A meta-analytic review. *Cognitive Behavioural Therapy*. 38: 66-82.
93. PORTNOY, D. B., L. A. J. SCOTT-SHELDON, B. T. JOHNSON & M. P. CAREY. 2008. Computer-delivered interventions for health promotion and behavioral risk reduction: A meta-analysis of 75 randomized controlled trials, 1988-2007. *Prev Med*. 47: 3-16.
94. CUIJPERS, P., A. VAN STRATEN & G. ANDERSSON. 2008. Internet-administered cognitive behavior therapy for health problems: A systematic review. *J Behav Med.* 31: 169-177.
95. RIPER, H., M. BLANKERS, H. HADIWIJAYA, J. CUNNINGHAM, S. CLARKE, R. WIERS, D. EBERT & P. CUIJPERS. 2014. Effectiveness of guided and unguided low-intensity internet interventions for adult alcohol misuse: a meta-analysis. *PLoS One.* 9: e99912.
96. DEDERT, E. A., J. R. MCDUFFIE, R. STEIN, J. M. MCNIEL, A. S. KOSINSKI, C. E. FREIERMUTH, A. HEMMINGER & J. W. WILLIAMS, JR. 2015. Electronic Interventions for Alcohol Misuse and Alcohol Use Disorders: A Systematic Review. *Ann Intern Med.* 163: 205-214.
97. COPELAND, J. & G. MARTIN. 2004. Web-based interventions for substance use disorders: A qualitative review. *J Subst Abuse Treat.* 26: 109-116.
98. POSTEL, M. G., H. A. DE HAAN & C. A. J. DEJONG. 2008. E-therapy for mental health problems: A systematic review. *Telemedicine and E-Health.* 14: 707-714.
99. TUMUR, I., E. KALTENTHALER, M. FERRITER, C. BEVERLEY & G. PARRY. 2007. Computerized cognitive behaviour therapy for obsessive-compulsive disorder: A systematic review. *Psychotherapy and Psychosomatics.* 76: 196-202.
100. GIBBONS, M. C., R. F. WILSON, L. SAMAL, C. U. LEHMANN, K. DICKERSIN, H. ABOUMATAR, J. FINKELSTEIN, E. SHELTON, R. SHARMA & E. B. BASS. 2009. *Impact of Consumer Health Informatics Applications, Evidence Report/Technology Assessment No. 188.,,* Vol. AHRQ Publication No. 09(10)-E019. Agency for Healthcare Research and Quality, Ed. Agency for Healthcare Research and Quality,. Rockville, MD.
101. EVERS, K. E., C. O. CUMMINS, J. O. PROCASKA & J. M. PROCASKA. 2005. Online health behavior and disease management programs: Are we ready for them? Are they ready for us? *J Med Internet Res*. 7: 3.
102. CARROLL, K. M. & B. J. ROUNSAVILLE. 2010. Computer-assisted therapy in psychiatry: be brave-it's a new world. *Curr Psychiatry Rep*. 12: 426-432.
103. COLLINS, L. M., S. A. MURPHY, V. NAIR & V. STRETCHER. 2005. A strategy for optimizing and evaluating behavior interventions. *Annals of Behavioral Medicine*. 30: 65-73.
104. COLLINS, L. M., S. A. MURPHY & V. STRETCHER. 2007. The Multiphase Optimization Strategy (MOST) and the Sequential Multiple Assignment Randomized Trial (SMART): New methods for more potent e-health interventions. *Am J Prev Med*. 32: S112-S118. PMCID: PMC2062525.
105. KILUK, B. D., D. E. SUGARMAN, C. NICH, C. R. GIBBONS, S. MARTINO, B. J. ROUNSAVILLE & K. M. CARROLL. 2011. A methodological analysis randomized trials of computer-assisted therapy for psychiatric disorders: Towards improved standards for an emerging field. *The American Journal of Psychiatry*. 168: 790-799.
106. CARROLL, K. M., B. D. KILUK, C. NICH, T. A. BABUSCIO, J. A. BREWER, M. N. POTENZA, S. A. BALL, S. MARTINO, B. J. ROUNSAVILLE & C. W. LEJUEZ. 2011. Cognitive function and treatment response in a

randomized clinical trial of computer-based training in cognitive-behavioral therapy. *Substance Use and Misuse*. 46: 23-34.

107. SUGARMAN, D. E., C. NICH & K. M. CARROLL. 2010. Coping strategy use following computerized cognitive-behavioral therapy for substance use disorders. *Psychol Addict Behav.* 24: 689-695.
108. KILUK, B. D., C. NICH, T. A. BABUSCIO & K. M. CARROLL. 2010. Quantity versus quality: Acquisition of coping skills in computer-assisted cognitive behavioral therapy for substance abuse. *Addiction.* 105: 2120-2127.
109. INSTITUTE OF MEDICINE. 2003. *Unequal Treatment: Confronting Racial and Ethnic Disparities in Healthcare.* National Academies Press. Washington, DC.
110. AMARO, H., S. AREVALO, G. GONZALEZ, J. SZAPOCZNIK & M. Y. IGUCHI. 2006. Needs and scientific opportunities for research on substance abuse treatments among Hispanic adults. *Drug Alcohol Depend.* 84S: S64-S75.
111. MCCRONE, P., M. KNAPP, J. PROUDFOOT, C. RYDEN, K. CAVANAGH, D. A. SHAPIRO, S. ILSON, J. A. GRAY, D. GOLDBERG, A. MANN, I. MARKS, B. EVERITT & A. TYLEE. 2004. Cost-effectiveness of computerized cognitive-behavioral therapy for anxiety and depression in primary care: Randomized controlled trial. *British Journal of Psychiatry*. 185: 55-62.
112. CARROLL, K. M., B. J. ROUNSAVILLE & C. NICH. 1994. Blind man's bluff: effectiveness and significance of psychotherapy and pharmacotherapy blinding procedures in a clinical trial. *J Consult Clin Psychol*. 62: 276-280.
113. CARROLL, K. M. 1997. Manual-guided psychosocial treatment. A new virtual requirement for pharmacotherapy trials? *Arch Gen Psychiatry*. 54: 923-928.
114. CARROLL, K. M., G. J. CONNORS, N. L. COONEY, C. C. DICLEMENTE, D. M. DONOVAN, R. R. KADDEN, R. L. LONGABAUGH, B. J. ROUNSAVILLE, P. W. WIRTZ & A. ZWEBEN. 1998. Internal validity of Project MATCH treatments: discriminability and integrity. *J Consult Clin Psychol*. 66: 290-303.
115. CARROLL, K. M., C. NICH, R. L. SIFRY, K. F. NURO, T. L. FRANKFORTER, S. A. BALL, L. FENTON & B. J. ROUNSAVILLE. 2000. A general system for evaluating therapist adherence and competence in psychotherapy research in the addictions. *Drug Alcohol Depend.* 57: 225-238.
116. CARROLL, K. M. & K. F. NURO. 2002. One size can't fit all: A stage model for psychotherapy manual development. *Clinical Psychology: Science and Practice.* 9: 396-406.
117. DECKER, S. E., T. FRANKFORTER, T. BABUSCIO, C. NICH, S. A. BALL & K. M. CARROLL. 2014. Assessment concordance and predictive validity of self-report and biological assay of cocaine use in treatment trials. *Am J Addict.* 23: 466-474.
118. O'MALLEY, S. S. & K. M. CARROLL. 1996. Psychotherapeutic considerations in pharmacological trials. *Alcohol Clin Exp Res*. 20: 17A-22A.
119. PETRY, N. M., J. M. ROLL, B. J. ROUNSAVILLE, S. A. BALL, M. STITZER, J. M. PEIRCE, J. BLAINE, K. C. KIRBY, D. MCCARTY & K. M. CARROLL. 2008. Serious adverse events in randomized psychosocial treatment studies: safety or arbitrary edicts? *J Consult Clin Psychol.* 76: 1076-1082.
120. ROUNSAVILLE, B. J., K. M. CARROLL & L. S. ONKEN. 2001. A stage model of behavioral therapies research: Getting started and moving on from Stage I. *Clinical Psychology: Science and Practice*. 8: 133-142.
121. ROUNSAVILLE, B. J., N. M. PETRY & K. M. CARROLL. 2003. Single versus multiple drug focus in substance abuse clinical trials research. *Drug Alcohol Depend*. 70: 117-125.
122. ROUNSAVILLE, D. B., K. HUNKELE, C. J. EASTON, C. NICH & K. M. CARROLL. 2008. Making consent more informed: preliminary results from a multiple-choice test among probation-referred marijuana users entering a randomized clinical trial. *J Am Acad Psychiatry Law*. 36: 354-359.
123. SANTA ANA, E. J., S. MARTINO, S. A. BALL, C. NICH, T. L. FRANKFORTER & K. M. CARROLL. 2008. What is usual about "treatment-as-usual"? Data from two multisite effectiveness trials. *J Subst Abuse Treat.* 35: 369-379.
124. SHOLOMSKAS, D. E., G. SYRACUSE-SIEWERT, B. J. ROUNSAVILLE, S. A. BALL, K. F. NURO & K. M. CARROLL. 2005. We don't train in vain: a dissemination trial of three strategies of training clinicians in cognitive-behavioral therapy. *J Consult Clin Psychol.* 73: 106-115.
125. SUAREZ-MORALES, L., J. MATTHEWS, S. MARTINO, S. A. BALL, C. ROSA, C. FARENTINOS, J. SZAPOCZNIK & K. M. CARROLL. 2007. Issues in designing and implementing a Spanish-language multi-site clinical trial. *Am J Addict.* 16: 206-215.

126. CARROLL, K. M., B. D. KILUK, C. NICH, E. E. DEVITO, S. DECKER, D. LAPAGLIA, D. DUFFEY, T. A. BABUSCIO & S. A. BALL. 2014. Toward empirical identification of a clinically meaningful indicator of treatment outcome: features of candidate indicators and evaluation of sensitivity to treatment effects and relationship to one year follow up cocaine use outcomes. *Drug Alcohol Depend.* 137: 3-19.
127. SERAFINI, K., B. MALIN-MAYOR, C. NICH, K. HUNKELE & K. M. CARROLL. 2016, in press. Psychometric properties of the Positive and Negative Affect Schedule (PANAS) in a heterogeneous sample of substance users. *Am J Drug Alcohol Abuse*.
128. BALODIS, I. M., H. KOBER, P. D. WORHUNSKY, M. C. STEVENS, G. D. PEARLSON, K. M. CARROLL & M. N. POTENZA. In press. Neurofunctional Reward Processing Changes in Cocaine Dependence During Recovery. *Neuropsychopharmacology*.
129. CARROLL, K. M., A. HERMAN, E. E. DEVITO, T. L. FRANKFORTER, M. N. POTENZA & M. SOFUOGLU. 2015. Catehol-O-Methyltransferase gene Val158Met polymorphism as a potential predictor of response to computer-assisted delivery of cognitive-behavioral therapy among cocaine-dependent individuals: Preliminary findings from a randomized controlled trial. *Am J Addict.* 24:443-451.
130. YIP, S. W., E. E. DEVITO, H. KOBER, P. D. WORHUNSKY, K. M. CARROLL & M. N. POTENZA. 2014. Pretreatment measures of brain structure and reward-processing brain function in cannabis dependence: an exploratory study of relationships with abstinence during behavioral treatment. *Drug Alcohol Depend*. 140: 33-41.
131. XU, J., H. KOBER, X. WANG, E. E. DEVITO, K. M. CARROLL & M. N. POTENZA. 2014. Hippocampal volume mediates the relationship between measures of pre-treatment cocaine use and within-treatment cocaine abstinence. *Drug Alcohol Depend.* 143: 74-80.
132. KILUK, B. D., K. SERAFINI, T. FRANKFORTER, C. NICH & K. M. CARROLL. 2014. Only connect: The working alliance in computer-based cognitive behavioral therapy. *Behav Res Ther.* 63C: 139-146.
133. WORHUNSKY, P. D., M. C. STEVENS, K. M. CARROLL, B. J. ROUNSAVILLE, V. D. CALHOUN, G. D. PEARLSON & M. N. POTENZA. 2013. Functional brain networks associated with cognitive control, cocaine dependence, and treatment outcome. *Psychol Addict Behav*. 27: 477-488.
134. KILUK, B. D., C. NICH & K. M. CARROLL. 2011. Relationship of cognitive function and the acquisition of coping skills in computer assisted treatment for substance use disorders. *Drug Alcohol Depend.* 114: 169-176.
135. JIA, Z., P. D. WORHUNSKY, K. M. CARROLL, B. J. ROUNSAVILLE, M. C. STEVENS, G. D. PEARLSON & M. N. POTENZA. 2011. An initial study of neural responses to monetary incentives as related to treatment outcome in cocaine dependence. *Biol Psychiatry.* 70: 553-560.
136. XU, J., E. E. DEVITO, P. D. WORHUNSKY, K. M. CARROLL, B. J. ROUNSAVILLE & M. N. POTENZA. 2010. White matter integrity is associated with treatment outcome measures in cocaine dependence. *Neuropsychopharmacology*. 35: 1541-1549.
137. KILUK, B. D., C. NICH & K. M. CARROLL. 2010. Neurocognitive indicators predict results of an informed-consent quiz among substance-dependent treatment seekers entering a randomized clinical trial. *J Stud Alcohol Drugs.* 71: 704-712.
138. MITCHELL, M. R., I. M. BALODIS, E. E. DEVITO, C. M. LACADIE, J. YESTON, D. SCHEINOST, R. T. CONSTABLE, K. M. CARROLL & M. N. POTENZA. 2013. A preliminary investigation of Stroop-related intrinsic connectivity in cocaine dependence: associations with treatment outcomes. *Am J Drug Alcohol Abuse*. 39: 392-402.
139. BALODIS, I. M., H. KOBER, P. D. WORHUNSKY, M. C. STEVENS, G. D. PEARLSON, K. M. CARROLL & M. N. POTENZA.In press, 2016. Neuro-Functional Reward Processing Changes in Cocaine Dependence during Recovery. *Neuropsychopharmacology*.
140. DECKER, S. E., T. FRANKFORTER, T. BABUSCIO, B. D. KILUK, C. NICH & K. M. CARROLL. in press. Just showing up is not enough: Homework competion and coaine abstinence in cognitve behavioral therapy for cocaine dependence. *J Consult Clin Psychol.*
141. DEVITO, E. E., T. A. BABUSCIO, C. NICH, S. A. BALL & K. M. CARROLL. 2014. Gender differences in clinical outcomes for cocaine dependence: Randomized clinical trials of behavioral therapy and disulfiram. *Drug Alcohol Depend.* 145C: 156-167.
142. MCCANCE-KATZ, E. F., K. M. CARROLL & B. J. ROUNSAVILLE. 1999. Gender differences in treatment-seeking cocaine abusers--implications for treatment and prognosis. *Am J Addict*. 8: 300-311.

143. MCHUGH, R. K., E. E. DEVITO, D. DODD, K. M. CARROLL, J. S. POTTER, S. F. GREENFIELD, H. S. CONNERY & R. D. WEISS. 2013. Gender differences in a clinical trial for prescription opioid dependence. *J Subst Abuse Treat*. 45: 38-43.
144. MILLIGAN, C. O., C. NICH & K. M. CARROLL. 2004. Ethnic differences in substance abuse treatment retention, compliance, and outcome from two clinical trials. *Psychiatr Serv*. 55: 167-173.
145. MONTGOMERY, L., K. M. CARROLL & N. M. PETRY. 2015. Initial abstinence status and contingency management treatment outcomes: Does race matter? *J Consult Clin Psychol*. 83: 473-481.
146. MONTGOMERY, L., N. M. PETRY & K. M. CARROLL. 2012. Moderating effects of race in clinical trial participation and outcomes among marijuana-dependent young adults. *Drug Alcohol Depend*. 126: 333-339.
147. SANTA ANA, E., S. MARTINO, S. A. BALL, C. NICH & K. M. CARROLL. 2008. What is usual about 'treatment as usual': Audiotaped ratings of standard treatment in the Clinical Trials Network. *Journal of Substance Abuse Treatment*. 35: 369-379 PMCID: PMC2712113.
148. HOFFMAN, K. A. & D. MCCARTY. 2013. Improving the quality of addiction treatment. *In Interventions for Addiction: Comprehensive Addictive Behaviors and Disorders*,, Vol. 3. Miller, P. M., Ed.: 579-588. Academic Press. San Diego, CA.
149. INSTITUTE OF MEDICINE. 1998. *Bridging the Gap Between Practice and Research: Forging Partnerships with Community-Based Drug and Alcohol Treatment*. National Academy Press. Washington, DC.
150. CARROLL, K. M. 1998. *A Cognitive-Behavioral Approach: Treating Cocaine Addiction*. NIDA. Rockville, Maryland.
151. CARROLL, K. M., C. NICH & S. A. BALL. 2005. Practice makes progress: Homework assignments and outcome in the treatment of cocaine dependence. *Journal of Consulting and Clinical Psychology*. 73: 749-755. PMCID: PMC2365906.
152. BURNS, D. D. & D. L. SPANGLER. 2000. Does psychotherapy homework lead to improvements in depression in cognitive-behavioral therapy or does improvement lead to increased homework compliance? *J Consult Clin Psychol*. 68: 46-56.
153. GONZALEZ, V. M., J. M. SCHMITZ & K. A. DELAUNE. 2006. The role of homework in cognitive-behavioral therapy for cocaine dependence. *J Consult Clin Psychol*. 74: 633-637.
154. KAZANTZIS, N., F. P. DEANE & K. R. RONAN. 2000. Homework assignments in cognitive and behavioral therapy: A meta-analysis. *Clinical Psychology: Science and Practice.* 7: 189-202.
155. MACKINNON, D. P. & L. J. LUECKEN. 2008. How and for whom? Mediation and moderation in health psychology. *Health Psycholology*. 27: S99-S100.
156. MACKINNON, D. P., C. M. LOCKWOOD, J. M. HOFFMAN, S. G. WEST & V. SHEETS. 2002. A comparison of methods to test mediation and other intervening variable effects. *Psychological Methods*. 7: 83-104.
157. LONGABAUGH, R. 2010. Commentary on Kiluk et al., 2010: The emperor has some new clothes: Coping is a mediator of cognitive-behavioral therapy's effectiveness. *Addiction.* 105: 2128-2129.
158. MORGENSTERN, J. & R. LONGABAUGH. 2000. Cognitive-behavioral treatment for alcohol dependence: A review of the evidence for its hypothesized mechanisms of action. *Addiction*. 95: 1475-1490.
159. FREEDMAN, R. 2014. Computerization of the therapeutic task of working through. *Am J Psychiatry.* 171: 388-390.
160. CARROLL, K. M., S. MARTINO, S. A. BALL, C. NICH, T. FRANKFORTER, L. M. ANEZ, M. PARIS, L. SUAREZ-MORALES, J. SZAPOCZNIK, W. R. MILLER, C. ROSA, J. MATTHEWS & C. FARENTINOS. 2009. A multisite randomized effectiveness trial of motivational enhancement therapy for Spanish-speaking substance users. *J Consult Clin Psychol.* 77: 993-999.
161. ANDRES-HYMAN, R. C., J. ORTIZ, L. M. ANEZ, M. P. PARIS & L. DAVIDSON. 2006. Culture and clinical practice: Recommendations for working with Puerto Ricans and other Latinas(os) in the United States. *Professional Psychology: Research and Practice.* 37: 694-701.
162. ANEZ, L. M., M. PARIS, JR., L. E. BEDREGAL, L. DAVIDSON & C. M. GRILO. 2005. Application of cultural constructs in the care of first generation Latino clients in a community mental health setting. *J Psychiatr Pract*. 11: 221-230.
163. CASTRO, F. G., M. BARRERA, JR. & L. K. HOLLERAN STEIKER. 2010. Issues and challenges in the design of culturally adapted evidence-based interventions. *Annu Rev Clin Psychol.* 6: 213-239.

164. NELSON, A. F., F. RICARDO, B. FORGES, E. D. S. LOPEZ & R. LEWY. 2008. Creando Nuestra Salud (Creating Our Health): Results and findings from a breast cancer education program with rural Hispanic women. *Florida Public Health Review.* 5: 99-103.
165. SILVA, M. L., L. ANEZ, M. A. GORDON, S. A. BALL, K. M. CARROLL & M. PARIS. Invited, under review. Vidas Cruzadas: Adaptation of computer-based training for cognitive behavioral therapy for Spanish-speaking substance users. *Psychiatric Rehabilitation J*.
166. SINGHAL, A. & E. M. ROGERS. 2002. A theoretical agenda for entertainment-education. *Communication Theory*. 12: 117-135.
167. FORSTER, M., J. P. ALLEM, N. MENDEZ, Y. QAZI & J. B. UNGER. 2016. Evaluation of a telenovela designed to improve knowledge and behavioral intentions among Hispanic patients with end-stage renal disease in Southern California. *Ethn Health.* 21: 58-70.
168. HERNANDEZ, M. Y. & K. C. ORGANISTA. 2013. Entertainment-education? A fotonovela? A new strategy to improve depression literacy and help-seeking behaviors in at-risk immigrant Latinas. *Am J Community Psychol.* 52: 224-235.
169. UNGER, J. B., L. J. CABASSA, G. B. MOLINA, S. CONTRERAS & M. BARON. 2013. Evaluation of a fotonovela to increase depression knowledge and reduce stigma among Hispanic adults. *J Immigr Minor Health*. 15: 398-406.
170. WILKIN, H. A., T. W. VALENTE, S. MURPHY, M. J. CODY, G. HUANG & V. BECK. 2007. Does entertainment-education work with Latinos in the United States? Identification and the effects of a telenovela breast cancer storyline. *J Health Commun*. 12: 455-469.
171. CENTRO PARA EL TRATEMIENTO DEL ABUSO DE SUSTANCIAS. 2010. *El alcohol y la depresion: El camino de Jorge hacia una vida mejor.* n, SAMHSA., Ed. Rockville, MD.
172. CARROLL, K. M., C. NICH & S. A. BALL. 2005. Practice makes progress? Homework assignments and outcome in treatment of cocaine dependence. *J Consult Clin Psychol.* 73: 749-755.
173. CARROLL, K. M., S. A. BALL, S. MARTINO, C. NICH, T. A. BABUSCIO, K. F. NURO, M. A. GORDON, G. A. PORTNOY & B. J. ROUNSAVILLE. 2008. Computer-assisted delivery of cognitive-behavioral therapy for addiction: a randomized trial of CBT4CBT. *Am J Psychiatry*. 165: 881-888.
174. DONOVAN, D. M., R. M. KADDEN, C. C. DICLEMENTE & K. M. CARROLL. 2002. Client satisfaction with three therapies in the treatment of alcohol dependence: results from project MATCH. *Am J Addict*. 11: 291-307.
175. CAETANO, R., B. A. MILLS, P. A. VAETH & J. REINGLE. 2014. Age at first drink, drinking, binge drinking, and DSM-5 alcohol use disorder among Hispanic national groups in the United States. *Alcohol Clin Exp Res.* 38: 1381-1389.
176. CAETANO, R., S. RAMISETTY-MIKLER & L. A. RODRIGUEZ. 2008. The Hispanic Americans Baseline Alcohol Survey (HABLAS): rates and predictors of alcohol abuse and dependence across Hispanic national groups. *J Stud Alcohol Drugs*. 69: 441-448.
177. CAETANO, R. 1988. Alcohol use among Hispanic groups in the United States. *Am J Drug Alcohol Abuse.* 14: 293-308.
178. CAETANO, R. 1983. Drinking patterns and alcohol problems among Hispanics in the U.S.: a review. *Drug Alcohol Depend*. 12: 37-59.
179. GONZALEZ SUITT, K., Y. CASTRO, R. CAETANO & C. A. FIELD. 2015. Predictive Utility of Alcohol Use Disorder Symptoms Across Race/Ethnicity. *J Subst Abuse Treat.* 56: 61-67.
180. FIELD, C. A., J. A. CABRIALES, R. H. WOOLARD, A. H. TYROCH, R. CAETANO & Y. CASTRO. 2015. Cultural adaptation of a brief motivational intervention for heavy drinking among Hispanics in a medical setting. *BMC Public Health*. 15: 724.
181. SUE, S. 2003. In defense of cultural competency in psychotherapy and treatment. *Am Psychol.* 58: 964-970.
182. BERNAL, G., J. BONILLA & C. BONITA. 1995. Ecological validity and cultural sensitivity for outcome research: Issues for cultural adaptation and development of psychosocial treatments with Hispanics. *J Abnorm Child Psychol.* 23: 67-82.
183. NOVAS, H. 1998. *Everything you need to know about Latino history*: Revised edition. Penguin Books. New York.
184. BARONA, A. & M. SANTOS DE BARONA. 2003. Recommendations for the psychological treatment of Latino/Hispanic populations. *In Psychological Treatment of Ethnic Minority Populations*. Council of

National Psychological Associations for the Advancement of Ethnic Minority Interests, Ed. Association of Black Psychologists. Washington, DC.

185. COMAS-DIAZ, L. 1996. Cultural considerations in diagnosis. *In Handbook of relational diagnosis and dysfunctional family patterns.* John Wiley & Sons. New York.
186. ANEZ, L. M., M. A. SILVA, M. P. PARIS & L. E. BEDREGAL. 2008. Engaging Latinos through the integration of cultural values and motivational interviewing*. Professional Psychology: Research and Practice*. 39: 153-159.
187. MARIN, B. V. 1990. *Hispanic Drug Abuse: Culturally Appropriate Prevention and Treatment*. Humana Press. New Jersey.
188. SHATTELL, M. M., D. HAMILTON, S. S. STARR, C. J. JENKINS & N. A. HINDERLITER. 2008. Mental health service needs of a Latino population: a community-based participatory research project. *Issues Ment Health Nurs.* 29: 351-370.
189. TREPPER, T. S., T. S. NELSON, E. E. MCCOLLUM & P. MCAVOY. 1997. Improving substance abuse service delivery to Hispanic women through increased cultural competencies: a qualitative study*. J Subst Abuse Treat*. 14: 225-234.
190. CHERAGHI-SOHI, S., P. BOWER, N. MEAD, R. MCDONALD, D. WHALLEY & M. ROLAND. 2007. Making sense of patient priorities: applying discrete choice methods in primary care using 'think aloud' technique. *Fam Pract.* 24: 276-282.
191. PARIS, M., L. BEDREGAL, L. M. ANEZ, G. SHAHAR & L. DAVIDSON. 2004. Psychmetric properties of the Spanish version of the therapeutic collaboration scale (TCS). *Hispanic Journal of Behavioral Sciences*. 26: 390-402.
192. PARIS, M., L. M. ANEZ, L. BEREDGAL, R. ANDRES-HYMAN & L. DAVIDSON. 2005. Help seeking and satisfaction among Latinas: The roles of setting, ethnic identity and therapeutic alliance. *Journal of Community Psychology*. 33: 299-312.
193. BAMATTER, W., C. K.M., L. M. ANEZ, M. PARIS, S. A. BALL, C. NICH, T. L. FRANKFORTER, L. SUAREZ-MORALES, J. SZAPOCZNIK & S. MARTINO. 2010. Informal discussions in substance abuse treatment with Spanish-speaking clients. *J Sub Abuse Treatment* 39: 353-363.
194. CARROLL, K. M., S. MARTINO, L. SUAREZ-MORALES, S. A. BALL, W. R. MILLER, C. ROSA, L. M. ANEZ, M. P. PARIS, C. NICH, T. L. FRANKFORTER, J. MATTHEWS & J. SZAPOCZNIK. 2009. A multisite randomized effectiveness study of motivational enhancement therapy for Spanish-speaking substance abusers. *Journal of Consulting & Clinical Psychology*. 77: 993-999 PMCID: PMC 2792592.
195. SANTA ANA, E. J., K. M. CARROLL, L. ANEZ, M. PARIS, JR., S. A. BALL, C. NICH, T. L. FRANKFORTER, L. SUAREZ-MORALES, J. SZAPOCZNIK & S. MARTINO. 2009. Evaluating motivational enhancement therapy adherence and competence among Spanish-speaking therapists. *Drug and Alcohol Dependence.* 103: 44-51 PMCID: PMC2692434.
196. SUAREZ, L., S. MARTINO, L. BEDEGRAL, B. E. MCCABE, I. V. CUZMAR, M. PARIS, D. J. FEASTER, K. M. CARROLL & J. SZAPOCZNIK. 2010. Do therapist cultural characteristics influence the outcome of substance abuse treatment for Spanish-speaking adults. *Cultural Diversity and Ethnic Minority Psychology*. 16:199-205
197. SUAREZ-MORALES, L., J. MATTHEWS, S. MARTINO, S. A. BALL, C. ROSA, C. FARENTINOS, J. SZAPOCZNIK & K. M. CARROLL. 2007. Issues in designing and implementing a Spanish-language multi-site clinical trial. *The American Journal on the Addictions*. 16: 206-215.
198. MTP RESEARCH GROUP. 2004. Brief treatments for cannabis dependence: Findings from a randomized multisite trial. *J Consult Clin Psychol.* 72: 455-466.
199. BALL, S. A., S. MARTINO, C. NICH, T. L. FRANKFORTER, D. VAN HORN, P. CRITS-CHRISTOPH, G. E. WOODY, J. L. OBERT, C. FARENTINOS, K. M. CARROLL & N. NATIONAL INSTITUTE ON DRUG ABUSE CLINICAL TRIALS. 2007. Site matters: multisite randomized trial of motivational enhancement therapy in community drug abuse clinics. *J Consult Clin Psychol*. 75: 556-567.
200. CARROLL, K. M., C. J. EASTON, C. NICH, K. A. HUNKELE, T. M. NEAVINS, R. SINHA, H. L. FORD, S. A. VITOLO, C. A. DOEBRICK & B. J. ROUNSAVILLE. 2006. The use of contingency management and motivational/skills-building therapy to treat young adults with marijuana dependence. *J Consult Clin Psychol.* 74: 955-966.

201. CARROLL, K. M., L. R. FENTON, S. A. BALL, C. NICH, T. L. FRANKFORTER, J. SHI & B. J. ROUNSAVILLE. 2004. Efficacy of disulfiram and cognitive-behavioral therapy in cocaine-dependent outpatients: A randomized placebo controlled trial. *Archives of General Psychiatry*. 64: 264-272.
202. CARROLL, K. M., S. A. BALL, C. NICH, P. G. O'CONNOR, D. EAGAN, T. L. FRANKFORTER, E. G. TRIFFLEMAN, J. SHI & B. J. ROUNSAVILLE. 2001. Targeting behavioral therapies to enhance naltrexone treatment of opioid dependence: Efficacy of contingency management and significant other involvement. *Archives of General Psychiatry*. 58: 755-761.
203. STOUT, R. L., P. W. WIRTZ, J. P. CARBONARI & F. K. DELBOCA. 1994. Ensuring balanced distribution of prognostic factors in treatment outcome research. *J Stud Alcohol.* Supplement 12: 70-75.
204. WEI, L. J. 1978. An application of an urn model to the design of sequential controlled clinical trials. *Journal of the American Statistical Association*. 73: 559-563.
205. CARROLL, K. M. 1997. *Improving Compliance with Alcoholism Treatment. In* Project MATCH Monograph Series, Vol. 6. Mattson, M. E., Ed. NIAAA. Bethesda, Maryland.
206. ZWEBEN, A., D. BARRET, K. CARTY, B. MCREE, P. MORSE & C. RICE. 1998. *Strategies for Facilitating Protocol Compliance in Alcoholism Treatment Research.* NIAAA. Bethesda, Maryland.
207. TWITCHELL, G. R., C. A. HERTZOG, J. L. KLEIN & M. A. SCHUCKIT. 1992. The anatomy of a follow-up. *Br J Addict.* 87: 1327-1333.
208. NICH, C. & K. M. CARROLL. 2002. Intention to treat meets missing data: Implications of alternate strategies for analyzing clinical trials data. *Drug and Alcohol Dependence*. 68: 121-130.
209. NICH, C. & K. M. CARROLL. 1997. Now you see it, now you don't: A practical demonstration of random regression versus traditional ANOVA models in the analysis of longitudinal follow-up data from a clinical trial. *J Consult Clin Psychol*. 65: 252-261.
210. CAMPBELL, A. N., E. V. NUNES, G. M. MIELE, A. MATTHEWS, D. POLSKY, U. E. GHITZA, E. TURRIGIANO, G. L. BAILEY, P. VANVELDHUISEN, R. CHAPDELAINE, A. FROIAS, M. L. STITZER, K. M. CARROLL, T. WINHUSEN, S. CLINGERMAN, L. PEREZ, E. MCCLURE, B. GOLDMAN & A. R. CROWELL. 2012. Design and methodological considerations of an effectiveness trial of a computer-assisted intervention: an example from the NIDA Clinical Trials Network. *Contemp Clin Trials*. 33: 386-395.
211. CARROLL, K. M., C. NICH, R. SIFRY, T. FRANKFORTER, K. F. NURO, S. A. BALL, L. R. FENTON & B. J. ROUNSAVILLE. 2000. A general system for evaluating therapist adherence and competence in psychotherapy research in the addictions. *Drug and Alcohol Dependence.* 57: 225-238.
212. BAMATTER, W., K. M. CARROLL, L. M. ANEZ, M. PARIS, JR., S. A. BALL, C. NICH, T. L. FRANKFORTER, L. SUAREZ-MORALES, J. SZAPOCZNIK & S. MARTINO. 2010. Informal discussions in substance abuse treatment sessions with Spanish-speaking clients. *Journal of Substance Abuse Treatment*. 39: 353-363.
213. MARTINO, S., S. BALL, C. NICH, T. L. FRANKFORTER & K. M. CARROLL. 2009. Correspondence of motivational enhancement treatment integrity ratings among therapists, supervisors, and observers. *Psychother Res*. 19: 181-193.
214. DE TORRES, L. A., E. M. REBOLLO, R. RUIZ-MORAL, J. A. FERNANDEZ-GARCIA, R. A. VEGA & M. M. PALOMINO. 2009. Diagnostic usefulness of the Alcohol Use Disorders Identification Test (AUDIT) questionnaire for the detection of hazardous drinking and dependence on alcohol among Spanish patients. *Eur J Gen Pract*. 15: 15-21.
215. BUTLER, S. F., J. P. REDONDO, K. C. FERNANDEZ & A. VILLAPIANO. 2009. Validation of the Spanish Addiction Severity Index Multimedia Version (S-ASI-MV). *Drug Alcohol Depend.* 99: 18-27.
216. BAMATTER, W., K. M. CARROLL, L. M. ANEZ, M. PARIS, JR., S. A. BALL, C. NICH, T. L. FRANKFORTER, L. SUAREZ-MORALES, J. SZAPOCZNIK & S. MARTINO. 2010. Informal discussions in substance abuse treatment sessions with Spanish-speaking clients. *J Subst Abuse Treat*. 39: 353-363.
217. KILUK, B. D., J. A. DREIFUSS, R. D. WEISS, V. E. HORIGIAN & K. M. CARROLL. 2013. Psychometric properties of a Spanish-language version of the Short Inventory of Problems. *Psychol Addict Behav*. 27: 893-900.
218. SANTA ANA, E. J., K. M. CARROLL, L. ANEZ, M. PARIS, JR., S. A. BALL, C. NICH, T. L. FRANKFORTER, L. SUAREZ-MORALES, J. SZAPOCZNIK & S. MARTINO. 2009. Evaluating motivational enhancement therapy adherence and competence among Spanish-speaking therapists. *Drug Alcohol Depend*. 103: 44-51.

219. SERAFINI, K., S. DECKER, B. D. KILUK, L. ANEZ, M. PARIS, JR., T. FRANKFORTER & K. M. CARROLL. 2015. Outcome expectations and associated treatment outcomes in motivational enhancement therapy delivered in English and Spanish. *Am J Addict.* 24: 732-739.
220. MCCARTY, C. A., W. HUGGINS, A. E. AIELLO, R. M. BILDER, A. HARIRI, T. L. JERNIGAN, E. NEWMAN, D. K. SANGHERA, T. J. STRAUMAN, Y. ZENG, E. M. RAMOS, H. A. JUNKINS & X. R. N. PHEN. 2014. PhenX RISING: real world implementation and sharing of PhenX measures. *BMC Med Genomics*. 7: 16.
221. PAN, H., K. A. TRYKA, D. J. VREEMAN, W. HUGGINS, M. J. PHILLIPS, J. P. MEHTA, J. H. PHILLIPS, C. J. MCDONALD, H. A. JUNKINS, E. M. RAMOS & C. M. HAMILTON. 2012. Using PhenX measures to identify opportunities for cross-study analysis. *Hum Mutat*. 33: 849-857.
222. FIRST, M. B., J. B. W. WILLIAMS, R. S. KARG & R. L. SPITZER. 2015. *Structured Clinical Interview for DSM-4; Clinical Trials Version* (SCID-4-RV). American Psychiatric Association. Arlington, VA.
223. CAETANO, R. 1987. Acculturation and drinking patterns among U.S. Hispanics. *Br J Addict.* 82: 789-799.
224. CAETANO, R., S. RAMISETTY-MIKLER & L. A. RODRIGUEZ. 2009. The Hispanic Americans Baseline Alcohol Survey (HABLAS): the association between birthplace, acculturation and alcohol abuse and dependence across Hispanic national groups. *Drug Alcohol Depend*. 99: 215-221.
225. CAETANO, R., S. RAMISETTY-MIKLER, L. S. WALLISCH, C. MCGRATH & R. T. SPENCE. 2008. Acculturation, drinking, and alcohol abuse and dependence among Hispanics in the Texas-Mexico border. *Alcohol Clin Exp Res.* 32: 314-321.
226. CAETANO, R., P. A. VAETH & L. A. RODRIGUEZ. 2012. The Hispanic Americans Baseline Alcohol Survey (HABLAS): Acculturation, Birthplace and Alcohol-Related Social Problems Across Hispanic National Groups. *Hisp J Behav Sci*. 31: 95-117.
227. FALS-STEWART, W., T. J. O'FARRELL, T. T. FREITAS, S. K. MCFARLIN & P. RUTIGLIANO. 2000. The timeline followback reports of psychoactive substance use by drug-abusing patients: Psychometric properties. *J Consult Clin Psycho*l. 68: 134-144.
228. SOBELL, L. C. & M. B. SOBELL. 1992. Timeline followback: A technique for assessing self-reported alcohol consumption. *In Measuring alcohol consumption: Psychosocial and biological methods*. Litten, R. Z. & J. Allen, Eds.: 41-72. Humana Press. New Jersey.
229. MILLER, W. R. & F. K. DELBOCA. 1994. Measurement of drinking behavior using the Form 90 family of instruments. *J Stud Alcohol*. 12, supplement: 112-117.
230. ALLEN, J. P., R. Z. LITTEN, J. B. FERTIG & T. F. BABOR. 1997. A review of research on the Alcohol Use Disorders Identification Test (AUDIT). *Alcoholism: Clinical & Experimental Research*. 21: 613-619.
231. SAUNDERS, J. B., O. G. AASLAND, T. F. BABOR, J. R. DE LA FUENTE & M. GRANT. 1993. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. *Addictio*n. 88: 791-804.
232. BOHN, M. J., T. F. BABOR & H. R. KRANZLER. 1995. The Alcohol Use Disorders Identification Test (AUDIT): Validation of a screening instrument for use in medical settings. *J Stud Alcohol.* 56: 423-432.
233. DEROGATIS, L. R. & N. MELISARATOS. 1983. The Brief Symptom Index: An introductory report. *Psychological Medicine*. 13: 595-605.
234. PEREDA, N., M. FORNS & M. PERO. 2007. Dimensional structure of the Brief Symptom Inventory with Spanish college students. *Psicothema.* 19: 634-639.
235. ACOSTA, F. X., L. H. NGUYEN & J. YAMAMOTO. 1994. Using the brief symptom inventory to profile monolingual Spanish-speaking psychiatric outpatients. *J Clin Psychol*. 50: 723-726.
236. CACCIOLA, J. S., A. I. ALTERMAN, B. HABING & A. T. MCLELLAN. 2011. Recent status scores for version 6 of the Addiction Severity Index (ASI-6). *Addiction*. 106: 1588-1602.
237. CACCIOLA, J. S., A. I. ALTERMAN, A. T. MCLELLAN, Y. T. LIN & K. G. LYNCH. 2007. Initial evidence for the reliability and validity of a "Lite" version of the Addiction Severity Index. *Drug Alcohol Depend*. 87: 297-302.
238. NAVALINE, H. A., E. C. SNIDER, C. J. PETRO, D. TOBIN, D. METZGER, A. I. ALTERMAN & G. E. WOODY. 1994. An automated version of the Risk Assessment Battery (RAB): Enhancing the assessment of risk behaviors. *AIDS Res Hum Retroviruses.* 10 (supplement 2): 281-283.
239. JOFRE-BONET, M., J. L. SINDELAR, I. PETRAKIS, C. NICH, T. FRANKFORTER, B. J. ROUNSAVILLE & K. M. CARROLL. 2004. Cost-effectiveness of disulfiram treatment in methadone maintained opioid addicts. *J Substance Abuse Treatment*. 26:225-232.

240. ETTER, J., M. M. BERGMAN & T. V. PERNEGER. 2000. On quitting smoking: Development of two scales measuring the use of self-change strategies in current and former smokers (SCS-CS and SCS-FS). *Addict Behav.* 25: 523-538.
241. FARABEE, D., R. A. RAWSON & M. J. MCCANN. 2002. Adoption of drug avoidance strategies among patients in contingency management and cognitive-behavioral treatments. *J Subst Abuse Treat.* 23: 343-350.
242. FRENCH, M. T., H. J. SALOME, J. L. SINDELAR & A. T. MCLELLAN. 2002. Benefit-cost analysis of addiction treatment: Methodological guidelines and empirical application using the DATCAP and ASI. *Health Serv Res.* 37: 433-455.
243. FRENCH, M. T., L. J. DUNLAP, G. A. ZARKIN, K. A. MCGEARY & A. T. MCLELLAN. 1997. A structured instrument for estimating the economic cost of drug abuse treatment: The Drug Abuse Cost Analyis Program (DATCAP). *Journal of Substance Abuse Treatment*. 14.
244. MARTINO, S., M. PARIS, L. ANEZ, C. NICH, M. CANNING-BALL, K. HUNKELE, T. A. OLMSTEAD & K. M. CARROLL. in press. The effectiveness and cost of clinical supervision for motivational interviewing: A randomized controlled trial. *. J Subst Abuse Treat.*
245. OLMSTEAD, T., K. M. CARROLL, M. CANNING-BALL & S. MARTINO. 2011. Cost and cost-effectiveness of three strategies for training clinicians in motivational interviewing. *Drug Alcohol Depend.* 116: 195-202.
246. OLMSTEAD, T. A. & N. M. PETRY. 2009. The cost-effectiveness of prize-based and voucher-based contingency management in a population of cocaine- or opioid-dependent outpatients. *Drug Alcohol Depend.* 102: 108-115.
247. OLMSTEAD, T. A., J. L. SINDELAR, C. J. EASTON & K. M. CARROLL. 2007. The cost-effectiveness of four treatments for marijuana dependence. *Addiction.* 102: 1443-1453.
248. CHANEY, E. F., M. R. O'LEARY & G. A. MARLATT. 1978. Skill training with problem drinkers. *J Consult Clin Psychol.* 46: 1092-1104.
249. NOCK, M. K. 2007. Conceptual and design essentials for evaluating mechanisms of change. *Alcoholism: Clinical & Experimental Research.* 31: 4S-12S.
250. KAZDIN, A. E. & M. K. NOCK. 2003. Delineating mechanisms of change in child and adolescent therapy: Methodological issues and research recommendations. *Journal of Child Psychology & Psychiatry*. 44: 1116-1129.
251. GIBBONS, R. D., D. HEDEKER, I. ELKIN, C. WATERNAUX, H. C. KRAEMER, J. B. GREENHOUSE, M. T. SHEA, S. D. IMBER, S. M. SOTSKY & J. T. WATKINS. 1993. Some conceptual and statistical issues in analyses of longitudinal psychiatric data. *Archives of General Psychiatry.* 50: 739-750.
252. HEDEKER, D. & R. J. MERMELSTEIN. 2000. Analysis of longitudinal substance use outcomes using ordinal random-effects regression models. *Addiction*. 95: s381-394.
253. INSTITUTE OF MEDICINE, P. O. H. D. I. C. T. 2010*. The Prevention and Treatment of Missing Data in Clinical Trials.* The National Academies Press. Washington, DC.
254. CARROLL, K. M., C. NICH, N. M. PETRY, D. A. EAGAN, J. M. SHI & S. A. BALL. 2016. A randomized factorial trial of disulfiram and contingency management to enhance cognitive behavioral therapy for cocaine dependence. *Drug Alcohol Depend.* 160: 135-142
255. BRYK, A. S. & S. W. RAUDENBUSH. 1987. Application of hierarchical linear models to assessing change. *Psychol Bull.* 101: 147-158.
256. HSIEH, F. 1991. SSIZE: A sample size program for clinical and epidemiological studies. *American Statistician*. 45.
257. KRAEMER, H. C., G. T. WILSON, C. G. FAIRBURN & W. S. AGRAS. 2002. Mediators and moderators of treatment effects in randomized clinical trials. *Arch Gen Psychiatry*. 59: 877-883.
258. HAYES, A. F. 2009. Beyond Baron and Kenny: Statistical medication analysis in the new milennium. *Communication Monographs*. 76: 408-420.
259. MACKINNON, D. P., M. S. FRITZ, J. WILLIAMS & C. M. LOCKWOOD. 2007. Distribution of the product confidence limits for the indirect effect: Program PRODCLIN. *Behav Res Methods.* 39: 384-389.
260. SAMPSON, J. P. & K. R. PYLE. 1983. Ethical issues involved with the use of computer-assessed counseling, testing, and guidance systems. Personnel and Guidance Journal. 61: 283-287.
261. WRIGHT, J. H. & A. S. WRIGHT. 1997. Computer-assisted psychotherapy. *Journal of Psychotherapy Practice and Research.* 6: 315-329.

262. SUBSTANCE ABUSE AND MENTAL HEALTH ADMINISTRATION. 2010. The NSDUH Report: Substance use among Hispanic adults. SAMHSA, Office of Applied Studies. Rockville, MD.