Study Protocol

Development and Pilot Testing of a Multimodal Web-based Program to Address Heavy Drinking During Smoking Cessation

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Principal Investigator: **Christopher W. Kahler, Ph.D.**
Co-Investigators: **Nichea Spillane, Ph.D.**
Amanda Graham, Ph.D.
Benjamin Toll, Ph.D.
Amy Cohn, Ph.D.

Description and Purpose of the Project

The combination of cigarette smoking and heavy drinking (HD) is a major public health concern. Previous research has shown that smokers are considerably more likely than non-smokers to engage in HD, and smoking and HD act synergistically to increase dramatically the risk of certain cancers. It has also been found that greater alcohol use is associated with reduced odds of quitting smoking in numerous community and clinical samples, with episodic HD being an especially important predictor of smoking relapse and cessation failure. Recent evidence suggests that face-to-face and telephone-delivered smoking cessation counseling that incorporates a brief alcohol intervention significantly increases the odds of smoking abstinence and reduces drinking. We believe web-based delivery of a combined intervention for HD smokers is a compelling next step for increasing the public health impact of this approach. A website specifically designed for HD smokers could provide an exceptional opportunity to: (a) improve smoking cessation rates in smokers at especially high risk for health problems and smoking cessation failure and (b) intervene on HD in individuals who otherwise might not otherwise receive a brief alcohol intervention.

The overall objective of this project is to pilot-test a web-based smoking cessation program that specifically addresses HD. The project builds upon a well-established, free evidence-based smoking cessation website, BecomeAnEX.org ("EX"), which enrolls approximately 2,300 new users each month and is supported by Truth Initiative, a national non-profit public health organization.

Primary Aims

Randomized Pilot Study

The aim of this project is to conduct a preliminary RCT. 120 HD smokers will be recruited through BecomeAnEX and randomly assigned to either the standard BecomeAnEX program (EX-S) or to EX-HD. Feasibility, acceptability and efficacy of EX-HD will be examined by comparing EX-S and EX-HD on site use metrics, text message utilization, and treatment satisfaction, and both smoking and alcohol use outcomes. We also will explore potential mechanisms of action for EX-HD including increased motivation for changing drinking and reduced odds of alcohol-involved smoking lapses.

Participant population

Inclusion: Eligible participants must 1) be a current daily smoker of 1 cig/day; 2) meet NIAAA criteria for past month heavy or at risk drinking (women-drinking 8+ drinks/week or consuming 4+ drinks on one occasion at least once in the past month) (Men – drinking 15+ drinks/week or consuming 5+ drinks on one occasion at least once in the past month); 3) be 18 years of age or older; 4) be willing to provide contact information; 5) be a member of BecomeAnEx; 6) have no prior use of the BecomeAnEx website.

Exclusion: Subjects will be excluded if they: 1) have a history of severe alcohol withdrawal symptoms (Hallucinations, seizures, delirium tremens).

Recruitment Procedures

We will recruit participants who are newly registering at BecomeAnEx.org and indicate that they want to quit smoking within the next 30 days. At the end of registering, users are asked whether they would be interested in participating in a research study. Those who are interested are asked an additional set of questions and based on their responses are invited to participate in specific studies. For this project, we will be adding four questions focusing specifically on alcohol to the research screener used by BecomeAnEX (see Appendix). The other questions on that screener vary based on the recruitment needs of other ongoing projects that recruit from the site.

Subjects meeting inclusion/exclusion criteria for this project will be asked: "Working with Brown University, we are currently conducting a study to develop and test a version of BecomeAnEX that is designed specifically for smokers who drink alcohol. Would you be interested in learning more about this project?" Those indicating an interest will be asked to read and sign an electronic informed consent form. They will be given written descriptions of the project including procedures, potential risks and benefits, and confidentiality. If participants choose not to sign the consent form or are not found eligible after completing their baseline survey, they will be directed back to the standard BecomeAnEX website, which they can use as they please free of charge.

Inclusion/Exclusion Criteria

Inclusion of Women, Minorities, and Children

We will aim to recruit a sample that approximates data from the most recent Census Bureau (http://www.census.gov/topics/population.html) adjusted for lower smoking rates among Asians and higher smoking rates among American Indian/Alaskan Natives. Targeted enrollment goals are as follows: 70% White, 20% Black/African American, 5% American Indian/Alaska Native, 1% Asian, 4% Native Hawaiian/Other Pacific Islander. Smoking prevalence among Hispanics is 12.5%, but we have struggled to achieve targeted enrollment goals for Hispanics in our previous and ongoing research using BecomeAnEX (Graham et al., 2013). We will aim to recruit a sample that is roughly 10% Hispanic. With our Study System, we can turn off recruitment by race/gender/ethnicity once we meet recruitment goals in a given category. Given the relatively small samples sizes we will be working with that preclude setting specific numbers for each possible race/gender/ethnicity combination, we will instead set a maximum number of non-Hispanic white participants who can enroll for any given month at 60% of our enrollment target for that month. After that number is reached, only ethnic or racial minorities will be screened into the trial until the monthly recruitment goal is met, guaranteeing that ethnic and racial minorities will comprise at least 40% of the sample. We expect to recruit an equivalent number of men and women since registered users are more likely to be female, but heavy drinking is more common in men.

The sample will include children aged 18 to 20 inclusive. Those under the age of 18 will be excluded. We believe that the cognitive, psychosocial and developmental differences of those under the age of 18 would require significant modification to the study protocols and is not feasible in a developmental project. Furthermore, the needs of adolescent smokers under the age of 18 appear different than those of adult smokers.

Procedures

Pilot Randomized Trial

We will recruit N=120 adult smokers who are newly registered users on BecomeAnEX. The procedures for recruitment, eligibility screening, informed consent, and the baseline assessment will mirror those from Stage 1a, with the exception that participants will be informed during the consent process that they will be randomly assigned to have access to either EX-S or EX-HD. Once the baseline assessment is complete, eligible participants will be randomly assigned to have access to EX-S or EX-HD each time they log in. EX-HD will only be available to those assigned to that condition. Participants will be directed to use their assigned website however they desire. At 1 month and 6 months after baseline enrollment, participants will complete online surveys about their smoking, alcohol use, experiences with quitting smoking, and their use of their assigned website.

Participants will receive $15 at baseline enrollment, $30 for the 1-month follow-up and $50 for the 6-month follow-up.

Intervention Content

EX-HD will build upon BecomeAnEX and includes a number of additions specific to addressing alcohol use and quitting smoking. Based on our combined interventions,[1,2] the section of BecomeAnEX on Health Consequences of smoking will be expanded to include consequences specific to combined smoking and heavy drinking. A *Smoking and Alcohol Connection* page will be added that describes the association between alcohol use and smoking, the pharmacologic and expectancy effects of alcohol on smoking urges and the ability to resist smoking based on our recent laboratory studies,[3-5] and data on the increased risks of having a lapse to smoking while drinking.[6-10] In addition, a *Managing Alcohol Use* tab will be added to the *My Quit Plan* page in EX. This will include a menu of options for goals participants can set around drinking, including stopping drinking for a specified time after quitting smoking, setting a maximum limit of how much to drink on any day, and creating plans for minimizing the risk of smoking when the person does decide to drink such as drinking only with a friend who is supportive of the goal to quit smoking. Participants also will be provided a list of strategies for cutting down on or avoiding drinking that they can select and save as part of My Quit Plan. The EX-HD site also will include normative feedback on drinking, a pros and cons of reducing drinking checklist, guidelines for "safe" drinking limits, and strategies for cutting down on drinking. These pages, in addition to pages defining a standard drink and the number of drinks in different alcohol containers, will build off of parallel pages in NIAAA's *Rethinking Drinking* website but will be adapted to fit the look and style of BecomeAnEX. In addition, EX-HD will include links to the interactive tools on *Rethinking Drinking* that calculate calories and costs of drinking and that estimate blood alcohol levels achieved with specific drinking rates. Finally, EX-HD will have educational pages on alcohol use disorders, alcohol withdrawal symptoms, and resources for seeking help with drinking.

We will also modify the existing BecomeAnEX text message library to include alcohol-specific content. The standard text message intervention with BecomeAnEx is modeled after the delivery schedule of the txt2stop program developed by Free and colleagues.[11] In their study, participants set a quit date and received 35 messages/week (5/day) for 5 weeks and then 3 messages/week for the remaining 26 weeks following their quit day. Our intervention is designed to be 8 weeks given the pilot nature of the R34 and the time and budgetary constraints of this

mechanism. We do not require participants to set a quit date since messages focus on ongoing engagement with BecomeAnEX as well as support around a quit date. Further, as this is a pilot study, setting a quit date will be an intermediary outcome of interest and metric of engagement. Therefore, all participants will receive 5 messages per day for 4 weeks, and 3 messages per week for 4 weeks after that. In EX-HD, 2 texts per day for the first 4 weeks following enrollment will be focused on alcohol, and 1 text per week will be focused on alcohol in the remaining 4 weeks after that. These texts will reiterate information on the association of HD and smoking relapse and HD and health, will encourage reductions in drinking, and will provide links to alcohol-focused content on EX-HD such as *Planning for Change* and *Tips for Reducing Drinking*.

Measures

Screening Measures for Inclusion/Exclusion Criteria

Stage 1a: Pilot Trial

The baseline survey and follow-ups will be conducted online and hosted on a secure server. Follow-ups will prompted by email and text with phone follow-ups for non-responders conducted by research staff at Brown.

Baseline Assessment. Eligible participants will complete a short online assessment comprised of smoking history and current smoking behavior measures. The Fagerström Test for Nicotine Dependence[12] will be used as a continuous measure of nicotine dependence, and the Short Inventory of Problems will be used as measure of past 30-day alcohol problem severity.[13-15] We will assess the perceived importance of cutting down or stopping drinking using a single-item 0-10 Likert scale.[1] Commitment to quitting smoking will be assessed with a reliable 8-item scale.[16] The Contemplation Ladder[17,18] and Readiness to Change Questionnaire[19,20] will assess motivation to change smoking and drinking (respectively) and the Smoking Cessation Self-Efficacy Scale[21] will assess confidence in ability to abstain from smoking in high-risk situations. Perceived associations between alcohol use and smoking will be assessed with the Alcohol and Smoking Interaction Expectancies Questionnaire.[22]

Website Utilization Metrics**.** We will extract the following utilization metrics from the BecomeAnEX Data Warehouse: number of logins, minutes spent using the site during each visit/session, number of interactive features used, and number of days logged in to the site (as a measure of treatment duration). Website utilization is recorded using Adobe/Omniture SiteCatalyst. Every page view by a participant is recorded into a relational database, and page views are grouped into sessions. The duration of a session is defined as the time elapsed between the first page view and the last page view in a given session. If a user does not view a new page for more than 30 minutes, the system marks them as inactive and their next return visit creates a new session. We will also extract data on use of the community (e.g., # wall posts made/received, number of forum posts/replies, number of personal messages sent/received) and practical counseling features (e.g., whether the user set a quit date, number of quit date changes, use of tools to identify triggers and develop coping strategies) . For those in EX-HD, we will extract utilization data for new alcohol-specific features (e.g., setting a drinking goal, creating a quit plan).

Follow-Up Assessments. At 2 weeks post enrollment, participants will be contacted to complete a semi-structured interview by phone regarding their experiences using EX-HD. Phone calls will be completed by study staff and investigators at Brown. The semi-structured interview will assess: (a) whether participants have completed each of the primary alcohol-focused

components of EX-HD and the reasons for doing or not doing so, and (b) reactions to each component and how useful they found it. Participants will also be asked to complete a second follow-up online at 1 month post-enrollment to assess whether they set a quit date, achieved 7-day smoking abstinence, and reduced HD frequency. They also will be asked to provide feedback on the persuasiveness and relevance of the alcohol-focused text messages, as well as intensity of message delivery. They will receive an email and text asking them to complete the survey. If participants do not complete the survey within two days, a second email/text will be sent. Those not completing the survey 5 days after receiving the second prompt will be called by staff at Brown to complete the assessment over the telephone.

Stage 1b: Pilot Randomized Trial

The baseline survey and follow-ups will be conducted online and hosted on a secure server. Follow-ups will prompted by email and text with phone follow-ups for non-responders conducted by research staff blind to treatment.

Baseline Assessment**.** As in Stage 1a, participants will complete the Fagerström Test for Nicotine Dependence,[12] the Short Inventory of Problems,[13-15] a measure of the perceived importance of cutting down or stopping drinking,[1] commitment to quitting smoking,[16] The Contemplation Ladder for smoking,[17,18] the Readiness to Change Questionnaire for alcohol,[19,20] the Smoking Cessation Self-Efficacy Scale,[21] and the Alcohol and Smoking Interaction Expectancies Questionnaire.[22]

Website Utilization Metrics**.** We will extract the following utilization metrics from the BecomeAnEX Data Warehouse: number of logins, minutes spent using the site during each visit/session, number of interactive features used, and number of days logged in to the site (as a measure of treatment duration). Website utilization is recorded using Adobe/Omniture SiteCatalyst. Every page view by a participant is recorded into a relational database, and page views are grouped into sessions. The duration of a session is defined as the time elapsed between the first page view and the last page view in a given session. If a user does not view a new page for more than 30 minutes, the system marks them as inactive and their next return visit creates a new session. We will also extract data on use of the community (e.g., # wall posts made/received, number of forum posts/replies, number of personal messages sent/received) and practical counseling features (e.g., whether the user set a quit date, number of quit date changes, use of tools to identify triggers and develop coping strategies) . For those in EX-HD, we will extract utilization data for new alcohol-specific features (e.g., setting a drinking goal, creating a quit plan).

Outcome Assessments**.** At 1- and 6-months post-enrollment, we will gather self-reported 7-day smoking abstinence, which is the primary outcome. We will also assess the circumstances surrounding the initial slip after quit date including positive moods, negative moods, presence of other smokers, and consumption of alcohol at the time.[1] Past 7-day alcohol consumption will be assessed with a shortened version of the Timeline Followback Interview, which has been recommended by co-I Toll for use in smoking cessation studies.[23] Participants will also complete a quantity-frequency measure of past 30-day drinking, including frequency of episodic HD in that time.

Follow-up Assessment**.** *Intervention satisfaction* will be assessed at the 1-month follow-up with the Client Satisfaction Questionnaire, an 8-item questionnaire that will be administered at the 8-week follow-up to assess participant satisfaction with provided services (CSQ-8[24]). The

CSQ has shown good reliability and in prior smoking cessation treatment development work[25,26] and can be readily adapted to assess satisfaction with a web-based intervention. *Quit methods* will be assessed with the Quitting Strategies Questionnaire[1] at the 1-month follow-up which assesses use of general smoking cessation strategies (e.g., planning for high-risk situations, use of pharmacotherapy) and specific strategies for managing alcohol use while quitting (e.g., limiting drinking, avoiding alcohol).

Biochemical confirmation of abstinence. Participants reporting smoking abstinence at 6 months will be invited to provide a saliva sample by mail to biochemically verify smoking status. Participants will be sent a Salimetrics© collection kit by mail from the research team at Brown, with clear directions on saliva collection, and instructions to return the sample with the enclosed return envelope to the PI's lab. These mail-in kits have been validated for the collection of saliva cotinine biomarkers.

Confidentiality

Participation in this study and information gathered from the study will be kept confidential to the extent of the law. The findings of the study may be published, but individual participants will not be identified.

The Principal Investigator, Co-Investigators, Data Analyst, Assessment Coordinator, Research Assistant, and software development team will have access to individually identifiable information about human subjects. Electronic data files with identifiable information will be maintained separately from other data files and will only be used for administrative purposes (e.g., tracking follow-up completion, managing subject payment). All personnel will receive certification in human subjects protection from the NIH Office of Human Subjects Research or Brown University's approved CITI training program prior to beginning work on this project. Brown University research staff will have secure access to an administrative interface of the web-based Clinical Trials Management System that interacts with BecomeAnEX. Each staff person will have a unique username and password that will be required for login. The interface will provide access to participants' information for study use only.

All Text messages, sent and received, will be encrypted and stored by the Legacy Software Development Team. This team maintains the text message system deployed within BecomeAnEX as well as the web-based clinical trials management system that will support all aspects of the study. They will have access to participant cell phone numbers and responses to the text messages but not names or other identifying information. They will not share this information with anyone other than Brown staff. We do advise participants to set up password protection on their cell phones and to erase messages after responding to reduce the chance of loss of private information.

Risks

The overall risks of participating in this study are minimal. Study participants who attempt to quit smoking will likely experience some withdrawal symptoms that may include anxiety, restlessness, anger, irritability, sadness, problems concentrating, appetite change and weight gain, insomnia, and decreased heart rate. It is possible that individuals who drink alcohol very heavily may experience some alcohol withdrawal symptoms if they decide to avoid drinking completely. Symptoms of alcohol withdrawal include insomnia, excessive physical restlessness, or hand tremor, as well as more severe symptoms such as delirium and seizures.

There is a remote possibility of loss of confidentiality, although we will take steps to protect participants confidentiality as described above. Answers are confidential and the findings of the study may be published, but individual participants will not be identified.

When we send a text message to a participant, there is a chance that other people could read that message. The texts will contain specific information and encouragement about quitting smoking and managing alcohol use that may be helpful when quitting.

Protection Against Risk

There is no reason to believe that participation in this study would worsen nicotine withdrawal symptoms. The questionnaires and interviews are commonly used in research and clinical practice so they should cause minimal discomfort or risk.

The eligibility screen will exclude participants who report a history of severe alcohol withdrawal. Participants will be informed that if they stop drinking and experience any disturbing effects that they should seek medical assistance. Withdrawal symptoms are typically mild and resolve within a few days.

Potential Benefits of the Proposed Research to the Subjects and Others

We cannot and do not guarantee or promise that participants will receive any benefits from this study. Participants may quit or reduce smoking or drinking, which could improve their health. They also have a chance to contribute to a scientific study that may help people in the future.

Informed Consent

Potentially eligible individuals are presented the informed consent page and provided detailed information about the study including the following: a) an overview of the study and the fact that they will be directed to a new version of the BecomeAnEX website that contains additional content and functionality related to alcohol use; b) financial incentives for participating; c) protection of confidentiality and the right to withdraw at any time; d) expectations regarding follow-up data collection, including compensation for time required to complete follow-up assessments; e) risks and benefits of study participation; and f) the availability of other cessation treatment resources. Smokers must type their initials into a box and click a button labeled "I want to participate" as active affirmation that they are providing informed consent for study participation. The name and telephone numbers of the Principal Investigator and the Brown University Human Subjects Research Protections Office will be included in the consent form. An email address will be appear on each enrollment Web page for participants to contact Brown staff should they encounter any technical difficulties during the enrollment process or have further questions about the research.

Following consent, participants are asked to provide their contact information. They are required to verify their email address within 24 hours to complete study enrollment. Once they provide contact information, they will be immediately directed to the online baseline questionnaires. It is possible that some participants may be found ineligible during the baseline. This will be explained in the informed consent. Those found ineligible will be directed back to the BecomeAnEX website to use it as they please.

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