YALE UNIVERSITY
HUMAN INVESTIGATION COMMITTEE

e-Application to Involve Human Subjects in Biomedical Research
100 FR 1e (2012-1)

For use with Electronic Protocol Submissions Only

HIC Protocol Number:

Title of Research Project: Text Messaging to Reduce Alcohol Relapse in Liver Transplant Patients	
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Investigator Interests:

Does the principal investigator, or do any research personnel who are responsible for the design, conduct or reporting of this project or any of their family members (spouse or dependent child) have an incentive or interest, financial or otherwise, that may affect the protection of the human subjects involved in this project, the scientific objectivity of the research or its integrity? Note: The Principal Investigator (Project Director), upon consideration of the individual's role and degree of independence in carrying out the work, will determine who is responsible for the design, conduct, or reporting of the research.

See Disclosures and Management of Personal Interests in Human Research
http://www.yale.edu/hrpp/policies/index.html#COI

Yes X No

Do you or does anyone on the research team who is determined by you to be responsible for the design, conduct or reporting of this research have any patent (sole right to make, use or sell an invention) or copyright (exclusive rights to an original work) interests related to this research protocol?

Yes X No

If yes to either question above, list names of the investigator or responsible person:

The Yale University Principal Investigator, all Yale University co-investigators, and all Yale University individuals who are responsible for the design, conduct or reporting of research must have a current financial disclosure form on file with the University's Conflict of Interest Office. Yale New Haven Hospital personnel who are listed as con-investigators on a protocol with a Yale University Principal Investigator must also 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.**

Billing Information: IRB Review fees are charged for projects funded by Industry or Other For-Profit Sponsors. If this study is funded by Industry or Other For-Profit Sponsor, 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:

SECTION I: 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/Smilow
- ☒ Yale-New Haven Hospital
- ☐ Specify Other Yale Location:
- ☐ Yale University 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)
- ☐ Other Locations, Specify:
- ☐ Haskins Laboratories
- ☐ John B. Pierce Laboratory, Inc.
- ☐ Veterans Affairs Hospital, West Haven
- ☐ International Research Site (Specify location(s)):

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

This project is expected to last 24 months. Participants will be enrolled in the treatment phase of the study for 8 weeks and will complete post-intervention assessments at 8 weeks. Medical chart review will be completed 3-months post-treatment. Participant recruitment will last for 12 months and data analysis will take an additional 12 months.

3. **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

4. Is this study a clinical trial? Yes ☐ No ☒
NOTE the current ICMJE (International Committee of Medical Journal Editors) definition of a clinical trial: "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes." Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example, drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events"
If yes, where is it registered?
Clinical Trials.gov registry ☐
Other (*Specify*)

*Registration of clinical trials **at their initiation** is required by the FDA, NIH and by the ICMJE.*

If this study is registered on clinicaltrials.gov, there is new language in the consent form and compound authorization that should be used.

For more information on registering clinical trials, including whether your trial must be registered, see the YCCI webpage, http://ycci.yale.edu/researchers/ors/registerstudy.aspx or contact YCCI at 203.785.3482)

5. 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

6. Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities? Yes X No *If Yes, please answer questions a through c and note instructions below. If No, proceed to Section II.*

a. Does your YNHH privilege delineation currently include the **specific procedure** that you will perform?

Yes, Dr. Toll's YNHH privilege delineation covers all procedures.

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

No, we will not be using any new equipment.

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

No, a novel approach with existing equipment will not be applied.

If you answered "no" to question 6a, or "yes" to question 6b or c, please contact the YNHH Department of Physician Services (688-2615) for prior approval before commencing with your research protocol.

SECTION II: RESEARCH PLAN

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

This study is an 8-week, randomized controlled pilot trial to investigate the feasibility and acceptability of a text-messaging intervention for alcohol relapse prevention and stress reduction in 20 liver transplant patients with alcohol-related liver disease. The scientific aims of the study are as follows:

(1) To develop a mobile, SMS-based stress reduction and alcohol use intervention for pre-liver transplant patients with alcohol-related liver disease (ALD).
(2) Evaluate the feasibility and acceptability of the mobile intervention and its effect on rates of alcohol consumption compared to a Standard Care condition in a liver transplantation center.

Text messaging is a novel mechanism for intervention in this population. Over the course of the study, participants randomized to the Text Message condition will receive messages targeting known predictors of alcohol abstinence and relapse, including (1) craving, (2) identification of high-risk situations, (3) identification of triggers, (4) stress level, (5) coping skills, and (5) quality of life. Because mobile interventions have not been utilized in studies of alcohol abstinence, we will base the protocol for this text message intervention on past studies that have used text messages interventions. Specifically, we will apply portions a large-scale RCT of a text message intervention for smoking cessation (Free et al., 2001) and of a smaller study on a text message intervention for reducing alcohol-related consequences in college students (Weitzel et al., 2007). The text messages will include motivational messages and behavior-change techniques (e.g. coping with cravings and urges to drink, trigger identification, high-risk situation identification). Messages will encourage participants to continue with sobriety and focus on the success they have achieved so far. After the first 4 weeks, they will receive 3 messages per week for the next 4 weeks. All text messages will be developed with the input of liver transplant professionals.

All patients will be assessed at 4-weeks and 8-weeks and will provide urine for EtG analysis to allow biological verification of sobriety. After the 8-week intervention, patients will complete a satisfaction survey about their experiences in the Text Message condition and Standard Care condition to assess intervention helpfulness, text message content, and the

east of using the text message program. These data will allow us to examine the feasibility and acceptability of the text message intervention.

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.

The liver is the second most commonly transplanted major organ, after the kidney. Heavy alcohol and illicit substance use are more likely to cause end-organ liver damage compared with other organs. Alcohol-related liver disease (ALD) is the most common type of liver disease in the United States and accounts for nearly 30% of all liver transplants (Belle et al., 1997). The main indication for liver transplant in males is ALD, and ALD is second only to viral hepatitis overall (Roizen, 1999; Organ Procurement and Transplantation Network, 2010). Although these patients may consume enough alcohol to acquire end-stage ALD, not all meet diagnostic criteria for alcohol dependence (DiMartini et al., 2001). Of those who consume the equivalent of 12 or more beers per day for more than 10 years, nearly 20% require a liver transplant (Alter et al., 1998). Thus, a significant range exists in the drinking patterns of those who are diagnosed with ALD.

Survival rates, at 1-year and 5-years, of patients that undergo liver transplant for ALD are similar to patients who are transplanted for other causes (Mackie et al., 2001). Despite these high overall survival rates, up to 50% of liver transplant patients with alcoholism return to alcohol use within 5 years (DiMartini et al., 2006). Relapse to drinking can lead to acute injury to the allograft and/or cause death or graft loss (Cuadrado et al., 2005). Especially important for predicting a patient's post-transplant relapse risk is pre-transplant sobriety. Numerous studies have concluded that duration of abstinence of less than 6 months prior to transplant best predicts post-transplant outcome (Cf. Miguet et al., 2004). These studies have provided support for the mandatory 6-month abstinence period routinely implemented by most transplant centers, though recent evidence indicates that transplantation before the 6-month mark could be beneficial for patients who are not responding to medical treatment (Mathurin et al., 2011). Patients with ALD are at significantly higher risk than non-ALD patients to return to heavy drinking post-transplant (Bravata et al., 2001). This is unfortunate given that survival rates of patients who resume excessive drinking after transplantation are significantly lower than the survival rates of abstinent patients or even patients who have a minor lapse to alcohol use post-transplant (Pfitzmann et al., 2007). Based on the relationship between pre-transplant drinking behavior and post-transplant outcome and survival, it is especially important to treat patients' alcohol use and alcohol dependence before liver transplant.

Despite the clear importance of clinical management and treatment of heavy alcohol use and alcohol dependence pre-transplant, only 1 randomized-controlled trial of a behavioral treatment (Motivational Enhancement Therapy) for alcohol versus treatment-as-usual exists for the liver transplant setting (Weinrieb et al., 2011). Results from this small-scale (n = 91) trial provide early evidence that behavioral treatment can reduce drinks per drinking day in pre-transplant patients with ALD. Other results from a study on the feasibility of a psychosocial intervention for pre-transplant patients indicated that a time-limited intervention was acceptable to patients and was readily integrated into the liver clinic (Georgiou et al., 2003). These studies provide initial evidence that behavioral interventions may be helpful to pre-liver transplant patients.

Mobile technologies and mobile telephone short-message service (SMS; e.g., text message) have become ubiquitous in the United States. SMS, in particular, is used by all people of all age groups and socioeconomic backgrounds (Rice & Katz, 2003; Ling, 2004). SMS delivers short messages (typically up to 160 characters) instantaneously to cell phone users; messages can be accessed by the user at any time and can be tailored to the needs of an individual, which increases the efficacy of a health behavior message (Dijkstra & De Vries, 1999; Ryan & Lauver, 2002). Because some of the highest rates of mobile phone usage are among socioeconomically disadvantaged populations (Faulkner & Culwin, 2006), SMS presents an optimal intervention strategy for targeting both patients who are in poorer health and those who are

socioeconomically disadvantaged. Liver transplant patients experience significant impact on their health-related quality of life, and the complications of liver disease, including hepatic encephalopathy, ascites, and recurrent variceal hemorrhages, can further impact patients' quality of life. Given their compromised health status, SMS interventions represent a promising intervention modality for these patients.

A key benefit to SMS interventions, and other mobile interventions, is that they provide more ecologically valid interventions. They have been used to target a variety of health behaviors, including smoking cessation, anxiety, diabetes management, alcohol use, and physical activity (Cf. Heron & Smyth, 2010). Mobile interventions have successfully decreased total drinking days, increased physical activity and vegetable intake, and improved blood glucose levels in diabetic patients. Because they occur in a patient's natural environment and are provided at specific moments during the day, SMS interventions can provide real-time support in the real world (Heron & Smyth, 2010). For medically compromised patients who already have a multitude of appointments with providers, SMS technology can provide a valuable source of care in their daily lives. With this additional support in their natural environment, patients report feeling better able to utilize new behavioral skills (Kazantzis & L'Abate, 2007; Newman et al., 1997). The ability to provide tailored messages based on patient characteristics, including self-efficacy and motivation, can improve message acceptance (Kreuter et al., 1999). Mobile technologies have also been effectively implemented without any additional treatment support (Weitzel et al., 2007; Whittaker et al., 2008). Given that the patient burden of attending additional appointments at a liver clinic that might be at a significant distance from their homes can be high, mobile technology can therefore provide additional and efficacious treatment for patients that have limited ability to attend a higher number of in-person appointments.

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.

This study has two phases: (1) Stage 1 – development of intervention text messages and (2) Stage 2 – pilot randomized controlled trial of Text Message intervention versus Standard Care.

In **Stage 1** – we will develop a text message bank approximately 200-300 text messages using empirically supported in-person intervention components for heavy alcohol use and alcohol dependence. Component areas will be craving, high-risk situations, identification of alcohol use triggers, stress, mood, quality of life, and coping skills. As text messages will be used both for assessment *and* for intervention content, the text message bank will contain both assessment messages and intervention messages. Following the development of the text message bank, the messages will be assessed by Consultants to this project, which will include liver transplantation medical and psychological care providers. Text messages will be rated on their: (1) readability, (2) acceptability, (3) relevance to patients' concerns, and (4) helpfulness. Consultants will also be asked to indicate if they think any messages should be eliminated. Obtaining this feedback prior to the RCT will enhance the Text Message Intervention's acceptability to liver transplant providers.

Stage 2 is a between-subjects, randomized clinical trial that will compare the effect of a Text Message intervention with Standard Care in a liver transplantation clinic on alcohol relapse rate and stress reduction. This trial will also examine the feasibility and efficacy of the Text Message intervention. A total of 20 subjects, at least 18 years of age, will be recruited to participate in the trial and will be randomized to receive either the Text Message intervention or Standard Care. There are three consecutive phases to the study: (1) a 1-week assessment period; (2) an 8-week treatment period; (3) follow-up post-treatment and at 3-months post-intervention.

In Stage 2, we will conduct a randomized controlled pilot study to test the feasibility, acceptability, and preliminary efficacy of the final Text Message intervention versus a Standard Care (SC) intervention. Patients in the SC condition will receive all elements of their usual care as part of the liver transplant service but will not receive any text messages.

Screening: Participants who express interest in the study will attend an in-person intake to learn about the study, provide informed, voluntary consent, be further evaluated for eligibility and complete baseline assessments for which they will be compensated. Participants will be randomized to either the Text Message intervention or to SC based on a preset randomization schedule generated via computer by a statistician. For participants in the Text Message condition, the RA will demonstrate how to use the text messaging service. A pre-paid mobile phone will be provided for the duration of the study for all participants. Study cell phones will have pre-paid text messaging coverage for the duration of the study.

Interventions: *In the SC condition, participants will receive only standard care provided by the liver transplantation team.* No additional behavioral or psychosocial interventions will be provided. These participants will receive only study-specific assessments. Participants in this condition will complete assessments at baseline, 4-weeks and 8-weeks that measure self-reported substance use, stress, and coping skills. At each in-person assessment, participants will provide urine for EtG analysis and will be compensated.

In the Text Message condition, participants will receive daily text messages in addition to receiving all elements of standard care in the liver transplant service. Daily text messages will be used to determine their current level of functioning and provide text message intervention messages in response. Text messages will be sent via Google Voice on a research computer. A study-specific phone number will be generated via Google and will be the number from which all participants receive text messages. Participants will receive these messages on their pre-paid study cell phones only. Participants will be asked to respond to the text messages either with a specified response (e.g. YES/NO) or with a generic response (e.g. “1”). This will allow the collection of feasibility data on number of responses to the messages and verify that participants are reading and receiving the intervention. Participants’ response messages will be received, via Google Voice, on a research computer. The research assistant will monitor and record whether a participant is responding at least once per day. As noted, some text messages will ask for a specific reply in response to a question (e.g. “Any cravings today?”). Based on the participant’s response (e.g. “high,” “med,” or “low”), the research assistant will respond with a text message tailored to the participant’s message. Participants will be informed that this account will be used for research purposes only and should not be used in the case of a clinical emergency, because all text messages have been pre-generated and it cannot be guaranteed that responses will be seen at the moment they are sent. All text messages will be sent to the HIC in an amendment to this protocol for approval.

Over the course of the study, participants will receive messages targeting known predictors of alcohol abstinence and relapse, including (1) craving, (2) identification of high-risk situations, (3) identification of triggers, (4) stress level, (5) coping skills, and (5) quality of life. Because mobile interventions have not been utilized in studies of alcohol abstinence, we will base the protocol for this text message intervention on past studies that have used text message interventions. Specifically, we will apply portions a large-scale RCT of a text message intervention for smoking cessation (Free et al., 2001) and of a smaller study on a text message intervention for reducing alcohol-related consequences in college students (Weitzel et al., 2007). Following randomization, participants will receive 2 text messages per day for the first 4 weeks of the study. Research on the elaboration likelihood model (ELM; Petty & Cacioppo, 1986) of attitude change has indicated that tailored messages are more effective than generic messages (Webb et al., 2007). Because intervention messages are most effective if they are tailored to the personal characteristics of the participant, the daily text messages (content: craving, trigger identification, high-risk situation identification and other efficacious components of alcohol abstinence interventions) will be tailored on variables known to be risk factors for pretransplant abstinence, including gender, family history of alcoholism, and level of social support (Pfitzmann et al., 2007). The text messages will include motivational messages and behavior-change techniques (e.g. coping with cravings and urges to drink, trigger identification, high-risk situation identification). Messages will encourage participants to continue with sobriety

and focus on the success they have achieved so far. After the first 4 weeks, they will receive 3 messages per week for the next 4 weeks. As noted, these messages will be developed with the input of liver transplant professionals.

As in the Standard Care condition, participants in the Text Message condition will return to the liver clinic for assessments at 4-weeks and 8-weeks and to provide urine for EtG analysis. Participants will be compensated for these in-treatment appointments.

End of Treatment Monitoring/Follow-Up: After the 8-week intervention, participants will be contacted via phone to schedule an in-person follow-up appointment. At follow-up participants will be asked to complete a satisfaction survey about their experiences with the Text Message or SC interventions. The survey will assess intervention helpfulness, text message content, and ease of using the text message program and will provide an end-of-treatment urine test. Participants will be compensated $30 for completing the in-person assessment.

At 3-months post-treatment, a chart review will be conducted for each enrolled participant to obtain liver transplant listing status, current Model for End-Stage Liver Disease (MELD) score, any incidence of major medical complications, and the results of any urine toxicology tests that have occurred since the end of treatment.

Assessments (b: baseline, t: treatment (Week 4 and Week 8)):

Demographics (b): This questionnaire assesses basic demographic information, including age, sex, weight, ethnic/racial identity, sexual orientation, and current residence type.

Mini-Mental Status Examination (b,t) (MMSE; Folstein et al., 1975). The MMSE is the most widely used brief measure of cognitive function. It is designed to specifically assess impaired cognition in diseased or very old populations. The total score of the 10-item measure indicates the severity of cognitive dysfunction.

Alcohol and Smoking History Questionnaire (b). At baseline, this will assess basic alcohol and smoking status and history. Alcohol questions will assess age of first use (sip), age when alcohol use began regularly, family history of alcohol problems, number of alcohol quit attempts, and concomitant alcohol-related health symptoms and syndromes. They will also report the highest number of drinks they have consumed in a 24-hour period, the number of hours it took them to consume these drinks and the number of times they drank at this level. Smoking questions will assess number of years smoked, age they began smoking, and whether they have ever attempted to quit smoking.

Ethyl Glucuronide (EtG; b, t): EtG provides a sensitive and reliable biomarker of recent alcohol consumption and is detectable in urine for up to three days after drinking, depending on the amount of alcohol consumed. A urine sample will be taken at baseline, Week 4, and at Week 8 post-treatment. Heavy exposure to non-beverage sources of ethanol such as some mouthwashes and hand washes, particularly the latter, can confound the interpretation of urinary EtG assays. Usage of these products will be monitored.

Timeline Followback (b, t): This standardized, validated and reliable experimenter-administered rating scale will be used to obtain quantity and frequency estimates of alcohol and nicotine consumption for a 30-day period prior to assessment. It uses a calendar prompt and a number of other memory aids (e.g. holiday, payday, and other personally relevant dates) to facilitate accurate recall of drug use during the targeted period, and it has demonstrated adequate levels of reliability and validity when administered as an in-person interview. We will use the calendar method to record alcohol and tobacco use (Sobell & Sobell, 1992, 2000).

Alcohol-Related Problems (b, t): The Impact of Beverage Intake on Behavior (IMBIBE) is a 15-item self-report questionnaire that assesses the frequency of negative alcohol consequences in the past month.

Alcohol Craving (b, t): The Obsessive Compulsive Drinking Scale (OCDS; Anton, Moak, & Latham,

1995) will be used to assess alcohol craving. It is a 14-item, self-report scale on which participants rate their experiences of craving over the previous 1- to 2-weeks. The OCDS has been found to be a robust predictor of drinking during treatment (Flannery et al., 2001)

Perceived Stress (b, t): The Perceived Stress Scale (PSS; Cohen et al., 1988) is a 10-item self-report assessment to measure the perception of stress and the degree to which situations in one's life are appraised as stressful. The scale assesses stress over the past month.

Quality of Life (b, t):Quality of Life will be assessed with the World Health Organization Quality of Life (WHOQOL) scale. We will use the WHOQOL-BREF version, which is a 26-item, self-report scale that assess overall quality of life, general health, and quality of physical health, psychological health, social relationships, and environment. The WHOQOL-BREF has been shown to have good to excellent psychometric reliability and has been tested in both well- and sick-populations (Skevington, Lotfy, & O'Connell, 2004).

Depression (b, t): The Center for Epidemiologic Studies- Depression Questionnaire (CES-D; Radloff, 1977) will assess depressive symptoms during the week prior to assessment. The CES-D is a 10-item self-report scale that has been shown to have high internal consistency and adequate test-retest repeatability.

Self-Efficacy (b,t): Self-efficacy will be assessed with a single item. Participants will rate their confidence to remain alcohol abstinent on a 10-point scale (1 = not at all confident; 10 = extremely confident). The midpoint (i.e. between 5 and 6) will be labeled as somewhat confident. This single item assessment has been demonstrated to be a significant predictor of alcohol use relapse (Hoeppner, Kelly, Ubanoski, & Slaymaker, 2011)

Treatment Feasibility and Acceptability (Week 8 only): This questionnaire will ask participants to rate the acceptability of the treatment dimensions (e.g., how easy the text messages are to read).

Medical Chart Review Form (3 month follow-up only): This questionnaire will be completed by a Research Assistant. The RA will review the chart and obtain information about the following: UNOS listing status, MELD scores, urinary toxicology results, major medical complications during post-treatment, diabetes status, and substance dependence diagnostic status.

4. **Genetic Testing** **N/A**☒
   - **A.** Describe
     - i. the types of future research to be conducted using the materials, specifying if immortalization of cell lines, whole exome or genome sequencing, genome-wide association studies, or animal studies are planned
     - ii. the plan for the collection of material or the conditions under which material will be received
     - iii. the types of information about the donor/individual contributors that will be entered into a database
     - iv. the methods to uphold confidentiality
   - B. What are the conditions or procedures for sharing of materials and/or distributing for future research projects?
   - C. Is widespread sharing of materials planned?
   - D. When and under what conditions will materials be stripped of all identifiers?
   - E. Can donor-subjects withdraw their materials at any time, and/or withdraw the identifiers that connect them to their materials?
     - i. How will requests to withdraw materials be handled (e.g., material no longer identified: that is, anonymized) or material destroyed)?
   - F. Describe the provisions for protection of participant privacy
   - G. Describe the methods for the security of storage and sharing of materials

5. **Subject Population** Provide a detailed description of the targeted population of human

subjects for this research project.

We will recruit 20 participants for the randomized trial through flyer advertisements and clinic referral in the liver transplant clinic at Yale-New Haven Hospital. Liver transplantation patients

who express interest in participating in the study will meet with a research assistant (RA) and provide written, informed consent. The RA or other study personnel will review study procedures, review eligibility, and study requirements. Patients will be eligible for the study if they report ≥ 1 drinking episode in the previous year, have a diagnosis of ALD, and have pre-transplant status.

6. **Subject Classifications:** 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.

No, this study will not enroll subjects who require additional safeguards.

a. 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)*

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

Eligibility criteria include: (1) at least 18 years of age; (2) diagnosis of alcohol-related liver disease; (3) currently in evaluation for UNOS listing as a liver transplant candidate; (4) last reported use of any alcohol within the past 1 year; (5) willingness to receive and respond to multiple text messages per day.

Exclusion criteria include: unstable psychiatric/medical conditions such as suicidal ideation, acute psychosis, or dementia.

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

Participants who express interest in participating will meet with a research assistant to review the study protocol and eligibility criteria. All participants will provide written, informed consent. Eligibility will be determined through individual interviews and self-report questionnaires. Initial eligibility will be determined by Amanda Palmer (research assistant) and final eligibility will be determined by the PI, Dr. Toll, and Co-Investigator/Project Coordinator, Dr. DeMartini.

9. **Risks:** Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects' participation in the research.

a) **Urine Collection** – Urine collection is performed for EtG testing to verify a participant's sobriety. This should add no risk other than those normally associated with this procedure.
b) **Rating Scales and Questionnaires** – The assessment of alcohol consumption by participants under the legal drinking age is a sensitive issue. Though we are recruiting any liver transplantation patients with alcohol-related liver disease, it is extremely unlikely that there will be any transplantation under 21 who have ALD and thus, extremely unlikely that any participants under the age of 21 will be enrolled. The major disadvantage of the remaining instruments are the time taken to complete them and possible breach of confidentiality. Our past experience with these measures indicates that they are acceptable to subjects. Careful efforts aimed at maintaining confidentiality will be made. Additionally, it is possible that during the course of assessments, a participant could disclose suicidal or homicidal ideation and/or report any form of

child/elder abuse or report plans to damage property. If that is the case, we will have to report this to appropriate authorities and/or provide the participant with referrals for immediate treatment.

c) **Text Message Prompts and Responses** - The major disadvantage of the assessment of alcohol consumption and craving via text message is the time taken to complete them on a daily basis and the potential breach of confidentiality. Our assessments used in the text messages will be taken from validated instruments used in the assessment of alcohol and these measures, in our experience, have been acceptable to subjects. Careful efforts aimed at maintaining confidentiality will be made.

d) **Medical Chart Review** - At the 3-month follow-up, a review of the participants' liver transplantation medical chart will be completed to verify transplant status, review any in-clinic urine test results that have occurred since the end of treatment, determine whether any serious medical complications have occurred, and obtain the participant's most recent Model for End-Stage Liver Disease (MELD) score. Chart reviews will be completed by the study research assistant.

10. Minimizing Risks: Describe the manner in which the above-mentioned risks will be minimized.

Rating Scales/Questionnaires/Confidentiality – The major risk of the assessments is the potential loss of confidentiality which is discussed under the section related to confidentiality below. To minimize any discomfort associated with reporting on sensitive behaviors, participants will be informed that they may refuse to answer questions that they are not comfortable answering. Further, the nature of the questions is such that they do not pose a threat of criminal prosecution. Questions about drinking and drug use do not include information about where these behaviors occurred. For example, participants do not indicate a specific location and time when they may have used illicit substances. In summary, we believe the general nature of the questions provides further protection against any adverse outcomes. To protect participants' privacy in the case of a mandated disclosure, we will only voluntarily disclose information about participants under these circumstances (e.g. reported suicidal or homicidal ideation, child/elder abuse, or a plan to damage property) and participants will be informed about this procedure during the consent process.

The data being collected in this study are sensitive (e.g. current substance use in patients that are being evaluated for liver transplant) due to the fact that substance use of any kind can render a patient ineligible for current listing on the UNOS transplant list. Therefore, it is of utmost importance that the clinical team of the liver transplant service is blind to the results of specific participants' urine toxicology reports and self-reports of substance use. All liver transplant treatment providers will be blind to the participation of any patients in the study and no specific patient's substance use results will be discussed with liver transplant team members. Dr. DeMartini, Co-Investigator and Project Coordinator, is the only exception to this blind. Dr. DeMartini is a current psychotherapy provider in the liver transplant service and a member of the Behavioral Medicine team at Yale-New Haven Hospital. As Project Coordinator, she will have access to participants' toxicology results. She will not share these results with any other medical staff in the liver clinic and will not participate in any listing decisions for any participants enrolled in the study.

Medical Chart Review - Participants in this study will have already been enrolled in the Liver Transplantation clinic, and as such, already have a medical chart. As part of the consent procedures, participants are advised of the distinction between the research record and the medical record, which is protected by HIPAA and the Code of Federal Regulations (CFR) Part 2, Subpart E. As part of the consent process, patients will be informed about the medical chart review that will occur at the 3-month follow-up. Participants will be informed that only specific variables will be documented from the medical chart in their research chart – specifically, urine drug and alcohol test results, liver transplantation status, current Model for End-Stage Liver Disease (MELD) score, and any incidence of major medical complications.

11. 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?

The overall nature of study participant and the safeguards outlined above should not place participants at significant risk. It is possible, however, that mandated reporting requirements or a voluntary disclosure to protect a participant's welfare could incur risk. Overall, we consider this to be a minimal risk study.

b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study? N/A

c. Data and Safety Monitoring Plan:

The principle investigator (PI) is responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews, and the specified frequency of the reviews at a minimum of every 6 months (including when reapproval of the protocol is sought). During the review process, the PI will evaluate whether the study should continue unchanged, require modification/amendment, continue or close to enrollment.

Either the PI or the Human Investigation Committee (HIC) have the authority to stop or suspend the study or require modifications.

This protocol presents minimal risks to the subjects and adverse events or other problems are not anticipated. In the unlikely event that such events occur, serious and unanticipated and related adverse events or unanticipated problems involving risks to subjects or others will be reported in writing within 48 hours to the HIC using the appropriate forms and any appropriate funding and regulatory agencies. The investigator will apprise fellow investigators and study personnel of all adverse events that occur during the conduct of this research project through regular study meetings with study personnel.

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?

12. Statistical Considerations: Describe the targeted number of subjects and the statistical analyses that support the study design.

Questionnaire data on the participants' ratings of the text message intervention will be analyzed descriptively, focusing on mean ratings of (1) acceptability, (2) helpfulness, and (3) feasibility. Data analyses will also be performed to evaluate the effect size of the Text Message intervention compared with standard care for improving alcohol abstinence rates and preventing relapse to alcohol, as seen in EtG analyses. In addition, changes in secondary outcomes to perceived stress and increased coping skills will be compared between the two conditions. A sample size of 20 will not be sufficient to establish statistical significance, but rather a pattern of results that suggest promising effects across alcohol and stress outcomes.

SECTION III: RESEARCH INVOLVING DRUGS, BIOLOGICS, RADIOTRACERS, 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.

A. DRUGS, BIOLOGICS and RADIOTRACERS

13. Identification of Drug ,Biologic or Radiotracer: What is (are) the **name(s)** of the drug(s), biologic(s) or radiotracer(s) being used? Identify whether FDA approval has been granted and for what indication(s).

N/A

5. **Use of Placebo:** ☒ **Not applicable to this research project**

6. **Use of Controlled Substances:**
Will this research project involve the use of controlled substances in human subjects?
☐ Yes ☒ No *See HIC Application Instructions to view controlled substance listings.*

7. **Continuation of Drug Therapy After Study Closure** ☒ **Not applicable to this project**

B. DEVICES

1. Are there any investigational devices used or investigational procedures performed at YNHH, e.g., YNHH Operating Room or YNHH Heart and Vascular Center? Yes ☐ No ☒
If Yes, please be aware of the following requirements:

SECTION IV: RECRUITMENT/CONSENT AND ASSENT PROCEDURES

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

   a. targeted for enrollment at Yale for this protocol__20_
   b. If this is a multi-site study, give the total number of subjects targeted across all sites___

2. **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	
☐ YCCI Recruitment Database	☐ Clinicaltrials.gov Registry (do not send materials to HIC)	
☐ Other (describe):		

3. **Recruitment Procedures:**

a. Describe how potential subjects will be identified.

Because all participants must be in-evaluation at Yale New-Haven Hospital's Liver Transplantation clinic, all recruitment will be done within the YNHH Liver clinic. Potential participants will either self-identify that they are interested in the study or will be referred by a member of the medical staff.

b. Describe how potential subjects are contacted.

Flyers in the YNHH Liver Clinic will include a telephone number for potential participants to call to schedule an in-person intake evaluation. Potential participants will then call the number to speak to a research assistant to schedule the evaluation. Participants who express interest in the study to their medical provider or who are referred by a provider will be given the telephone number to contact the research assistant.

c. Who is recruiting potential subjects?

All participants will be recruited from the YNHH Liver Transplantation Clinic. Patient recruitment will be completed by the research assistant and final eligibility will be determined by Drs. Toll and DeMartini.

4. **Screening Procedures**

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 TO BE COLLECTED:

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

5. **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.

As noted above, Dr. DeMartini is a current member of the Behavioral Medicine team in the Liver Transplant service at YNHH and is a Co-Investigator/Project Coordinator of this study. She provides psychotherapy to liver transplant patients with ALD, and as such, has a direct clinical relationship with some potential research subjects.

Drs. Fehon, Emre, and Schilsky are all members of the liver transplant team. Dr. Emre, in his role as Chief of Transplant, has a clinical relationship with all transplant patients. Drs. Shilsky and Fehon also have clinical relationships with all transplant patients. All of these clinicians will be blind to the results of self-report data collected during the study and to urine toxicology results.

6. **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.)

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.

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

8. **Consent Personnel**: List the names of all members of the research team who will be obtaining consent/assent:

Benjamin Toll, PhD, Kelly DeMartini, PhD, Dwain Fehon, PsyD, and Amanda Palmer.

9. **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.

The entire consent form will be reviewed in detail with the subject in a private, one-on-one setting at the first intake appointment. All risks and benefits will be described. Any questions the subject may have will be addressed. If the subject wishes, they may take the consent form home and consider it further before signing. They may also request to speak to anyone on the research team about questions they have or to consult others, including their physician and family members. Once the subject has signed the consent, they may withdraw consent at any time. This informed consent will serve as documentation of the major aspects of the consent process. The informed consent form will be signed and dated by the participants and countersigned and dated by the staff member obtaining consent. A copy of the signed informed consent form will be given to the participant. Informed consent will be obtained prior to performance of any protocol specific procedures.

10. **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.

    We will not be enrolling participants with limited decision-making capacity. We plan to exclude individuals with current serious psychiatric or unstable medical illnesses. During the consenting process, the research assistant will read and review the consent form with the prospective participant. The research assistant will then ask the potential participant various questions about the consent form and study protocol to ensure the prospective participant sufficiently understands the study and the nature of their consent to participate.

11. **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.

The Compound Consent and HIPAA Authorization form is appended for your review.

12. **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.

N/A – We will not enrolling non-English speaking subjects in this project.

13. **Consent Waiver: In certain circumstances, the HIC may grant a waiver of signed consent, or a full waiver of consent, depending on the study.** If you will request either a waiver of consent, or a waiver of signed consent for this study, complete the appropriate section below.

    ☒ **Not Requesting a consent waiver**
    ☐ **Requesting a waiver of signed consent**

☐ **Requesting a full waiver of consent**

A. Waiver of **signed** consent: (Verbal consent from subjects will be obtained. **If PHI is collected, information in this section must match Section IV, Question 6**)

☐ **Requesting a waiver of signed consent for <u>Recruitment/Screening</u> only**

If requesting a waiver of signed consent, please address the following:

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 activity pose greater than minimal risk?
☐ Yes ***If you answered yes, stop. A waiver cannot be granted.*** Please note: Recruitment/screening is generally a minimal risk research activity
☐ No

AND

d. Does the research include any activities that would require signed consent in a non-research context? ☐ Yes ☐ No

☐ **Requesting a waiver of signed consent for the <u>Entire Study</u> (**Note that an information sheet may be required.)

If requesting a waiver of signed consent, please address the following:

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 ***If you answered yes, stop. A waiver cannot be granted.*** ☐ No

AND

d. Does the research include any activities that would require signed consent in a non-research context? ☐ Yes ☐ No

B. **Full waiver** of consent: (No consent from subjects will be obtained for the activity.)

☐ **Requesting a waiver of consent for <u>Recruitment/Screening</u> only**

a. Does the research activity pose greater than minimal risk to subjects?
☐ Yes ***If you answered yes, stop. A waiver cannot be granted.*** Please note: Recruitment/screening is generally a minimal risk research activity
☐ 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?

☐ **Requesting a full waiver of consent for the Entire Study (Note: If PHI is collected, information here must match Section IV, question 6.)**

If requesting a full waiver of consent, please address the following:

a. Does the research pose greater than minimal risk to subjects? ☐ Yes ***If you answered yes, stop. A waiver cannot be granted.*** ☐ 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?

SECTION V: PROTECTION OF RESEARCH SUBJECTS

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?

The following protected health information will be collected from each participant: name, address, telephone number(s), birth date, electronic mail address, admission date to the liver transplantation program, liver transplant/YNHH medical chart number, liver transplantation diagnosis (e.g. alcohol-related liver disease) and diagnostic status (e.g. pre-transplant evaluation, work-up complete, UNOS listed, transplant denied), MELD scores, and major medical diagnoses in addition to liver disease (e.g. diabetes mellitus type I or II, cardiac status.

In addition, we will obtain contact information (name, address, telephone number) of a collateral contact that we can contact in case a participant cannot be reached to schedule follow-up appointments. All participants will be notified about this procedure in the consent process and will provide separate informed consent to give us permission to contact their collateral.

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

Research data will be collected using interviews, laboratory testing, self-reports, and through text-message based methods.

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?

Several steps will be taken to safeguard the confidentiality of subjects and their data. All research data collected will be coded by participant study number rather than name. Daily text message assessments will be completed by participants using a study administered phone, which will be a phone purchased in cooperation with Yale's ITS department and meet Yale standards for security. Each participant's phone will be set-up with a password so that only the participant has access to any text messages sent to it. Text messages will contain no personal information and phones will be set-up with participant study numbers rather than names, therefore no personal health information (PHI or ePHI) will be transmitted, stored, or received via text message. The names of participants will not be associated with this data and assessments will be maintained according to participant study number. A master list connecting participant study numbers to participant names will be kept in a locked file cabinet where it can

be accessed only by senior level project staff. Identifiable information will be collected and used to enroll and contact participants. It will only be used for this purpose. All identifiable information will be stored in a locked research cabinet. Hard research data will be generated into digital data, kept confidential, and scored on a secure server. Only research staff, including Drs. Toll, and DeMartini, research assistants, and a data manager will have access to participant data, including identifiable information.

The YNHH medical records are maintained under the person's name, but the study number is not entered anywhere into the medical record. Right to privacy for participation in this research will be protected through coding of data and proper storage of research records. We advise participants that in the case of child abuse or neglect, threat of injury to self or others, or intention to destroy property, that we will need to intervene and report that information to the proper authorities. Subjects will be informed of this limit to confidentiality as it is stated in the informed consent document.

Do all portable devices contain encryption software? ☒ Yes ☐ No
If no, see http://hipaa.yale.edu/guidance/policy.html

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.

The data will be stored in a locked room for 7 years after the final data is collected. We anticipate that the final data will be collected by January 1, 2014, so the date that the research data will be destroyed or de-identified is February 28, 2021.

f. Who will have access to the protected health information (such as the research sponsor, the investigator, the research staff, all research monitors, FDA, Yale Cancer Center Data and Safety Monitoring Committee (DSMC), SSC, etc.)? (please distinguish between PHI and de-identified data)

The PI and the research staff will have access to the protected health information obtained in the study. As noted above, however, all members of the liver transplant clinical team, except for Dr. DeMartini, will not have access to toxicology results or the results of questionnaire data indicating substance use. Members of the liver transplant clinical team will have access to only deidentified data on substance use. Dr. DeMartini will provide research data to the clinical treatment team. Research monitors will have access to de-identified data.

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

Because this is a brief pilot study, a Certificate of Confidentiality will not be obtained.

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.

There are no study procedures that are likely to yield information that is subject to these mandatory requirements. All information collected will remain confidential except when we are legally required to disclose such information by law. These circumstances include knowledge of abuse of a child or elderly person, threats of harm to self or others, and threats of harm to property. Subjects will be informed of this limit to confidentiality as it is stated in the informed consent document.

SECTION VI: 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. *(Note: Payment of subjects is not considered a benefit in this context of the risk-benefit assessment.)*

All participants will complete alcohol assessments. Research has consistently shown that assessments of alcohol and drug use behavior trigger self-initiated change, it is possible that the completion of assessments will increase participants' awareness of their drinking patterns. Participants will also have a 50% chance of receiving the Text Message intervention condition that may help them avoid relapse to alcohol and reduction in the stress associated with coping with a chronic medical condition.

The results of this study should help develop a psychosocial approach to the treatment of alcohol use and relapse to alcohol use in liver transplant candidates with ALD and thus may eventually benefit society in general.

SECTION VII: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

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

All patients in the liver transplantation clinic are provided with individual psychotherapy and are also given the option to receive treatment in local outpatient facilities and AA. In addition, there are support groups for liver transplant candidates to provide psychosocial support.

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

We will pay each participant up to $50 depending upon their compliance with the various aspects of the study. The payment breaks down as follows: $10 for intake appointment, $15 for the Week 4 appointment, and $25 for completion of the Week 8 post-treatment follow-up.

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.

Participants will not incur any costs as a result of their participation in this research.

4. **In Case of Injury:** This section is required for any research involving more than minimal risk.

   N/A

   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?

References

1. Belle SH, Beringer KC, Detre KM. Liver transplantation for alcoholic liver disease in the United States: 1988-1995. *Liver Transplant Surg* 1997; 3: 212-209.
2. Roisen, R, Kerr WC, Filmore KM. Cirrhosis mortality and per capita consumption of distilled spirits, United States 1949-94 trend analysis. *BMJ* 1999; 319: 666-70.
3. DiMartini A, Weinrieb R, Fireman, M. Liver transplantation in patients with alcohol and other substance use disorders. *Psychiatry Med Ill* 2002; 25: 195-209.
4. Alter MJ, Margolis HS, Bell BP, et al. Recommendations for prevention and control of Hepatitis C Virus (HCV) infection and HCV-related chronic disease. 1998. Atlanta, Centers for Disease Control, pp 1-39.
5. Mackie J, Groves, K, Hoyle A, Garcia C, Garcia R, Gunson B, Neuberger J. Orthotopic liver transplantation for alcoholic liver disease: a retrospective analysis of survival, recidivism, and risk factors predisposing to recidivism. *Liver Transpl* 2001; 7: 418-427.
6. DiMartini A, Day N, Dew MA, Javed L, Fitzgerald MG, Jain A, Fung JJ, Fontes P. Alcohol consumption patterns and predictors of use following liver transplantation for alcoholic liver disease. *Liver Transpl* 2006*;* 12: 813-820.
7. Cuadrado A, Fabrega E, Casafont F, Pons-Romero F. Alcohol recidivism impairs long-term patient survival after orthotopic liver transplantation for alcoholic liver disease. *Liver Transpl* 2005; 11: 420-426.
8. Miguet M, Monnet E, Vanlemmens C, Gache P, Messner M, Hruskovksy S, et al. Predictive factors of alcohol relapse after orthotopic liver transplantation for alcoholic liver disease. *Gastroenterol Clin Bio* 2004; 28: 845-851.
9. Mathurin P, Moreno C, Samuel D, Dumortier J, Salleron J, Durand F, Castel H et al. Early liver transplantation for severe alcoholic hepatitis. *New England Journal of Medicine* 2011; 365: 1790-1800.
10. Pfitzmann R, Schwenzer J, Rayes N, Seehofer D, Neuhaus R, Nussler NC. Long-term survival and predictors of relapse after orthotopic liver transplantation for alcoholic liver disease. *Liver Transpl* 2007; 13: 197-205.
11. Weinrieb RM, Van Horn DHA, Lynch KG, Lucey MR. A randomized controlled study of treatment for alcohol dependence in patients awaiting liver transplantation. *LiverTranspl* 2011; 17: 539-547.
12. Georgiou G, Webb K, Griggs K, Copello A, Neuberger J, Day E. First report of a psychosocial intervention for patients with alcohol-related liver disease undergoing liver transplantation. *Liver Transpl* 2003; 9: 772-775.
13. Rice R, Katz J. Comparing internet and mobile phone usage: digital divides of usage, adoption and dropouts. *Telecommunications Policy* 2003; 27: 597-623.
14. Ling R. The mobile connection: the cell phone's impact on society. San Francisco: Morgan Kaufmann Publishers, 2004.
15. Dijkstra A, De Vries H. The development of computer-generated tailored interventions, *Patient Educ Couns* 1999; 36: 193-203.
16. Ryan P, Lauver D. The efficacy of tailored interventions. *J Nurs Scholarsh* 2002; 34: 331-337.
17. Koivusilta K, Lintonen T, Rimpela A. Orientations in adolescent use of information and communication technology: a digital divide by socio-demographic background, educational career and health. *Scandinavian J Public Health* 2007; 35: 95-103.
18. Faulkner X, Culwin F. When fingers do the talking: a study of text messaging. *Interacting Comput* 2005: 17; 167-85.
19. Heron KE, Smyth, JM. Ecological momentary interventions: incorporating mobile technology into psychosocial and health behavior treatments. *Brit J Health Psych* 2010: 15; 1-39.
20. Kazantiz N, L'Abate L. Introduction and historical overview. In N. Kazantis & L. L'Abate (Eds.), *Handbook of homework assignments in psychotherapy: Research, practice, and prevention* (pp. 1-15). New York: Springer Science + Business Media, LLC., 2007.

21. Newman M, Consoli A, Taylor C. Computers in assessment and cognitive behavioral treatment of clinical disorders: anxiety as a case in point. *Behavior Therapy* 1997; 28; 211-235.
22. Kreuter M, Strecher V, Glassman B. One size does not fit all: The case for tailoring print materials. *Annals Behav Med* 1999; 21: 276-283.
23. Weitzel J, Bernhardt J, Usdan S, Mays D, Glanz K. Using wireless handheld computers and tailored text messaging to reduce negative consequences of drinking alcohol. *J Stud Alc Drug* 2007; 68; 534-537.
24. Petty R, Cacioppo J. *Communication and persuasion: Central and peripheral routes to attitude change*. New York: Springer-Verlag; 1986.
25. Webb MS, Hendricks PS, Brandon TH. Expectancy priming of smoking cessation messages enhances the placebo effect of tailored interventions. *Health Psychology*. 2007;26(5):598-609.
26. Whittaker R, Maddison R, McRobbie H, Bullen C, Denny S, Dorey E, et al. A multimedia mobile phone-based youth smoking cessation intervention: Findings from content development and piloting studies. *J Med Internet Research* 2008; 10; e49.
27. Free C, Knight, Robertson S, Whittaker R, Edwards P, Zhou W, Rodgers A, Cairns J, Kenward MG, Roberts I. Smoking cessation support delivered via mobile phone text messaging (txt2stop): a single-blind, randomized trial. *Lancet* 2011; 378: 49-55.
28. Sobell LC, Sobell, MB. (1992). Timeline Follow-back: A technique for assessing self-reported alcohol consumption. In R.Z. Litten & J. Allen (Eds.), *Measuring alcohol consumption: Psychological and biological methods* (pp. 41-72). Towota, NJ: Humana Press.
29. Sobell LC, Sobell, MB. (2000). Alcohol Timeline Followback (TLFB). In American Psychiatric Association (Ed.), *Handbook of psychiatric measures* (pp. 477-479). Washington DC: American Psychiatric Association.
30. Anton RF, Moak, DH, Latham, PK. The Obsessive Compulsive Drinking Scale: A self-rated instrument for the quantification of thoughts about alcohol and drinking behavior. *Alcoholism: Clinical and Experimental Research*. 1995; 19:92-99.
31. Cohen S. (1988). Perceived stress in a probability sample of the United States. In S. Spacapan & S. Oskamp (Eds.), *The social psychology of health. The Claremont symposium on applied social psychology* (pp. 31-67). Thousand Oaks, CA: Sage Publications.
32. Skevington SM, Lofty M, O'Connell KA. The World Health Organization's WHOQOL-BREF quality of life assessment: Psychometric properties and results of the international field trial. A report from the WHOQOL Group. *Quality of Life Research* 2004; 13: 299-310.
33. Radloff LS. The CES-D Scale: a self-report depression scale for research in the general population. *Applied Psychological Measurement* 1977; 1: 385-401.
34. Hoeppner BB, Kelly JF, Urbanoski KA, Slaymaker V. Comparative utility of a single-item versus multiple-item measure of self-efficacy in predicting relapse among young adults. *Journal of Substance Abuse Treatment* 2011; 41: 305-312.