A Guided Imagery Tobacco Cessation Intervention Delivered by a Quitline and Website

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The Study Team in collaboration with the Arizona Smokers' Help Line (ASHLine)

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Not Applicable

Tool Revision History

Version Number: 8.0

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Summary of Revisions Made:

- Remove 8-week cotinine assay.

- Change 6-month cotinine assay collection procedure.

- Increase feasibility enrollment from 100 to up to 120 subjects, which will increase total enrollment to up to 178. This changes the number of subjects assigned to control group from 50 to up to 60, and the number of subjects assigned to the intervention group from 50 to up to 60.

- Remove two staff people who are no longer with the project.

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PRÉCIS

Study Title: A Guided Imagery Tobacco Cessation Intervention Delivered by a Quitline and Website

Objectives: This clinical protocol has the following three objectives: 1) *Develop a theory-based, guided mental imagery tobacco cessation intervention for quitline callers* with input from expert consultants in health disparities and a Community Advisory Board representing diverse populations and tobacco control stakeholders, 2) Develop training and competency standards for, and train, two imagery coaches in the implementation of the guided imagery intervention, and two behavioral strategy coaches for implementation of control condition, 3) Conduct a feasibility and acceptability trial (N= up to 120) to gather preliminary data on the effects of the guided imagery intervention on quitline callers' tobacco abstinence, number of quit attempts, number of cigarettes smoked, and self-efficacy to quit smoking.

Design and Outcomes

The study consists of two phases: 1) Developmental; and 2) Randomized Feasibility Trial.

Phase 1: As shown in Table 1 below, the development of the intervention will occur iteratively and include the following 7 stages: 1) the development of protocols for the guided imagery intervention and control conditions for use in a telephone-based coaching model; 2) a website containing instructions, and testimonials regarding the use of guided imagery and control conditions; 3) focus group testing of materials and the website (N=48); 4) the development of a training program for the study coaches; 5) Programming of the website and internal quality assurance/quality control (QA/QC) testing; 6) Usability testing of the study website; and 7) Modification of the ASHLine's 2.0 electronic data system to gather and transfer study information, and development of a REDCap system for protocol implementation, participant management and data storage.

Phase 2: Prior to beginning the trial, we will user test all recruitment and data collection systems with up to 10 user test participants to identify and correct any problems. We will randomize up to 10 user-test participants to test the ASHLine 2.0/REDCap systems and correct any errors identified. Once any identified errors are corrected, we will begin the feasibility trial. The Feasibility Trial will employ a two-group randomized controlled design. While developing the intervention, we will also develop an attention-control condition that will control for treatment length and contact time of the intervention. The trial will enroll up to 120 smokers (males and females age 18 and older) who will be randomly allocated to either the Imagery Intervention (IIC) or control condition (CC). Participants will be recruited and screened for eligibility by ASHLine staff and study staff. Informed consents and surveys will be obtained by ASHLine and study staff at baseline. Study staff will collect follow-up surveys at 8-weeks and 6-months post-enrollment, including demographics, tobacco use, self-efficacy for quitting, cravings, and imagery expectancies for both groups. Participants will also complete measures of their imagery experiences, system usability, and other evaluations of their experiences with the website and study protocol. All participants who report abstinence at the 6-month assessment will be asked to perform a biochemical test using a saliva test kit to validate self-reported smoking abstinence. Participants meeting this criteria will be mailed a saliva kit in the mail and then join a video chat with staff who will instruct the participant and monitor the collection of saliva and reading of the test strip. Participants will be offered $25 for completing the saliva assessment.

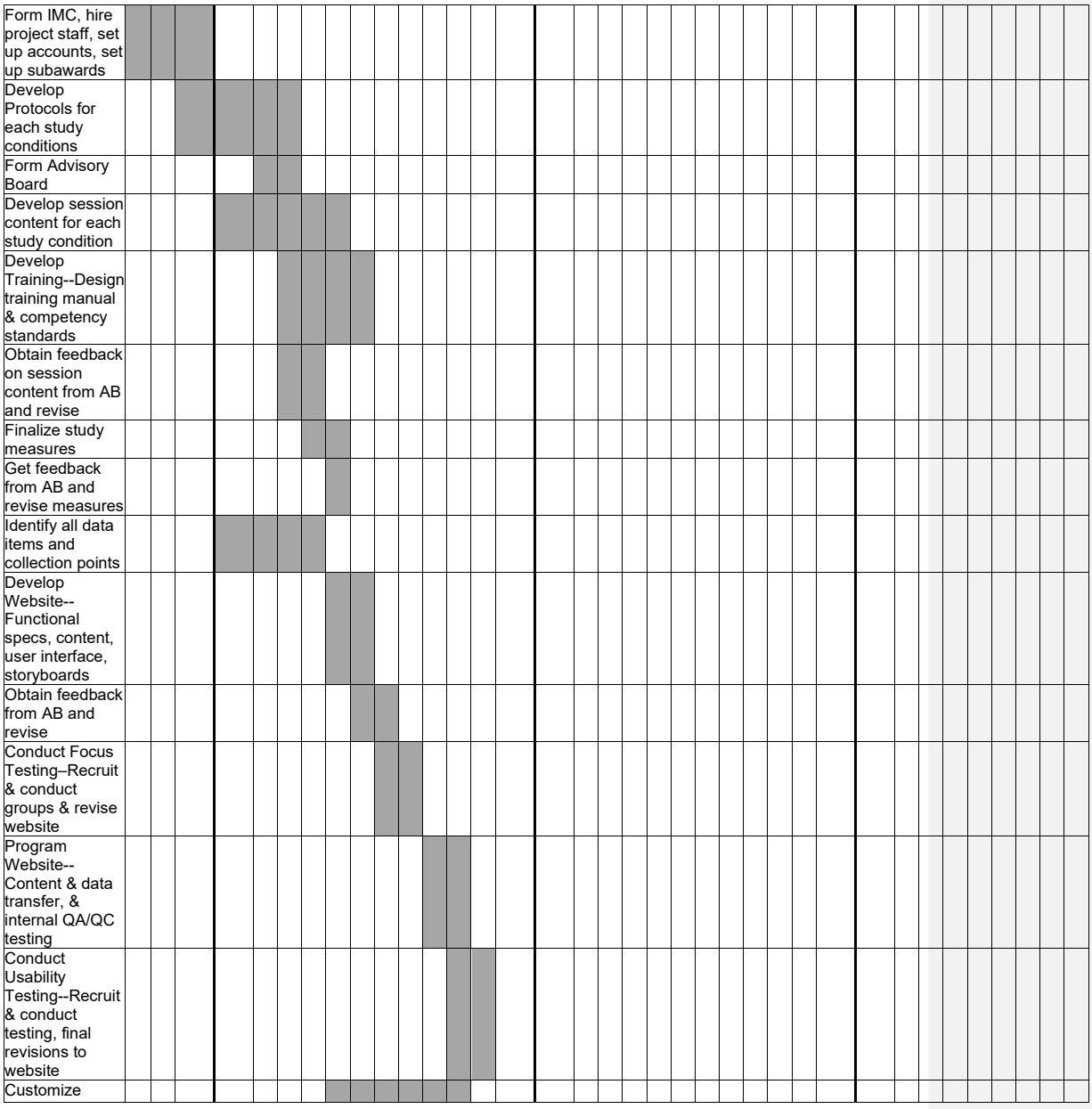
Commented [PG-(1]: Define abstinence: e.g. 7 day (not 30 day)

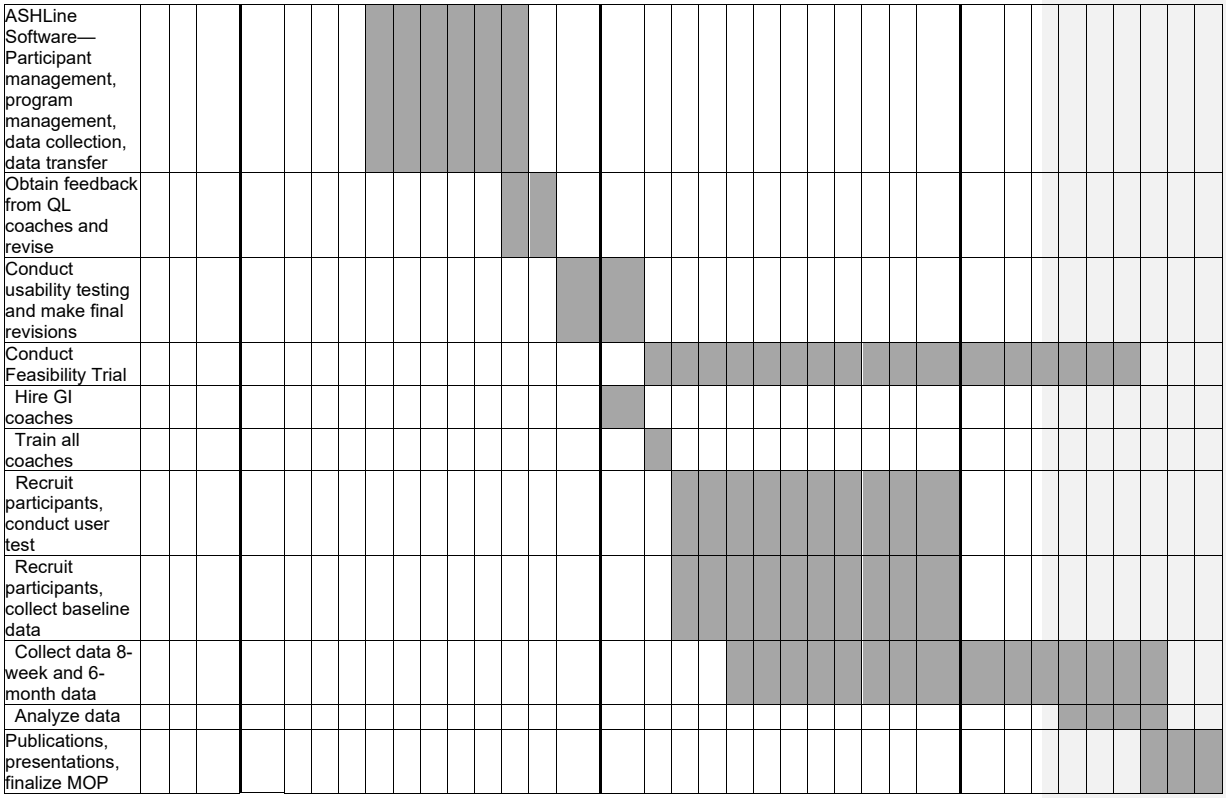
Total participants to be enrolled for Phase 1 equal 48. Total participants to be enrolled in Phase 2 will be up to 10 user-test participants, and up to 120 feasibility trial participants. Total enrollment for all phases of this study will be up to 178.

The remainder of this protocol will describe procedures for the randomized feasibility trial.

Table 1. Project Timeline

QLI Project Time Line	2016												2017																				2018	2019	
Activities	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep


Form IMC, hire project staff, set up accounts, set up subawards
Develop Protocols for each study conditions
Form Advisory Board
Develop session content for each study condition
Develop Training--Design training manual & competency standards
Obtain feedback on session content from AB and revise
Finalize study measures
Get feedback from AB and revise measures
Identify all data items and collection points
Develop Website--Functional specs, content, user interface, storyboards
Obtain feedback from AB and revise
Conduct Focus Testing–Recruit & conduct groups & revise website
Program Website--Content & data transfer, & internal QA/QC testing
Conduct Usability Testing--Recruit & conduct testing, final revisions to website
Customize



Interventions and Duration

For the feasibility trial, we will randomize up to 120 participants to either the Imagery Intervention (IIC) or Control (CC) condition. We anticipate that participants will receive 6 sessions. All sessions will be approximately 20-50 minutes long. All participants will be instructed to log into the project website, which will contain a repository of study and intervention information tailored to condition.

Participants will be assessed at 8-weeks post-enrollment, and at 6 months post-enrollment via online survey (or phone for non-responders) by project personnel. All participants who report abstinence at the 6-month assessment will be asked to perform a biochemical test using a saliva test kit to validate self-reported smoking abstinence. Participants meeting these criteria will be invited to receive a saliva kit in the mail and then join a video chat with staff who will instruct the participant and monitor the collection of saliva and reading of the test strip. Participants will be offered $25 for completing the saliva assessment.

Sample Size and Population

The target population for the feasibility intervention will be a racially and ethnically diverse sample of male and female smokers (N= up to 120) who will be randomized to the IIC or CC.

1. STUDY OBJECTIVES

1.1 Primary Objective

The primary outcome will be self-reported tobacco abstinence. We will measure 7-day point prevalence, 30-day point prevalence and prolonged abstinence at the 6-month follow-up assessment. All participants who report abstinence at the 6 month assessment and agree to perform a saliva test will be biochemically validated. We hypothesize that participants in the Imagery Intervention Condition will report equal or higher rates of cessation than those in the Control Condition.

Our feasibility outcomes include: at least 50% of participants will complete the 6-session intervention program; 50% Of the IIC participants will report listening to the guided imagery audio files at least 5 times per week; 50% will visit the website at least one time; and 75% of participants will complete both follow-up assessments.

1.2 Secondary Objectives

Secondary outcomes will include reduced tobacco use (for non-quitters), increased self-efficacy for quitting, and reduced nicotine cravings. We hypothesize that participants in the Imagery Intervention Condition will report equal or lower levels of tobacco use and cravings, and equal or higher levels of self-efficacy for quitting.

In addition, we will explore the demographics of study participants to assess how they may differ from the general population of ASHLine callers.

2. BACKGROUND AND RATIONALE

2.1 Background on Condition, Disease, or Other Primary Study Focus

Tobacco use continues to be a leading preventable cause of death in the United States accounting for about 480,000 deaths each year (USDHHS, 2014). For every death related to smoking-related diseases there are 30 people who suffer from serious illnesses directly related to smoking that include stroke, chronic obstructive pulmonary disease, heart disease, and lung cancer. According to a recent report by the Surgeon General, the total economic cost of tobacco use in the United States was $289 to $332 billion from 2009-2014.

2.2 Study Rationale

Several meta-analytic reviews have shown that proactive telephone-based tobacco cessation services are an effective way to reduce cravings for and use of tobacco (Fiore et al., 2008; Hopkins et al., 2001; Lichtenstein et al., 2010). Telephone Quitlines (QLs) are an efficient, centralized, and highly scalable way to help individuals quit their use of tobacco that are available in all fifty states plus the District of Columbia. The North

American Quitline Consortium reported that 515,000 users, or 1.2% of all smokers, contacted QLs in 2009: this represents an increase of 129.7% since 2005. In Arizona, the Arizona Smokers' Help Line (ASHLine) is run through the University of Arizona, Mel and Enid Zuckerman College of Public Health, and is funded by the State of Arizona, Department of Health. The ASHLine, where the proposed study will be implemented, enrolled 10,824 individuals from July 2013 to June 2014, which represented a 7% increase from the previous year. Of these, about 73% were Caucasian, 57% were female, 17% were Hispanic, 8% were African American, and 2% were American Indian. The ASHLine uses a "Coaching Model," and reported an average of 3.9 calls per enrollee--two calls for medication only enrollees, and nine calls per coaching enrollees.

Researchers have also demonstrated the cost-effectiveness of telephone QLs in the United States and Europe over the past 25 years (Cromwell, Bartosch, Fiore, Hasselblad, & Baker, 1997; Fiore et al., 2008; Kahende, Loomis, Adhikari, & Marshall, 2009; Lichtenstein et al., 2010). Despite these findings, many state agencies that oversee the implementation of QLs are cutting funds at a time when there is record utilization of services (NAQC, 2010). This situation has prompted many state sponsors to try to improve their effectiveness by focusing recruitment on under-represented groups and reducing human capital with increased web-based services: approximately 1/3 of US QLs include some type of internet service to supplement counseling. Theoretically-based website services and alternative intervention approaches that are more appealing to diverse groups may increase the reach, engagement, and effectiveness of QLs.

Guided imagery is a mind-body technique that involves the visualization of mental images and is similar to mindfulness meditation (MM). Both mindfulness meditation and mental imagery can create awareness and direct attention to one's thoughts, feelings, and health behaviors. Guided imagery and other mindfulness interventions can effectively assist tobacco users to quit (Brewer et al., 2011; Wynd, 2005; Zernig et al., 2008). One randomized controlled trial with 779 adult smokers compared the use of bupropion with brief psychotherapy that was taught to participants over 2 days lasting 8 hours (Zernig et al., 2008). The latter condition consisted of exposure to guided imagery intended to enhance self-management, decidedness, assertiveness, self-determination, and self-assurance. Intent-to-treat analysis showed 12-month abstinence rates of 39.1% and 12.3% for the psychotherapy and bupropion groups, respectively. These rates were 39.9% (psychotherapy) and 22.5% (bupropion) for those who completed the study. In another four week randomized controlled trial, 33 adults were taught mindfulness and encouraged to practice at home (Elwafi et al., 2013). Results showed that home practice predicted reduced cigarette use, and informal mindfulness practice moderated the relationship between craving and cigarette use (Elwafi et al., 2013). Another smaller trial compared those receiving education and counseling with education/counseling plus imagery training (Wynd, 2005). Results of that study indicated abstinence rates of 12% and 26%, respectively (Wynd, 2005). These studies support the efficacy of guided mental imagery for smoking cessation.

However, these studies employed in-person interventions that are prohibitively expensive and limit larger scale implementation and overall reach. Combining the use of guided imagery with tobacco QL services offer a highly scalable, innovative, and a cost-effective strategy for delivering a guided imagery intervention. We will develop, using input from expert consultants, a community advisory board, and our target population, a guided imagery intervention, attention-control condition, and recruitment strategies. The intervention has little potential risk and may increase the use of telephone-based tobacco cessation counseling by male and racially-/ethnically-diverse smokers.

3. STUDY DESIGN

As shown in Figure 1, we will use a two-group randomized control design. Participants will be recruited through IRB-approved flyers and advertising, and the ASHLine, screened for eligibility by ASHLine or study staff, consented by ASHLine or study staff, administered the baseline survey by ASHLine or study staff, and automatically randomized by the REDCap system (using a randomization algorithm) to either the Imagery Intervention (IIC) or Control (CC) Condition. We will enroll and randomize up to 120 feasibility trial participants (approximately equal numbers per condition).

Participants in both conditions will receive a screening call and 6 telephone coaching sessions delivered over 6 weeks by trained ASHLine or project staff. The screening call will be conducted by ASHLine or study staff to assess study eligibility, collect consent for study participation, and collect baseline survey items. The coaching sessions will be approximately 20-50 minutes long. We will develop baseline survey items to be administered to participants during the screening call. We will develop content for each coaching call for each study condition, including instructions for using the study website. The IIC sessions 1-4 will include an introduction to guided imagery, setting a quit date, setting a guided imagery schedule, and helping the participant develop a guided imagery script which the coach will record as an audio file and send to the participant to listen to. Sessions 5-6 will focus on quitting issues and relapse prevention. The CC sessions 1-4 will include an introduction to cognitive behavioral telephone coaching, setting a quit date, an introduction to the quitting booklet [in development], and setting a schedule for using the booklet, and assistance in developing the first part of the quit plan. Sessions 5-6 will focus on quitting issues and relapse prevention strategies. Sessions 2 – 4 will review progress and build skills according to study condition, culminating in a quit day at approximately 4 weeks post-enrollment. Sessions 5-6 will reinforce quitting smoking or help participant recommit to quit. Between sessions, participants in both conditions will receive occasional text messages (e.g. motivational messages, call reminders). During the enrollment process participants are asked for a phone number at which they can receive texts. By providing the number they are agreeing to receive occasional texts. During the coaching sessions, the coach asks the participant if they wish to receive more messages (e.g., motivational messages, tips for quitting, etc.).

Participants in both conditions who request it will receive up to 4 weeks of Nicotine Replacement Therapy (NRT), either nicotine patches or lozenges based on level of nicotine

dependence. All participants requesting NRT will be screened by trained project staff for contraindications for use, assessed for level of dependence, and informed of potential side effects (AEs and SAEs) of using NRT. The screening, assessment, and informational scripts are under development and will be submitted to the IRB for approval prior to these activities occurring with participants.

Participants will be assessed by project staff at 8-weeks and 6-months post-enrollment. Self-report surveys will be administered online or by phone. All participants who report abstinence at the 6-month assessment will be asked to perform a biochemical validation. Biochemical validation will be performed via saliva test kit sent to the participant's home and a video chat with University of Arizona project staff.

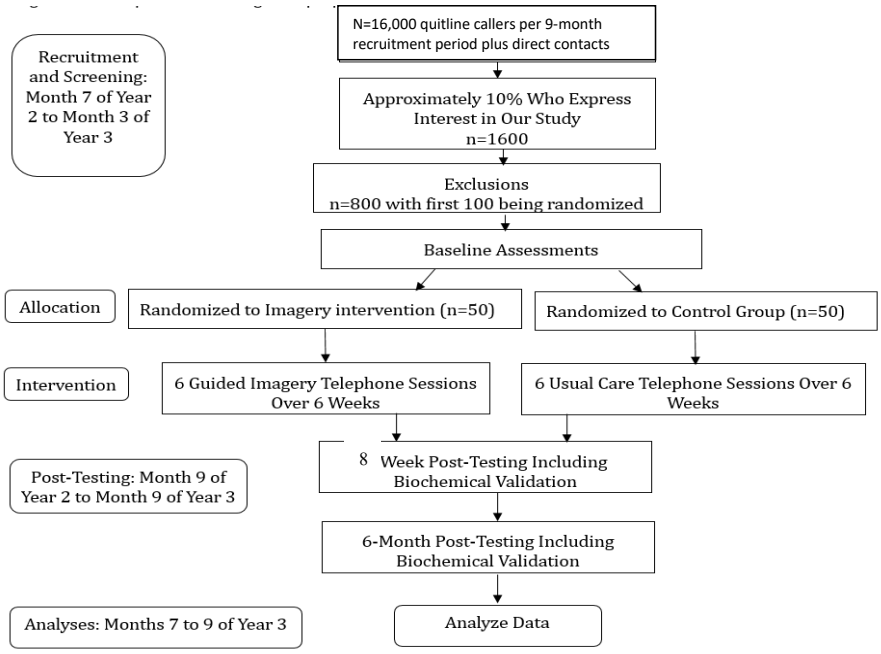
The primary outcome will be self-reported tobacco abstinence. We will measure 7-day point prevalence, 30-day point prevalence and prolonged abstinence at each follow-up assessment. We hypothesize that participants in the Imagery Intervention Condition will report equal or higher rates of cessation than those in the Control Condition.

Our feasibility outcomes include: at least 50% of participants will complete the 6-session intervention program; 50% will report listening to the guided imagery audio files at least 5 times per week; and 50% will use the website at least one time; and 75% of participants will complete both follow-up assessments.

Secondary outcomes will include increased number of quit attempts, reduced tobacco use (for non-quitters) and increased self-efficacy for quitting. We hypothesize that participants in the Imagery Intervention Condition will report equal or lower levels of tobacco use, and equal or higher levels of quit attempts and self-efficacy for quitting.

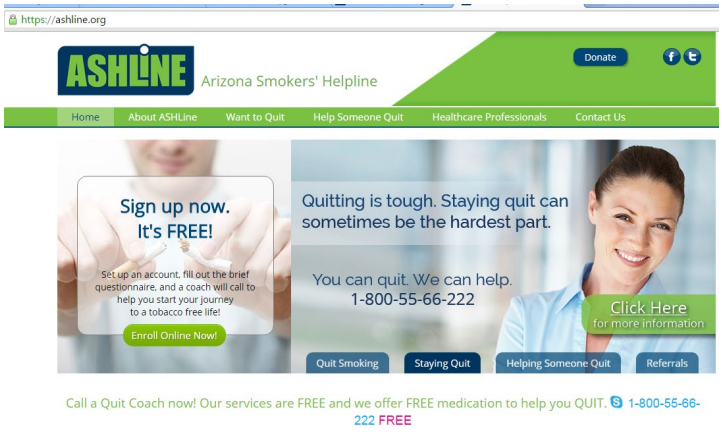
In addition, we will explore the demographics of study participants to assess how they may differ from the general population of ASHLine callers. Our goal is to increase the diversity of ASHLine callers.

Figure 1. Study Flow Diagram - Minimum Number of Participants Noted, Up to 120 (60 Per Condition) Will be Randomized



4. SELECTION AND ENROLLMENT OF PARTICIPANTS

Participants will be male and female smokers over the age of 18 who are interested in quitting and call the ASHLine or respond to flyers or advertising. During the study period, we will actively recruit underrepresented smokers to call the ASHLine. The ASHLine has agreed to display tailored recruitment information on their website (as developed by our consultants and community advisory board [CAB]), and we will employ additional recruitment strategies (e.g., swap meets, churches, medical providers, identified by the CAB and consultants) to attract diverse potential participants. Additional participant recruitment may occur through the Arizona ASHLine using special features on their study website (see Figure 2). ASHLine staff may embed a link about the research study that will be tailored for racially- and ethnically-diverse audiences and feature content about the use of guided imagery.



4.1 Inclusion Criteria

Participants must meet all of the inclusion criteria to participate in this study.

Inclusion Criteria:

- Current smokers or those whose primary tobacco product is cigarettes (e.g., dual cigarette and smokeless tobacco users).
- Current callers and former callers who have not enrolled in the ASHLine for the previous 12 months
- At least 18 years of age
- Have email access
- Speak English
- Ability to understand study procedures and to comply with them for the entire length of the study.
- Contraception is not necessary or required.

4.2 Exclusion Criteria

All candidates meeting any of the exclusion criteria at baseline will be excluded from study participation.

Exclusion Criteria:

- Individuals with serious mental illness
- Tobacco users who have used the ASHLine in the past 12 months
- Tobacco users who are currently receiving any form of tobacco cessation treatment
- Refusal to be randomized to one of the study conditions.

4.3 Study Enrollment Procedures

The REDCap system will be used to document information during all phases of the study. The REDCap system will track the name and contact information of the participants, date of contact with ASHLine or study staff, the staff person who took their telephone call, eligibility/screening information, consent, baseline survey, and randomization information. Informed consent will occur over the telephone with ASHLine or study staff reading an IRB-approved abbreviated version of the consent document to participants. Participants will provide verbal consent and be emailed a copy of the full-length consent form for their records. Upon completion of informed consent, ASHLine or study staff will administer the baseline survey via the phone. Upon completion of the baseline survey, the data from ASHLine 2.0 will be transferred to the REDCap system. Study staff will then call the participant and confirm consent. The REDCap system will be used to randomize the participant to either the IIC or CC. The REDCap system will automatically assign the participant to condition using a randomization algorithm. Following randomization, study staff will assign the participant to an appropriate study coach. The coach will then schedule the first session with the participant.

5. STUDY INTERVENTIONS

5.1 Interventions, Administration, and Duration

The Imagery Intervention will consist of 6 weekly telephone coaching sessions delivered by trained project staff plus a companion website containing study materials. As shown in Table 2, the first session will include an overview of guided imagery, setting a quit date, setting a guided imagery schedule, description of the Intervention website and instructions for using the website. Sessions 2-4 will include follow-up and review of progress and use of the imagery files. Session 5 will include instructions using / modifying the guided imagery script. Session 6 will review progress and creating a plan for continued use of guided imagery for relapse prevention and/or cessation.

Table 2. Activities in the Intervention and Control Conditions by Week

Week 1-Imagery Intervention Condition **Theme:** Intro and planning **Goal:** Set quit date, define GI, determine reasons/benefits of quitting, create script and set times to practice script. **Content**: Basic definition of GI, intro to breathing, relaxation. Draft one GI sentence for each reason/benefit.	**Week 1-Control Condition** **Theme:** Intro and planning **Goal:** Set quit date, determine reasons/benefits of quitting and set time to do portion of booklet. **Content:** Define and discuss behavioral treatment. Discuss previous quit attempts.
Week 2-IIC **Theme:** Triggers **Goal:** Develop GI strategies to address triggers.	**Week 2-CC** **Theme:** Triggers **Goal:** Develop behavioral strategies to address triggers.

Content: Identify participant's primary trigger and coping strategy; develop script. Practice previous script and this one together.	**Content:** Review triggers and coping strategies participant identified in booklet. Recommend practicing new coping strategy in the trigger setting each day.
Week 3-IIC **Theme:** Cravings and Withdrawal **Goal:** Have client understand 2 types of urges (habitual and physiological reaction). Develop strategies to address cravings and withdrawal. Discuss NRT. **Content:** Create script to manage cravings and withdrawal. Make listening to GI a new habit.	**Week 3-CC** **Theme:** Cravings and Withdrawal **Goal:** Have client understand 2 types of urges (habitual and physiological reaction). Develop strategies to address cravings and withdrawal. Discuss NRT. **Content:** Identify replacement behaviors for cravings and withdrawal issues.
Week 4-IIC (On or slightly before quit date) **Theme:** Handling withdrawal and preparing to quit **Goal:** Determine strategies to handle withdrawals, discuss use of NRT and quit preparation. **Content:** Make edits or additions to script if necessary. Practice entire script throughout week, or just a portion if too long.	**Week 4-CC** (On or slightly before quit date) **Theme:** Handling withdrawal and preparing to quit **Goal:** Determine strategies to handle withdrawals, discuss use of NRT and quit preparation. **Content:** Review strategies previously identified and any new ones, as needed.
Week 5-IIC **Theme:** Relapse prevention/recommit to quit **Goal:** Support quitting among those who quit and encourage quitting among those who didn't or who relapsed. **Content:** Check whether participant wants any changes to the script. If so, identify changes and re-record.	**Week 5-CC** **Theme:** Relapse prevention/recommit to quit **Goal:** Support quitting among those who quit and encourage quitting among those who didn't or who relapsed. **Content:** Revise behavioral strategies as needed to cope with anything that came up during the week.
Week 6-IIC **Theme:** Relapse prevention/recommit to quit **Goal:** Prepare participants to be successful on their own. Give post-quit resources. **Content:** Revise script if necessary. Provide GI and relaxation resources.	**Week 6-CC** **Theme:** Relapse prevention/recommit to quit **Goal:** Prepare participants to be successful on their own. Give post-quit resources. **Content:** Revise behavioral strategies if needed.
8 Week Follow-up Survey Assess for 7 day and 30 day point prevalence.	8 Week Follow-up Survey Assess for 7 day and 30 day point prevalence.
6 Month Follow-up Survey Assess for 7 day and 30 day point prevalence as well as prolonged abstinence.	6 Month Follow-up Survey Assess for 7 day and 30 day point prevalence as well as prolonged abstinence.

Participants are also eligible to use nicotine replacement therapy as per study guidelines. The study will provide nicotine lozenge or patch for up to 4 weeks if the participant has no medical contraindications for use.

Participants can opt in to receive text messages from the quit coaches throughout the quitting process. Quit coaches will ask participants during the coaching sessions if

they wish to receive additional, optional text messages (e.g., motivational messages, quitting tips, etc.).

5.2 Handling of Study Interventions

For a description of the intervention protocol, see section 5.1. As part of the R34 we will develop a Manual of Procedures to document all study-related policies, procedures, measures and materials. In addition, we will work with the Arizona Research Labs (ARL) to modify the ASHLine 2.0 system to collect study-related information, and contract with BMISR to create a REDCap data and participant management system that will be integrated with the ASHLine 2.0 system and the project website. ARL is responsible for programming and maintaining the ASHLine 2.0 system and the project website. Therefore, these systems will be integrated and maintained by ARL.

As this is a behavioral intervention, it is not possible to employ masking procedures with participants or study coaches. However, ASHLine staff and project staff who obtain informed consent and conduct baseline assessments and confirm consent will not know participants' study assignment prior to obtaining consent or baseline assessments.

5.3 Concomitant Interventions

Those calling the ASHLine who request only medications will be excluded (see above).

We will provide NRT to all study participants who request it, and have no medical contraindications for use. We will screen all participants for contraindications for use of NRT, and assess level of dependence to determine whether participants should use nicotine patches or lozenges. We will offer up to 4 weeks of NRT.

5.3.1 Allowed Interventions

Participants are allowed to take nicotine replacement medication as per study policies and any other medication prescribed by their physician.

5.3.2 Required Interventions

The participants must agree to be randomized to one of the two study conditions and to participate in 6 weekly sessions, and use the project website.

5.3.3 Prohibited Interventions

Participants may not be currently enrolled in the ASHLine or any other tobacco cessation treatment program or have been enrolled in the ASHLine in the past 12 months.

5.4 Adherence Assessment

Adherence will include: 1) Coach collected participant attendance of coaching sessions; 2) Participant self-reported listening to guided imagery audio files (IIC only); 3) Participant self-reported use of cognitive-behavioral techniques (CC only); and 4) Automatically collected use of the study website.

Adherence feasibility outcomes will be measured as: at least 50% of participants will complete the 6-session intervention program; 50% of IIC participants will report listening to the guided imagery audio files at least 5 times per week; and 50% will use the website at least one time.

6. STUDY PROCEDURES

The study procedures are outlined below. See also Figure 1 and Table 3.

1. Potential participants will call the ASHLine or study staff.
2. ASHLine or study staff will describe the study and screen callers for eligibility.
3. Eligible participants will be consented by the ASHLine or study staff, who will also administer the baseline survey. If participants are consented by ASHLine, study staff will call participants and confirm consent.
4. Participants who complete the survey will be enrolled in the study and automatically randomized by the REDCap system to one of the two study conditions.
5. Participants will be assigned to a study coach depending on condition.
6. The study coach will schedule the first and subsequent telephone coaching visits.
7. All visits will be conducted via phone at the initiation of the study coach.
8. All follow-up assessments will be scheduled and conducted by project assessment staff (not study coaches).
9. Study staff will administer the follow-up assessments at 8-weeks and 6-months post-enrollment.
10. A link to a REDCap or Qualtrics online questionnaires will be sent by email at 8 weeks and 6 months post-enrollment and participants will be instructed to complete the surveys.
11. Participants who have not completed a survey after one week will receive a reminder email.
12. Participants who have not completed a survey after two weeks will receive a phone reminder and offered the opportunity to complete the survey by phone or online.
13. Participants who have not completed a survey after three weeks will receive a phone reminder to complete the survey.
14. All participants who report abstinence on the 6-month survey will be asked to perform a biochemical validation using saliva.
15. Participants who have not completed a survey at four weeks will be considered lost to follow-up but retained in analyses.

Table 3. Schedule of Evaluations

Assessment	Screening, Consent, Baseline, Randomization Visit 0	Treatment Visit 1 (W1)	Treatment Visit 2 (W2)	Treatment Visit 3 (W3)	Treatment Visit 4 (W4)	Treatment Visit 5 (W5)	Treatment Visit 6 (W6)	Followup (W6)	Followup (W24)
Informed Consent Form	X								
Inclusion/Exclusion Criteria	X								
Enrollment/Randomization	X								
Demographics	X								
Tobacco Use	X	X	X	X	X	X	X	X	X
Dependence	X							X	X
Cravings	X							X	X
Self-Efficacy	X							X	X
Expectancy/Credibility	X							X	X
Biochemical Validation								X	X
Website Use								X	X
Imagery File Use								X	X
Imagery Vividness								X	X
Consumer Satisfaction								X	X
Treatment Administration Form		X	X	X	X	X	X		
Concomitant Medications	X	X	X	X	X	X	X	X	X
Adverse Events		X	X	X	X	X	X		

6.2 Description of Evaluations

All activities in this study (except for biochemical validation) will occur online or via telephone. The ASHLine 2.0 system and/or REDCap data base will be used to automate, deliver and track all study-related activities. The ASHLine 2.0 system or REDCap will provide the prompts and scripts for ASHLine or study staff to describe the study, screen for eligibility, read the abbreviated informed consent document, obtain and document informed consent, obtain and document the baseline assessment and confirm and document consent. The REDCap system will perform and track randomization, assign participant to study coach, and track all follow-up assessments.

Table 3 above shows the schedule of assessments. Baseline assessments will be administered by ASHLine or study staff via phone as per "Visit 0". All participants will be administered the Treatment Administration Form which will document their participation in the telephone coaching calls during Visits 1 to 6. Use of the websites will be collected automatically. Eight-week and 6-month assessments will be conducted by study staff. Links to online surveys will be sent via email, with reminder calls and emails for up to four weeks. Surveys can be completed online or via phone with study staff. Biochemical validation will be done on all participants who report abstinence on the 6-month assessment and agree to perform a saliva test monitored via video chat by study staff.

6.2.1 Screening Evaluation

Smokers who express interest in our study will eligible if they:

- Have smoked any cigarettes in the past 30 days.
- Are willing to quit smoking within 30 days.
- Want help / information about quitting.
- Are not currently receiving any type of tobacco cessation treatment.
- Are at least 18 years of age.
- Have not enrolled and participated in Quitline services in the past 12 months.
- Have never been diagnosed with schizophrenia by a health care professional.
- Have current valid email address.
- Are willing to receive occasional text messages from us.

Consenting Procedure

The potential participants who are eligible to participate in the study will be read the abbreviated informed consent document verbatim by ASHLine or study staff. The abbreviated and full informed consent documents and the study were reviewed and approved by the University of Arizona IRB prior to recruitment.

Participants are called by study staff to confirm consent and are then emailed the full

informed consent and are told that if after reading the full consent they decide not to participate to inform study staff.

All ASHLine and study staff are trained in Human Subjects Protection and the Responsible Conduct of Research. ASHLine staff are employed by the College of Public Health and regularly participate in recruitment for research studies. The PI will train the ASHLine and study staff in the procedures for the study and ensure that all staff demonstrate understanding before they begin enrolling participants.

All procedures and systems will be thoroughly tested prior to implementation. ASHLine and study staff will be instructed to inform the PI or Dr. Nair if they experience problems using the informed consent document or the ASHLine 2.0 and REDCap systems. If any study procedures affecting participants change, appropriate changes will be made to the informed consent document and resubmitted to the University of Arizona IRB for approval.

ASHLine or study staff will read the abbreviated informed consent document as many times as requested by the caller. The caller will provide verbal consent which will be documented in the ASHLine 2.0 or REDCap system. Study staff will send an email of the full-length informed consent document to each participant for their records.

Screening

All screening will be performed at the time of the first call to the ASHLine (Visit 0). Participants will be eligible if they:

- Have smoked any cigarettes in the past 30 days.
- Are willing to quit smoking within 30 days.
- Want help / information about quitting.
- Are not currently receiving any type of tobacco cessation treatment.
- Are at least 18 years of age.
- Have not enrolled and participated in Quitline services in the past 12 months.
- Have never been diagnosed with schizophrenia by a health care professional.
- Have current valid email address.
- Are willing to receive occasional text messages from us.

At any time, if the caller is not eligible, staff will inform the caller that they are not eligible to participate in the study and will offer standard ASHLine coaching.

6.2.2 Enrollment, Baseline, and/or Randomization

Enrollment

Enrollment in the study will occur upon completion of the informed consent document, the baseline assessment, confirmation of consent and randomization to one

of the study conditions. All screening, consent, assessment and randomization activities will be prompted and tracked by the ASHLine 2.0 system and REDCap data base.

Assessments

All of the measures proposed for use in this study have been used successfully in our previous work. All baseline assessments will be administered by ASHLine or study staff. See Table 4.

Table 4. Measures			
Both Conditions	**T0**	**T1**	**T2**
Demographics	✓		
Tobacco Use	✓	✓	✓
Dependence	✓	✓	✓
Cravings	✓	✓	✓
Self-Efficacy	✓	✓	✓
Expectancy/Credibility	✓	✓	✓
Biochemical Validation			✓
Consumer Satisfaction		✓	
Website Use		Dai	ly
Intervention Only	**Daily**	**T1**	**T2**
Imagery File Use	✓		
Imagery Mastery	✓		

Measures for All Participants

Demographics. At baseline, we will collect gender, age, race/ethnicity, level of education, insurance, prior use of tobacco cessation resources (including quitline and medication) and guided mental imagery experience.

Tobacco use. At baseline, at every session, 8-weeks and 6-months post-enrollment, we will collect tobacco use status using a series of questions that have been standardized and employed in previous studies (Severson, Gordon, et al., 2008, Gordon et al., 2007; Severson et al., 2000), and level of dependence using the the Fagerström Tolerance Nicotine Dependence scale (Fagerstrom & Schneider, 1989). We will conduct biochemical validation using a saliva test kit on all participants who report abstinence at the 6-month assessment and agree to perform a saliva test. Participants meeting these criteria will be mailed a saliva kit in the mail and then join a video chat with staff who will instruct the participant and monitor the collection of saliva and reading of the test strip. Participants will be offered $25 for completing the saliva assessment. As all participants will be current smokers, there is no need for biochemical testing at baseline.

Self-efficacy for quitting. We will measure self-efficacy for quitting smoking with items from the 15-item version of the Condiotte & Lichtenstein Confidence Questionnaire (Condiotte & Lichtenstein, 1981).

Cravings. All participants will be asked to rate their experience with withdrawal symptoms and cravings using items from the 5-item Shiffman rating scale (Shiffman, 2004) at each baseline and each follow-up assessment.

Imagery expectancies and credibility. We will include items adapted from the Borokov and Nau (1972) Treatment Credibility Scale, and used in our on-going guided imagery mobile app study, to measure expectancies and perceived credibility of guided imagery for smoking cessation.

Consumer satisfaction measure. At both follow-ups, participants will complete a consumer satisfaction survey that we have used in our previous research (Gordon et al., 2013; Severson, Gordon, et al., 2008) consisting of 8 items (using a 5-point Likert scale), measuring overall satisfaction with the program, perceived usefulness and relevance of the information, likeability, level of interest, ease of use, and whether they

Commented [PG-(2]: Note that the checkmark for T1 has been removed.

would recommend the program to others.
Website use. We collect usage data and can analyze use of all components of the site. Data most likely related to outcome will include, but not be limited to: (a) the length of time participants interact with the site; (b) the number of pages they visit within the site, and (c) the number of links they click on while using the site.
System usability. At both follow-up assessments, we will use Tullis and Stetson's (2008) 10-item adaptation of Brooke's widely used System Usability Scale (Brooke, 1996) to rate the usability of our website.

Measures for Only Imagery Intervention Condition Participants
Imagery files use. We will collect number of times imagery files were listened to , and if the participant modified or created their own file.
Imagery mastery. Ratings of imagery vividness and controllability will be measured weekly via the coach in order to verify compliance with the protocol (Marks, 1973).

Randomization

Eligible participants who are consented and complete the baseline assessment will be automatically randomized immediately by the REDCap system using a randomization algorithm. The assignment will be documented and tracked in the REDCap system, and the participant will be assigned to a study coach.

6.2.3 Blinding

Due to the nature of the study with two different behavioral interventions it would not be possible to blind participants or study coaches.

6.2.4 Follow-up Visits

All measures by follow-up are listed in Table 3. There will be two follow-up assessments: 1) 8 weeks post-enrollment; and 2) 6 months post-enrollment. All items will be asked at each follow-up assessment of every participant. In addition, biochemical validation of self-reported tobacco use will be conducted on all participants who report abstinence at the 6-month assessment and agree to perform a saliva test. Participants meeting these criteria will be mailed a saliva kit in the mail and then join a video chat with staff who will instruct the participant and monitor the collection of saliva and reading of the test strip. Participants will be offered $25 for each sample.

6.2.5 Completion/Final Evaluation

The items assessed at the final follow-up assessment are listed in Table 3. If a participant does not complete a follow-up assessment within 4 weeks of their initial reminder, they will be considered lost to follow up. However, their data will be retained and will be used in intent-to-treat analyses. We will make every effort to track and determine reasons for participant dropout including the unlikely possibility of an adverse event related to participation in this study.

7. SAFETY ASSESSMENTS

This is an extremely low risk study. However, participant safety will be monitored throughout the study by project staff. During Visits 1-6, study coaches will monitor participants withdrawal symptoms (if the participant quits tobacco), and provide assistance or referral to the patient's primary care physician.

7.1 Specification of Safety Parameters

The primary safety risk is the loss of privacy. However, all data will be stored on the secured ASHLine 2.0 and REDCap systems. We will be collecting usage data on the website, and participants could be concerned about the related lack of privacy.

If the participant quits smoking, s/he could experience withdrawal symptoms from nicotine cravings such as hunger, anxiety, restlessness, or sleep disturbance. Individuals who quit their addiction to tobacco products commonly experience these symptoms. Project coaches will be prepared to assist participants in handling these symptoms.

If a participant experiences adverse events as a result of using NRT, the coaches will be prepared to assist participants in handling these symptoms. In the event of an SAE, participants will be instructed to call 911 or schedule an appointment with their primary care provider. All AEs will be documented by project staff. Serious AEs will be reported to the University of Arizona IRB and the NCCIH Program Officer.

7.2 Methods and Timing for Assessing, Recording, and Analyzing Safety Parameters

Methods to assess, record, and analyze safety parameters will be ongoing throughout the study by study staff. The PI will be responsible for ongoing evaluation of the procedures used by the study coaches.

7.3 Adverse Events and Serious Adverse Events

An **adverse event (AE)** is generally defined as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during the study, having been absent at baseline, or if present at baseline, appears to worsen. Adverse events are to be recorded regardless of their relationship to the study intervention.

A **serious adverse event (SAE)** is generally defined as any untoward medical occurrence that results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly.

It is possible that some questions about personal behaviors (e.g. smoking) might cause emotional discomfort to participants. Care will be taken to ensure that all participants understand that they may choose not to answer any question. Quitting smoking may result in physical symptoms (e.g., sleep disturbance) and changes in mood (e.g., irritability).

Participants who use NRT may experience adverse events. Most adverse events are rare. The most common adverse events are skin irritation and itching (nicotine patch), and mouth/throat soreness or ulcers (nicotine lozenges), vivid dreams and insomnia. Rarer, more serious adverse events include dizziness, headache, rapid heartbeat, and nausea. Participants will be screened for contraindications for use of NRT (e.g., recent heart attack, uncontrolled high blood pressure). Participants using NRT will be queried about AEs at each phone contact by coaches. Participants reporting AEs will be advised how to minimize side effects. Participants reporting SAEs will be advised to stop using the NRT and call 911 or their primary care physician. All participants will be given a study telephone number to contact the study staff if they have any concerns about an untoward medical event.

SSL and TLS security protocols will be used to protect all communications between the website and/or mobile devices and the project database. These protocols use certificate-based authentication to ensure that the user is communicating with the correct server. In addition, the protocols validate data and use public-key cryptography to guard against eavesdropping. Users will also be required to be authenticated by logging into the application with both their user name and password. This authentication data, as well as all other communications, will be transmitted securely using the SSL or TLS protocols.

7.4 Reporting Procedures

It is highly unlikely that any of the study procedures will cause an AE or SAE. Should an AE or SAE occur, ASHLine personnel and research study staff are trained to immediately report AEs connected to implementation of the intervention to Dr. Nair (co-I) or Dr. Gordon (PI). Dr. Nair will report AEs to Dr. Gordon who will keep a log of AEs and SAEs. In the event of an SAE, we will file a report with the University of Arizona (UA) IRB. As part of this process the UA IRB will determine if the event is directly related to project procedures, so that It can be determined if project procedures should be modified.

7.5 Followup for Adverse Events

Dr. Gordon will monitor all AEs until resolved or considered stable up to the end of the study. Information about all AEs and SAEs will be provided in annual progress reports to UA IRB and NCI.

7.6 Safety Monitoring

The NCCIH requires that all Human Subjects research studies undergo independent monitoring, and NCCIH Program Officials will provide specific guidelines to the PI for the study.

Once approved by the UA IRB, the following aspects of the study and study conduct are monitored: all procedures to ensure conformity with the approved study protocol; unforeseen circumstance that might arise and affect participant safety; all reports of serious adverse events and defined in 38 CFR 46 (death, new or prolonged hospitalization, persistent or significant disability or incapacity; congenital anomaly

or birth defect); Other significant adverse events that lead to participant dropout, participant termination by the principal investigators, or termination of participation in the intervention.

8. INTERVENTION DISCONTINUATION

Participation in the study is voluntary. Participants may withdraw from the study at any time without penalty. Participants will continue to be followed with their permission if study intervention is discontinued (i.e., if they do not participate in all the coaching calls or use the website). Participants who wish to withdraw from all study activity will not be assessed at follow-up.

Possible reasons for participant withdrawal may include, but are not limited to, dissatisfaction with the intervention or study coaches/staff, lack of desire to quit smoking, or lack of time. No modifications to the study protocol will be permitted in terms of time spent with coaches, and the use of the study websites and audio files will be monitored.

Participants will be informed that: "You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with the University of Arizona or the Arizona Smokers Help Line (ASHLine). If you are a student or employee at the University of Arizona, your decision will not affect your grades or employment status. If you are a patient at Banner University Medical Center, your decision will not affect your healthcare."

9. STATISTICAL CONSIDERATIONS

9.1 General Design Issues

This is a feasibility study using a two arm parallel randomized controlled design. We chose this design in order to run the definitive trial in miniature, so that we can reliably address the aim of our feasibility study, which is to give assurance that we can do the future study. Expanding upon this, we aim to answer: will we be able to recruit, randomize and retain participants?; are the trial procedures working?; are we using the correct measures?; what are the relevant variance components in order to design the future study; and is there any preliminary evidence that the intervention is effective?

We have defined feasibility outcomes as % completing the 6-session intervention program; % listening to the guided imagery audio files at least 5 times per week, % using the other website functions at least one time.

Our primary efficacy outcome is tobacco use. We hypothesize that the participants in the intervention group will have lower rates of tobacco use than in the control arm. Our secondary outcomes are dependence, cravings and self-efficacy. We hypothesize that the intervention group will have lower scores for dependence, cravings and higher score for self-efficacy, in comparison to the control arm.

Tobacco use. At baseline, and 8-weeks and 6-months post-enrollment follow-ups, we will collect tobacco use status using a series of questions that have been standardized

and employed in previous studies (Severson, Gordon, et al., 2008, Gordon et al., 2007; Severson et al., 2000), and level of dependence using the the Fagerström Tolerance Nicotine Dependence scale (Fagerstrom & Schneider, 1989). At each visit, we will ask for participants' current tobacco use status. We will conduct biochemical validation using saliva test kit on all participants who report abstinence at the 6-month assessment and agree to perform a saliva test. Participants meeting these criteria will be mailed a saliva kit in the mail and then join a video chat with staff who will instruct the participant and monitor the collection of saliva and reading of the test strip. Participants will be offered $25 for each sample.

Self-efficacy for quitting. We will measure self-efficacy for quitting smoking with items from the 15-item version of the Condiotte & Lichtenstein Confidence Questionnaire (Condiotte & Lichtenstein, 1981).

Cravings. All participants will be asked to rate their experience with withdrawal symptoms and cravings using items from the 5-item Shiffman rating scale (Shiffman, 2010) at baseline and each follow-up assessment.

9.2 Sample Size and Randomization

9.2.1 Sample size

Because this is a feasibility study, our primary objective is to assess feasibility. A minimum sample size of 50 participants per group will yield a margin of error (95% confidence interval half-width) of no more than 1% for all binary outcomes, such as feasibility outcomes (% completing the 6-session intervention program; % listening to the guided imagery audio files at least 5 times per week, % using the other website functions at least one time), smoking prevalence, and dropout rates. This sample size is large enough to reasonably estimate, in conjunction with sensitivity analysis, relevant variance components, recruitment, and dropout rates for use in a future definitive trial (Julious, 2005). This sample size will also help us to assess the potential efficacy of the intervention, by giving 80% power to detect large effects for continuous outcomes (standard effect size 0.7) assuming a type I error rate of 0.05, a dropout rate of 20%, and a two sample t-test. We will use clinically meaningful effect sizes (not pilot effect sizes) to estimate the future R01 sample size.

9.2.2 Treatment Assignment Procedures

Randomization will be performed by REDCap using a randomization table created by a biostatistician who will have no contact with the participants. The allocation sequence will be automated, unpredictable, and concealed from study staff.

9.3 Definition of Populations

We will be using maximum likelihood based mixed models for all outcomes measured over time, using all available data. Mixed models are consistent with an intention to treat analysis due to their implicit imputation of missing data.

(Molenberghs et al., 2004). The per protocol population is defined as users who complete the 6-session intervention session.

9.4 Interim Analyses and Stopping Rules

No interim analyses or stopping rules are planned, as there are no potential safety issues, and because this is a feasibility study.

9.5 Outcomes

9.5.1 Primary Outcome

The primary efficacy outcome is tobacco cessation at 6 months.

The primary feasibility outcomes will be 50% of participants completing the 6-session intervention program; 50% of IIC participants listening to the guided imagery audio files at least 5 times per week, and 50% of participants using the website at least one time; and 75% of participants completed both follow-up assessments.

9.5.2 Secondary Outcomes

Secondary outcomes include number of quit attempts, number of cigarettes smoked, tobacco dependence, self-efficacy for quitting, and cravings. We will also explore the demographics of participants in the study compared to those of ASHLine callers in general.

9.5.3 Process and Exploratory Outcomes (Intervention Condition Participants)

All Participants

Website use. We collect usage data and can analyze use of all components of the site. Data most likely related to outcome will include, but not be limited to: (a) the length of time participants interact with the site; (b) the number of pages they visit within the site, and (c) the number of links they click on while using the site.

System usability. At both follow-up assessments, we will use Tullis and Stetson's (2008) 10-item adaptation of Brooke's widely used System Usability Scale (Brooke, 1996) to rate the usability of our website.

Imagery files use. These data will be collected automatically by the website. We will collect number of times and which imagery files were listened to completely, and if the participant created their own file.

Website use. We collect usage data and can analyze use of all components of the site. Data most likely related to outcome will include, but not be limited to: (a) the length of time participants interact with the site; (b) the number of pages they visit within the site, and (c) the number of links they click on while using

the site.

Imagery Intervention Condition Participants Only

Imagery files use. We will collect number of times and which imagery files were listened to completely, and if the participant modified and/or created their own file.

Imagery mastery. Ratings of imagery vividness and controllability will be measured weekly via the website in order to verify compliance with the protocol (Marks, 1973).

9.6 Data Analyses

Feasibility outcomes, including recruitment and dropout, will be described using frequencies and percentages, and 95% confidence intervals. Questionnaires will be scored according to developer instructions. Tobacco use outcome measures will use appropriate mixed models (linear for continuous outcomes and generalized linear with a logistic link for binary) using time categorically. Comparisons between the intervention and control group at 8 weeks and 6 months will be carried out using contrasts within these models. Mixed models are robust to missing outcome data (including dropout) and model misspecification, and are consistent with an intention to treat analysis (Bell and Fairclough, 2014; Mallinckrodt et al., 2004; Molenberghs et al., 2004). Mixed models will also be used to model self-efficacy, cravings, and consumer satisfaction, and to estimate intervention effects. Outcomes measured in the intervention group (e.g., imagery file use, website use), appropriate descriptive statistics will be computed, including means, standard deviations, ranges and frequencies/proportions. Linear regression and chi-square tests of trend will be used to assess the stability of the system usability and website/file use over time. We are underpowered to detect any subgroup analyses, but will conduct exploratory analyses in anticipation of the larger trial by including appropriate interactions within the mixed models. We will compare guided imagery use with tobacco outcome measures using linear regression in order to investigate a “dose-response” effect of the intervention. Demographics will be described with means, standard deviations, ranges and frequencies/ proportions and will be explored as correlates for successful tobacco outcomes.

10. DATA COLLECTION AND QUALITY ASSURANCE

10.1 Data Collection Forms

All baseline data collection will take place over the telephone by ASHLine staff who will be blinded to the participants’ allocation to the intervention or control groups or by study staff. All data will be collected within the ASHLine 2.0 system and/or the REDCap system, which follows HIPAA standards for privacy and security. The study website will be integrated with the ASHLine 2.0 system and will also be HIPAA compliant. Follow-up assessments will be collected online and stored via REDCap on our secure servers. Data from follow-up assessments conducted on the

phone by study staff will be entered directly into the REDCap system on our secure server.

10.2 Data Management

Data and Safety Monitoring Plan
Based upon the NIH definitions of clinical trials, this is not a Phase III clinical trial, therefore, no data and safety monitoring board is required. Only a data and safety monitoring plan is required.

Entities conducting monitoring of the study:
The Human Subjects Committee (institutional Review Board [IRB]) at the University of Arizona (UA) will review and provide oversight for the proposed research.

What is monitored:
Once approved by the UA IRB, the following aspects of the study and study conduct are monitored: all procedures to ensure conformity with the approved study protocol; unforeseen circumstance that might arise and affect participant safety; all reports of serious adverse events and defined in 38 CFR 46 (death, new or prolonged hospitalization, persistent or significant disability or incapacity; congenital anomaly or birth defect); Other significant adverse events that lead to participant dropout, participant termination by the principal investigators, or termination of participation in the intervention.

Data Monitoring
Data handling and quality
Assessments will be administered to study participants as described in E1.
All aspects of data collection and data storage will be carefully monitored to ensure rapid detection or errors, inconsistencies or other problems. Study personnel involved in data collection will follow a strict written protocol that describes study measures for protecting data privacy, clearly explains to study participant that she has the right to refuse to participate or refuse to answer any individual question that she wishes to not answer, and emphasizes reporting as accurately and truthfully as possible. The Principal Investigator and co-Investigators are experienced in training study staff in handling sensitive and confidential data, and in the storage and processing of such data.

No survey data resides on the website. It is used solely as a collection and submission device through a broadband internet connection to the University of Arizona Computer Science data center. The transmission of survey data between the web and database server where it is stored, is encrypted via a 128-bit SSL certificate.

Physical access to the data center is restricted to authorized personnel. All servers are housed in a locked rack and secured from the Internet and other university departments through the use of a hardware-based firewall and virtual LAN. A host-based firewall is installed and configured on each server as a secondary level of defense from outside intrusion. All servers and computer systems on the network are

configured with domain-managed accounts and password controls with audit logs. Access to server resources such as project data are restricted to authorized users only as approved by the project's Principal Investigator.

All servers and data are backed up daily to disc and tape with secure offsite storage at the University of Arizona's Computer Center.

Safety monitoring plan

Population: The proposed study involves smokers who want to quit tobacco. Since the study intervention is empirically based, and all participants are interested in quitting, it is unlikely that completing assessments or interacting with the website will cause an "adverse event" among the study populations. However, quitting smoking can cause discomfort, with physical symptoms and changes in mood.

Adverse events: We will use the definition of adverse events in the NIH OHRP document "Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events."

Adverse event (AE): Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research

Serious adverse event: Any adverse event that: (1) results in death; (2) is life-threatening (places the subject at immediate risk of death from the event as it occurred); (3) results in inpatient hospitalization or prolongation of existing hospitalization;(4) results in a persistent or significant disability/incapacity; (5) results in a congenital anomaly/birth defect; or (6) based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

It is possible that some questions about personal behaviors (e.g. smoking) might cause emotional discomfort to participants. Care will be taken to ensure that all participants understand that they may choose not to answer any question. Quitting smoking may result in physical symptoms (e.g., sleep disturbance) and changes in mood (e.g., irritability). Participants will be queried about AEs at each phone contact by coaches, and participants will be given a study telephone number to contact the study staff if they have any concerns about an untoward medical event.

Reporting: It is highly unlikely that any of the study procedures will cause an AE or SAE. Should an AE or SAE occur, ASHLine personnel and research study staff are trained to immediately report AEs connected to implementation of the intervention to Dr. Nair (co-I) or Dr. Gordon (PI) who will keep a log of AEs and SAEs. In the event of an SAE, we will file a report with the University of Arizona (UA) IRB. As part of this process the UA IRB will determine if the event is directly related to project

procedures, so that It can be determined if project procedures should be modified. Information about all AEs and SAEs will be provided in annual progress reports to UA IRB and NCI.

10.3 Quality Assurance

10.3.1 Training

All ASHLine and study staff will complete CITI training in the protection of human subjects and responsible conduct of research prior to engaging in any study-related activities. ASHLine personnel who will describe the study, screen, and enroll participants will be trained by Dr. Gordon and Dr. Nair, who will ensure that these staff demonstrate understanding and proficiency in all tasks prior to implementation. Project coaches will be trained by Drs. Gordon and Giacobbi on the use and administration of either the guided imagery intervention or the attention-control protocol. Dr. Giacobbi has previously developed and applied theory-based principles for training individuals to use and train others to administer guided imagery for behavior change. This included readings about the use of guided imagery and role playing exercise. These training sessions will occur in person and over ongoing/weekly telephone conversations prior to the implementation of the feasibility trial. Similar training (e.g., method, duration, etc.) will occur for coaches in both conditions.

10.3.2 Quality Control Committee

There will be no quality control committee. However, randomly selected telephone conversations will be audio-recorded and coaches in both conditions will be given immediate corrective feedback about the implementation of the protocols.

10.3.3 Metrics

A rating scale similar to the one shown below will be used to assess coaches' protocol adherence (1 = poor compliance; 5 = excellent). A rating system similar to the one proposed has been used by Dr. Giacobbi in previous studies and by Dr. Nair to monitor adherence to ASHLine protocols.

Scoring Criteria	**1**	**2**	**3**	**4**	**5**
Meeting day/time (record keeping and reliability)					
Follow protocol (followed reminder list)					
Application of guided imagery					
Use of open-ended questions that stimulate vivid images					

10.3.4 Protocol Deviations

When deviations of the protocol are observed, these deviations will be documented in the REDCap system, and coaches will be given immediate corrective feedback by Drs. Gordon, Nair or Giacobbi. These coaches will be monitored until adherence to the protocol is achieved, or will be replaced with coaches who can achieve adherence.

10.3.5 Monitoring

We will perform ongoing oversight of data capture by reviewing the project databases. All data will be collected and housed at the University of Arizona. Dr. Gordon will be responsible for ongoing oversight of project databases.

11. PARTICIPANT RIGHTS AND CONFIDENTIALITY

11.1 Institutional Review Board (IRB) Review

This protocol and the informed consent documents (See Appendix for the Informed Consent Forms) and any subsequent modifications will be reviewed and approved by the University of Arizona IRB, which will be the IRB of record for this study. The consent forms will be separate from the protocol document.

11.2 Informed Consent Forms

All participants must be able to speak English and demonstrate understanding of the consent process. All participants will provide verbal consent on the telephone. The consent form will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation. A copy will be mailed to each participant and this fact will be documented in the participant's record in the ASHLine 2.0 and/or REDCap system.

11.3 Participant Confidentiality

Efforts will be made to keep study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, all study records may be reviewed by the following groups:

- Office for Human Research Protections or other federal, state, or international regulatory agencies
- The University of Arizona Institutional Review Board
- The sponsor supporting the study, their agents or study monitor.
- If the results of this study are published, your identity will remain confidential.

11.4 Study Discontinuation

The study may be discontinued at any time by the IRB, the NCCIH, the OHRP, the FDA, or other government agencies as part of their duties to ensure that research participants are protected.

12. COMMITTEES

A community advisory board will be formed to guide our overall efforts, help us recruit racially and ethnically diverse participants, and tailor the intervention.

13. PUBLICATION OF RESEARCH FINDINGS

Efforts will be made to present our findings to all stakeholders (e.g., ASHLine, community advisory board, etc.), academic conferences, and publish the results in high impact journal outlets.

14. REFERENCES

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15. SUPPLEMENTS/APPENDICES

See Appendices for the Informed Consent Forms, measures, and other supplemental documents.