PROTOCOL AND STATISTICAL PLAN

Mindfulness Mobile App to Reduce Adolescent Substance Use (The Qlarity Study)

Grant Number/Protocol ID: DA043288-02
Clinical Trials.gov ID: NCT04027075
Federal Award Date: 5/17/2019

This Phase II SBIR will be conducted in two stages: 1) Product development and usability testing, and 2) product evaluation testing. Stage 1 and Stage 2 are outlined below and are expected to take approximately 12 months each.

Stage 1: Product development

The Qlarity app is proposed to include 12 modules focused on mindfulness techniques for substance use cessation, each of which will involve 2 components: a teaching component and a practice component. During Phase I, we developed the initial 4 modules of the Qlarity app in order to examine the feasibility and usability of the app, as well as the likeability and satisfaction among our target audience. The initial 4 modules developed during Phase I are as follows: 1) Introduction to Mindfulness: Understanding its Application to Substance Use and Cessation, 2) Focusing on Current Mind and Body States: Becoming Aware of Internal States and their Connection to Substance Use, 3) Being In the Moment: Observing without Judging, and 4) Making Mindful Decisions About Substance Use. We propose to use feedback from Phase I to inform the development of the full 24-component a; (12 teaching + 12 practice components) that will include the following additional concepts aimed at reducing and eliminating substance use: 5) Understanding and Taking Charge of Your Emotions: Using Mindfulness Techniques to Manage Emotional States, 6) Identifying Personal and Contextual Triggers for Use, 7) Managing High-Stress Situations: Advanced Mindfulness Skills, 8) Mindful Decision-making and Refusal Skills, 9) Establishing a Support System, 10) Effectively Utilizing Existing Supports, 11) Planning for the Future: Maintaining Sobriety, and 12) Emergency Planning: Getting Back on Track When You Slip-up.

We will use feedback from the Phase I evaluation of the initial four modules to inform and guide the development of the full app. Feedback on usability and attractiveness will be used to modify the initial modules and to provide consistency in the development of the modules. Based on this information, we will develop prototype versions of each module using Marvel, a design and rapid prototype development tool that yields functional mockups for users to interact with before any programming takes place. During an iterative process we will refine the mockups, present them to five test users, solicit their feedback, and continue to modify and refine the mockups until we arrive at an acceptable design and feature set. We will recruit adolescent test users who report current substance use from the community for this iterative process.

Next, we will finalize and create all the media assets for the app, including text and graphics, images, and narration or other audio elements; build all program screens and user controls, and determine scoring algorithms and programming logic for knowledge checks and quizzes. We will incorporate a simple user registration component to allow for tracking of app usage while also ensuring security of user-collected data.

Stage 2: Product evaluation

We will conduct an evaluation of the Qlarity app with 380 high-risk adolescents who are involved in the juvenile justice system. Feasibility, usability, participant satisfaction, and intervention outcomes of substance use will be evaluated in an efficacy trial. Data on: 1) frequency and duration of app use, 2) number of modules completed, 3) changes in attitudes, emotions and behaviors, and 4) type and frequency of substance use will be examined. Participants will be compensated using gift cards to Amazon in the following increments: $20 for each of the baseline, 4 week and 3-month assessments, and $50 bonus for completion off all three assessments. Participants in the focus groups and usability testing will receive a $30 gift card for their time and effort.

Study Design: Our evaluation of the program will be conducted with 380 adolescents ages 13- 18 who are referred from the Oregon Department of Youth Services (DYS) in Lane and Multnomah Counties, Oregon. Adolescents will be randomly and equally assigned to one of two conditions: 1) Qlarity, or 2) an active comparison condition that is standard treatment through the DYS (i.e., drug court, group therapy, and case management). All participants will be instructed to attempt to reduce substance use with a target quit date of 1 month after program initiation (day 28). Self-reported 7-day and 30-day point prevalence abstinence for all substances will be measured 1 and 3 months after treatment initiation. In addition, we will collect biochemical verification of self-reported substance use; urinary drug tests will be conducted at the baseline, 1- and 3-month follow ups and will follow the same UA drug testing protocol that we have found to be successful in our current NIH funded study with adolescents in the juvenile justice system.

Participants: Participants will include both male and female high risk adolescents recruited from the Department of Youth Services (DYS) in Lane and Multnomah Counties, Oregon. We have a long history of successful collaborations with the DYS and have received their support for the current proposal. Inclusion criteria will be as follows: 1) ages 13-18, 2) involvement with the juvenile justice system, 3) documented substance use, 4) English-speaking, and 5) living in the community (e.g., biological/adoptive/foster parents).

Focus Groups and Usability Testing: Twenty high-risk adolescents will be recruited to participate as test users in the development phase to give us initial reactions to mockup of modules, and a subgroup of 10 of these participants will be recruited to participate in preliminary usability testing of the modules. Feedback from usability testing will be used to inform adaptations to the app. The prototype app will then be evaluated in an efficacy trial with 380 additional high-risk adolescents. The primary outcomes of the evaluation-testing phase will be changes in adolescent substance use attitudes and behaviors and emotion regulation measured at three time points: baseline, 4 weeks post- baseline (end of treatment), and three months post-baseline. The proposed efficacy trial will evaluate the extent that the Qlarity app influences positive behavior change and will provide power estimates for later larger scale evaluation.

Efficacy Trial: Based on our power calculations, we will recruit 380 adolescents who are involved in the juvenile justice system. We have a long history of cooperation with the DYS and have well-established recruitment procedures. Eligible adolescents and their consenting parents will be recruited on a continual basis and will be included in the study for 3 months post-baseline. The participants will be randomly and equally assigned to the Qlarity condition (n = 190) or the DC standard treatment condition (n = 190) following adolescent assent and parent consent. Given that all youth will be involved in the juvenile justice system, we will assess all services offered and accessed by youth in both conditions.

Based on our prior experience, we expect many of the youth to be under orders to be participating in urine screening or other intervention services through DYS. Data from our current and prior studies with this population suggest that despite receiving random urine screens as part of their probationary status, 90% of youth are involved in ongoing alcohol, tobacco or other drug use (79% alcohol; 68% tobacco; 81% marijuana, and 53% other drug; 90% positive for one or more substance) at the time of referral. We will track additional services, including mandated urine screens, via official DYS reports and using a services utilization measure at each follow-up time point.

Overview of the Proposed Intervention Conditions

We propose to randomize youth into one of two conditions, outlined below.

Qlarity. Subjects randomized to Qlarity will be provided in-person assistance in loading the Qlarity app onto their phone immediately following their baseline interview and assessment. Once the app is loaded onto their phone, participants will generate a username and password. The proposed modules will each include a teaching and a practice component that uses mindfulness techniques to reduce or avoid substance use. Modules will be “unlocked” in ascending order as participants move through the program (i.e., module 2 will be “unlocked” after completion of module 1, etc.).

Drug Court, Group Therapy and Case Management (DC). The DC youth will receive the usual services provided by the DYS for youth who present with drug and alcohol use, which includes involvement in drug court, and case management services for the youth and their parents that span the duration of the youth’s probation or formal accountability contract. The drug court and case management services are provided by probation officers through the DYS. The DYS will manage each case and will make all decisions on referrals to community resources, including individual therapy, family therapy, mandated urine screens, and/or inpatient or outpatient substance use treatment that might occur in addition to the typical youth skill building groups and case management services. None of the usual services that youth in the respective study conditions receive will be affected by their participation in the study. We will track the youths’ and parents’ use of services as part of the interviews with a service utilization measure and official DYS reports of urine screens at each assessment. With these data, we will examine the type and length of treatment received for youth in both conditions, as well as the timing and outcome of urine screens over the course of the study. This services utilization measure has been used in previous work and has been useful for examining treatment impact.

Data Collection Procedures

Overview and timeline for the proposed data collection: In the proposed study, a total of at least 380 youth will be recruited and baseline assessed for the study. We anticipate that approximately 10% of these will fail to complete the study, resulting in a sample of at least 342 youth with complete data and an intent-to-treat analysis strategy which will include all 380 youth. We will conduct baseline assessments and follow-up assessments at treatment completion (1 month), and at 3 month post-baseline.

Assessments: The *baseline assessment* primarily measures youth risk factors, as well as past and current substance use, and will consist of an in-person interview including questionnaires with the youth.

The *treatment completion (1-month), and 3-month assessments* are aimed at assessing short and longer term outcomes and will consist of two components: (a) an in-person interview and questionnaires with the youth, and (b) usability and satisfaction ratings for the Qlarity app. Because every participant has unique needs, we have standardized guidelines that allow for minor modifications to our procedures when needed. For example, staff will read aloud questionnaires for participants who are nonreaders, and computer-assisted questionnaires will be available in hardcopy format. We will travel to participant residences or other locations to conduct the interviews as needed.

Measures: The following measures will be used to examine baseline demographic and pre- and post-changes in mindfulness skills, emotion regulation, and substance use: 1) Demographics, 2) Alcohol and Drug Use Survey, 3) Cigarette Use, 4) Adolescent Attitudes Questionnaire, 5) Emotion Regulation Scale, 6) Five Facet Mindfulness Questionnaire, 7) Youth Substance Use Interview (including Services Utilization), and 8) Qlarity usability and satisfaction rating. The Alcohol and Drug Use Survey is a 48-item scale that combines the Michigan Alcohol Screening Test (MAST) and the Drug Abuse Screening Test (DAST) and the Self-Efficacy for Limiting Substance Use. These scales are widely used as measures to assess the level and frequency of alcohol and drug use, use of mindfulness skills, as well as the ability to limit substance use, and have been shown to have good psychometric properties. In addition, urinary drug tests will be conducted at the baseline, 1- and 3-month follow ups. UA results will be photocopied after completion, and the UA cups will be discarded immediately; no identifying information will be recorded on the UA cups. We will use the same UA drug testing procedure that we have found to be successful in our current NIH funded study with adolescents in the juvenile justice system. All data will immediately be moved to a secure, locked location within ORI/Influents Innovations accessible only to the PI and research staff. The Services Utilization Survey is an interviewer-administered instrument that collects information about a respondent's use of a wide range of services such as in- and out-patient medical care (hospital, clinic, or office based), mental health treatment, drug and alcohol abuse treatment, and health-related groups (e.g., Narcotics or Alcoholics Anonymous, or physical health groups). For each type of service accessed, there are questions regarding frequency, reason for the service (e.g., physical, mental health, substance-use related), insurance coverage and out-of-pocket expenses. The Five Facet Mindfulness Questionnaire is a 36-item self-reported questionnaire that queries aspects of mindfulness such as non-judgment. The Adolescent Attitudes Questionnaire is a measure of attitudes and beliefs regarding drug and alcohol that was adapted from an interview developed to test 12 mediators of drug use in adolescents. For this study, we will use the normative beliefs, lifestyle incongruence, beliefs about consequences, and commitment scales. The Emotion Regulation Scale is a 36-item self-report questionnaire designed to assess multiple aspects of emotion dysregulation. Program navigation and usability will be assessed for all participants and will include reports of: 1) ease of use, 2) perceived benefits of using the app, 3) likeability, and

Table 1. *Measures*

	Assessments		
Measure	**Baseline**	**1 Month**	**3 Month**
Adolescent Attitudes Questionnaire	O	O	O
Alcohol and Drug Use Survey (MAST/DAST)	O	O	O
Qlarity Usability and Satisfaction		O	O
Cigarette Use	O	O	O
Demographics	O		
Emotion Regulation Scale	O	O	O
Five Facet Mindfulness	O	O	O
Urine Drug Screens	O	O	O
Youth Substance Use Interview (Services Utilization)	O	O	O

4) suggestions for product development and modifications. Participants will provide ratings on product satisfaction and usability on a 7-point Likert Scale. Qualitative data gathered from the focus groups will be recorded and evaluated with the goal of identifying challenges to using the app, product satisfaction, and suggested product modifications. In addition to qualitative data gathered during the pilot evaluation study, login tracking information from the app will be used to assess each participant's: 1) frequency and duration of app use and 2) number of modules completed. These data will be used to evaluate treatment engagement and adherence.

Statistical design and power overview: This project will test the efficacy of the Qlarity app in Year 2 with a randomized trial that nests multiple assessments nested with 380 youth within each of two conditions. Half of the participants will receive the Qlarity app intervention and half will maintain business-as-usual. We hypothesize that Qlarity app will increase youth's emotional regulation, mindfulness and self-efficacy and decrease alcohol, tobacco, and other drug use. Within this study design, we will test for main effects, moderation, mediation, and acceptability of the Qlarity app intervention and expect to detect effect sizes of 0.25 standard deviations. Program feasibility will be demonstrated via significant pre-post differences, a high and consistent level of app use, and a high degree of youth satisfaction ratings. See Human Subjects Statistical Design and Power section for complete details.

Feasibility benchmarks: Program feasibility will be demonstrated by the achievement of the following benchmarks: (a) significant pre-post increases (e.g., Cohen's d > .35) in emotional regulation, mindfulness, and self-efficacy, (b) significantly greater decreases in alcohol, tobacco, and other drug use for Qlarity participants; (c) a high consistent level of app usage (e.g., over 70% of users used the app at least 12 times over the 12 weeks); and (d) a high degree of youth satisfaction and ratings of app acceptability and usability (mean ratings > 4.0 on the 5-point scale). Benchmarks are based on meta-analysis quantitative methods that recommend effect sizes of at least d >.25 to demonstrate educationally meaningful change; a desire to show at least an average of weekly app use by a majority of participants; and a level of participant satisfaction that meets or exceeds that of Phase I.

Data Analysis

Preliminary analyses. Prior to analysis, all variables will be checked for out-of-range values and inter- and intra-measure consistency; frequency distributions and plots will be examined for unusual data distributions or data points. Any necessary data transformations will be employed. Initial analyses will evaluate the baseline equivalence of conditions and examine attrition effects. Baseline equivalence will consist of chi-square and grouped t-tests analyses comparing intervention condition on demographic characteristics and all baseline measures. Results of the baseline equivalency will be a test of the effectiveness of randomization. Any group differences will be treated as covariates in subsequent main-effect, moderation, and mediation analyses. Attrition analyses will consist of chi-square and grouped t-tests comparing proportion of participants in each condition who fail to complete follow-up assessments (i.e., drop-outs vs. completers); the independent variables will include intervention condition, demographic characteristics, and baseline measures. Results of main effects concerning attrition will provide information about the external validity of the study, and interaction effects will provide information about potential confounding.

Main-effects analyses. Tests of the general effectiveness of the Qlarity app within this three-panel (pretest, 1- month, and 3-month follow-up) randomized trial requires an analysis that accounts for the dependence of multiple assessments nested within participants that were assigned to conditions. Thus, we will test most of our research hypotheses with random effects growth models within the hierarchical and structural equation modeling (SEM) frameworks with individual variability in change in study outcomes from pretest to 3-months nested within individuals. Following Singer and Willet when constructing the longitudinal model, we will (a) examine empirical growth plots; (b) fit an unconditional means model; (c) fit an unconditional linear growth model; (d) fit unconditional non-linear models; and (e) compare models of longitudinal change from the previous two steps using the Akaike Information Criterion. Individual variability change in the outcomes from baseline to the 3-month follow-up assessment will be modeled as a function of intervention condition. Intervention condition by time interactions will test whether groups differ on individual trajectories over the course of the study period. We will also use logistic regression models reporting odds ratios (OR) to test for differential rates of abstinence at the 3-month follow-up assessments with intervention condition a two-level predictor.

Moderator effects. Moderating effects of demographics (gender and minority status) and number of baseline offenses will be explored by adding the moderator to the random effects growth models described above. The multiplicative interaction term between the participant level moderators constitute a three-way cross-level interaction with time in the growth models and addresses whether the level of the baseline moderator impacted the magnitude of intervention condition on change in the outcome. All significant cross-level interactions will be probed by computing sample-estimated intercepts and slopes of the trajectories of the outcomes at conditional levels of the moderator, separately, within the Qlarity and usual care group (i.e., simple trajectories) using methods described by Curran (Curran, Bauer et al. 2006).

Mediation effects. Growth-curve models implemented in an SEM framework will be used to explore whether observed condition effects on tobacco, alcohol, and drug use are mediated by adolescent attitudes and mindfulness. Following Preacher et al., models will be constructed by individually fitting growth models for mediators and outcomes using the growth curve model-building sequence described above to develop the best longitudinal change model. Then mediator and outcome growth curves will be combined in a single model. We will test whether (a) condition predicts change in each mediator, (b) condition predicts change in each outcome, (c) mediator change predicts outcome change, and (d) the condition effect on the outcome is significantly weaker when controlling for level or change in the mediator. Significance of indirect effects will be tested using bias-corrected bootstrapped confidence intervals.

Process analyses. A critical element to the program evaluation is the acceptability of the intervention to the target population, which will be assessed via rate of attrition, level of program

use, and degree of program satisfaction. Dose-response analyses will be conducted to examine the degree to which treatment engagement and retention (e.g., frequency and duration of app use, number of modules completed) predict change in the outcome measures at the post-intervention and follow-up assessments. Canonical correlation analyses will be used to examine the association between the dosage measures and outcome measures within the Qlarity condition. We will also test the hypothesis that those participants who report greater satisfaction with the intervention will have greater improvement in baseline-post scores using residual gain score analyses. Lastly, treating participant satisfaction as a process variable, we will examine the correlations between the satisfaction ratings and the amount of treatment engagement/retention.

Missing data. Missing data in outcome measures may result from dropout or item non-response. The mixed- growth models described above make use of maximum likelihood estimates and allow for use of all available outcome data from all assessments, reducing bias and increasing power. In general, maximum likelihood procedures, as well as imputation methods, will be used as they can provide unbiased estimates even in instances of substantial attrition. Multiple imputation procedures will follow best-practice recommendations.

Power considerations. The assumptions for the power estimates include a sample size of 380 participants, Type II error rate of 20% (β = .20) and a 2-tailed alpha = .05. Power estimates for multilevel growth models require assumptions that are not easily established in longitudinal studies (e.g., complete data, homogeneous random-effects covariance structures within conditions). Thus we rely on the fact that power for multilevel growth models has been shown to surpass that of the mixed-model ANCOVA. The proposed growth models, then, will detect smaller differences between conditions than the ANCOVA models on which power estimates were based. Allowing for intent-to-treat analyses that makes use of all available data using missing data techniques described above and a pretest covariate r^2= .25, there is sufficient power to detect main effects for condition of Cohen's d = .25 (small effect size) and detect condition by moderator effects of d = .35 (small to medium effect). The smallest subsample expected for decomposition of significant moderating effects is approximately 150 minority participants (75 per condition) which will provide sufficient power (>.80) to detect condition effects of d = .40 (medium effect). The study is also powered to detect small to medium between condition effect size differences (ORs = 2.05 – 2.25) for the logistic regression models predicting an estimated 15-20% substance use abstinence rates at follow-up. Using mediation effect size guidelines from Kenny for a model containing a dichotomous independent variable and a continuous mediator, effect sizes of .02, .15, and .40 derived from the product of d and r, represent small, medium, and large effect sizes respectively.
Assuming small to moderate effects for the indirect pathway (r = .20), the proposed sample size has sufficient power (>.94) to detect small effect sizes or greater (dr = .04) for tests of mediation. Process analyses involving correlation coefficients will have adequate power to detect small to medium effects (*r* = .20).

Feasibility benchmarks. Program feasibility will be demonstrated by the achievement of the following benchmarks: (a) significant pre-post increases (e.g., Cohen's d > .35) in emotional regulation, mindfulness, and self-efficacy, (b) significantly greater decreases in alcohol, tobacco, and other drug use for Qlarity participants; (c) a high consistent level of app usage (e.g., over 70% of users used the app at least 12 times over the 12 weeks); and (d) a high degree of youth satisfaction and ratings of app acceptability and usability (mean ratings > 4.0 on the 5-point scale). Benchmarks are based on meta-analysis quantitative methods that recommend effect sizes of at least d >.25 to demonstrate educationally meaningful change; a desire to show at least an average of weekly app use by a majority of participants; and a level of participant satisfaction that meets or exceeds that of Phase I.