Text Message Quit Vaping Intervention for Adolescents

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Supplement 1: Study Protocol

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BACKGROUND

The popularity of electronic cigarettes (or e-cigarettes) has grown exponentially over the past few years, with the surgeon general calling the use of e-cigarettes among young people an "epidemic".[1] E-cigarettes are now the most commonly used tobacco product among youth, and youth and young adults are more likely than adults to use e-cigarettes in the U.S. Many younger e-cigarette users have never used another tobacco product. Among current e-cigarette users aged 45 years and older in 2015, most were either current or former regular cigarette smokers, whereas, among current e-cigarette users aged 18-24 years, 40.0% had never been regular cigarette smokers.[2] E-cigarette use has grown even faster in recent years due to the popularity of products such as JUUL, a small-USB like e-cigarette with high nicotine content that is easy to conceal. Between 2016 and 2019, use of e-cigarettes more than doubled among American high school students (from 11.3% to 27.5%) and middle school students (from 4.3% to 10.5%).[3]

Young people should never use nicotine in any form. While there is some evidence that e-cigarettes are less harmful than traditional cigarettes, they are not harmless and early exposure to nicotine can have long-lasting adverse effects. The majority of e-cigarettes contain nicotine, which has known health effects on brain development which occurs into the mid-20s. Specific risks include nicotine addiction, mood disorders, permanent lowering of impulse control, as well as negative impacts on attention and learning. The aerosol produced by e-cigarettes contains cancer-causing chemicals and tiny particles that reach deep into the lungs. E-cigarettes have also produced unintended injuries such as fires and explosions from defective batteries and poisonings from acute nicotine exposure through e-cigarette liquids. Finally, there is strong evidence that e-cigarette use can lead to the use of other tobacco products such as cigarettes.[4,5] Reversing the dramatic gains over the past decade in reducing cigarette smoking among young people would be nothing short of a public health tragedy.

In response to this epidemic and given no available quitting resources for young people (cessation resources such as medication have no demonstrated effectiveness for young people[6,7]), Truth Initiative launched a first-of-its kind e-cigarette cessation program designed specifically for young people in January 2019. The program is called *This is Quitting* and it is delivered entirely via text message. Mobile phone ownership is ubiquitous among young people and text messaging is a preferred communication modality in this age group. Text messaging is also easy to use, discreet, anonymous, and there is strong evidence supporting its effectiveness as a cessation intervention modality.[8] *This is Quitting* was developed using best practices from smoking cessation research with young people, our extensive experience delivering digital tobacco cessation interventions to people of all ages, as well as formative research with young e-cigarette users and quitters.

Young people enroll by texting "DITCHVAPE" to a short code and responding to the initial message with their age and first name (used for tailoring the program). Terms of Service and Privacy Policy are provided via a link in a text message. Users receive one age-appropriate message per day tailored to their enrollment date or quit date, which can be set and reset via text message. Those not ready to quit receive 4 weeks of messages focused on building skills and confidence. Those who set a quit date receive messages for a week before and 8 weeks afterward that include encouragement and support, skill- and self-efficacy building exercises, coping strategies, and information about the risks of vaping, benefits of quitting, and cutting down to quit. Keywords COPE, STRESS, SLIP, and MORE provide on-demand support. Sample text messages can be found at the end of this protocol. Users can unsubscribe by texting STOP. E-cigarette use and abstinence are assessed via text message at 14, 30, 60, and 90 days following an enrollee's quit date or enrollment date. At 14 days, enrollees are asked, "Have you cut down how much you vape in the past 2 weeks? Respond w/letter: A=I still vape the same amount, B=I vape less, C=I don't JUUL at all anymore." At 30, 60, and 90 days, enrollees are asked, "When was the last time you vaped, even a puff of someone else's? Respond w/ letter: A: in the past 7 days, B: 8–30 days ago, C: More than 30 days ago."

As of July 27, 2021, over 350,000 young people have enrolled, including over 130,000 adolescents aged 13-17, demonstrating the appeal of this treatment approach and the urgent need for quit vaping resources

among young people. Preliminary evaluation data collected among an initial cohort of roughly 27,000 users has shown high levels of engagement in the program and high rates of abstinence among responders.[9] Roughly ¾ of users set a quit date, with the most common quit date being the day of enrollment. Interactive keywords were used by 45.5% of teens and 38.4% of YA. Response rates to follow-up assessment questions were 36.9% at 14 days and 21.0% at 90 days. At 14 days, 60.8% of respondents indicated they had reduced or stopped using e-cigarettes altogether. At 90 days, 7-day point prevalence abstinence (ppa) was 25% and 30-day ppa was 16%. The high volume of enrollment in a short period of time, high levels of engagement with the program, and e-cigarette reduction and cessation results demonstrate that young people are interested in quitting vaping and can be engaged in an easily accessible, anonymous digital platform.

We recently completed an evaluation of This is Quitting with 2,588 young adults aged 18-24. Under an intention-to-treat analysis with missingness coded as vaping, abstinence rates were 24.1% among participants assigned to the intervention (This is Quitting) and 18.6% among participants in the assessment only control arm, a statistically significant difference (Odds Ratio=1.39, 95% CI 1.15-1.68, $p< 0.001$).[10]

Building on previous research, the primary aim of the current study is to conduct a comparative effectiveness trial to evaluate the effectiveness of *This is Quitting* in promoting abstinence from e-cigarettes among adolescents aged 13-17. This study is a 2-arm randomized controlled trial conducted among young users aged 13-17 recruited through online channels. Participants will be randomized to *This is Quitting* or an assessment-only control condition and followed for 7 months to roughly correspond to 6-months post-treatment. The secondary aim is to examine potential mediators of program effectiveness, including treatment engagement and changes in self-efficacy and perceived social support for quitting.

We will also include a waitlist control arm to evaluate the influence of assessment reactivity and retention incentives given relatively high quit rates among assessment-only control participants in the previous YA trial and the dearth of data on adolescent vaping cessation. This arm was not included in sample size calculations.

The scientific, clinical, and public health communities are desperate for proven, evidence-based cessation resources to address the vaping epidemic among young people. We are uniquely positioned to address this urgent need given our extensive experience in conducting large-scale, rigorous research trials of digital tobacco cessation interventions and our expertise in working with young people. We plan to rapidly disseminate study results to benefit other researchers/service providers and use these results to further enhance the program.

METHODS

Subjects

We will randomize 1800 e-cigarette users aged 13-17 years old who are interested in quitting in the next 30 days to the two main intervention arms (900/arm). We will aim to randomize 450 to the waitlist control arm. Other eligibility criteria include past 30-day e-cigarette use and US residence. To fully enroll in the study, individuals must text a study-specific phone number and respond to the system-generated message.

Recruitment and Enrollment

Potential participants will respond to online ads on various social media platforms (Facebook, Instagram, etc.) if they are current e-cigarette users who are interested in quitting and willing to participate in a research study. Clicking on the ad will lead them to a webpage that provides details about what participation in the study entails and describes incentives for participation. Those who are interested will complete an eligibility screener followed by informed consent and a baseline assessment. Those who complete the baseline will be randomized into one of three arms (see below for additional details) and instructed to text a specific keyword corresponding to their treatment assignment to the same phone number. Only those who respond to the first message from the text message program within 24 hours will be fully enrolled into the study. This requirement will be made explicit.

Randomization

Randomization occurs after completion of the online enrollment process (completed baseline survey). A computer algorithm that is part of the survey software will automate random allocation.

Interventions

This is Quitting: Participants will be enrolled to receive messages from This is Quitting as described above.

Assessment-only control: After an initial enrollment message, participants will be contacted monthly to assess e-cigarette use. At the end of the study, participants will receive information about how to sign up for This is Quitting if they are interested.

Waitlist control: After an initial enrollment message, participants will only be contacted at 1 and 7 months to complete the follow-up assessments; there will be no other contact via text message. At the end of the study, participants will receive information about how to sign up for This is Quitting if they are interested.

Potential Problems and Solutions

Loss to follow-up is the primary concern in trials involving digital interventions, especially ones that employ an assessment only or minimal contact controls. For the treatment and assessment only control arms, we expect at least 75% follow-up at 1-month and 65% at 7-months based on our previous and ongoing digital mobile-based evaluations. If follow-up rates are lower than expected early in the trial, we will consider shortening the 7-month follow-up to gather only abstinence outcomes.

To maximize follow up rates we will:

1) provide clear information about the study at the outset, including expectations for follow-up;
2) reimburse participants up to $30 per follow-up assessment;
3) collect interim abstinence assessments via text ("Retention Messages": $5 incentive for each response) for intervention and assessment-only control arms;
4) send reminders about follow-up surveys via email and text messages;
5) conduct phone follow-ups for those unreachable by email and text messages;
6) contact participants via social media private messaging function (if permission given); and,
7) emphasize the importance of survey completion regardless of abstinence status.

Conducting research online involving incentives carries the potential for fraud and participant deception as there are often no direct interactions with the participants.[11] To prevent fraudulent enrollments and participation from bots, we will utilize the following features on the Qualtrics survey platform:

1) Prevent multiple submission: Enabling this option allows Qualtrics to place a cookie on the browser the first time someone takes the survey. The user will be flagged as duplicate if they come back to take the survey from the same browser and device without having cleared their cookies.
2) Bot detection: Enabling bot detection flags responses that are likely completed by bots by assigning a score to each response. This feature uses Google's invisible reCaptcha technology to assign a score to each response, with a score of less than 0.5 meaning that the respondent is likely a bot.
3) Relevant ID: This feature analyzes a user's browser, operating system, and location to calculate a fraud score that indicates whether the respondent is attempting to take the survey multiple times.

We also require a valid email address for completion of the baseline survey (users must click on a survey link in their email to launch the baseline and complete enrollment), which has been shown to prevent bots.[12] We will monitor emails and phone numbers used to enroll in the study on a daily basis and exclude any duplicates. We anticipate these measures will prevent the majority of any potentially fraudulent enrollments.

Measures

All randomized participants in both arms will be asked to complete all assessments. Assessments will occur at baseline and 1 month and 7 months post-randomization. The baseline survey will be conducted online and hosted on a secure server. Mixed-mode follow-up (email, phone, text) will be employed. Telephone surveys will be conducted by research staff blind to treatment. Text messages have demonstrated moderately high reliability (k=.66) compared with web-based surveys in assessing smoking outcomes[13] and will be used as a final means of gathering abstinence data from non-responders. Most measures listed below are standard instruments used in cessation studies, and are reliable when administered via the Internet.[14,15]

Screening Variables. Individuals located outside the U.S. (as determined by IP address captured by the survey platform) will be ineligible to participate. To characterize the sample of users interested in the study and assess study eligibility, we will gather: demographics (age, education, income level, sexual and gender identity, race, and ethnicity); current e-cigarette use (use of e-cigarette containing nicotine or THC in the past 30 days)[16]; interest in quitting; contact information (e-mail and phone number to send baseline survey to and link text message sign-up data). These questions are being asked during screening so we can determine whether enrolled participants are representative of the wider population of e-cigarette users.

Baseline Variables. To characterize the sample and explore potential moderators of treatment effectiveness, we will gather: additional demographics (student status, employment status); current e-cigarette use and history (frequency and rate,[16,17] age of first use, motivation to quit and quitting history[18]); nicotine dependence will be assessed with the Penn State Electronic Cigarette Dependence Index[19], EDS/PROMISE-E,[20] the Hooked on Nicotine Checklist,[21] and the E-cigarette Fagerström Test of Cigarette Dependence (e-FTCD)[22]; other substance use (other tobacco products, alcohol) and mental health symptoms[23]; and adverse childhood events.[24,25] For co-morbidities and adverse childhood events, we chose measures that are validated for use among adolescents. In order to minimize risk to participants, we deliberately avoided measures or deleted questions that assessed sensitive topics such as suicidality. Given evolving trends of e-cigarette use and perception, we will also ask about perception about harm from e-cigarettes, reasons for wanting to quit, and reasons for joining the study. To account for potential predictors of dropout, we will ask about motivation to use or quit e-cigarettes and potential barriers to quitting (e.g., social influences). We will assess baseline levels of perceived level of social support,[26,27] perceived social norms, and perceived self-efficacy for quitting and examine changes in these variables as potential mediators of treatment effectiveness.

Mediating Variables. We hypothesize that treatment engagement will mediate the relationship between treatment assignment and abstinence outcomes. We will extract data regarding replies to interactive text messages (e.g., setting a quit date, keyword use) as well as unsubscribe status, number of days enrolled, and total number of messages received. All text message interactions are date/time stamped.

Outcome Measures. The primary outcome is self-reported 30-day point-prevalence abstinence (ppa) at 7-months but we will gather abstinence data at all follow-ups. Other quitting-related outcomes include change in motivation to quit, quit attempts, reduction in e-cigarette use, 7-day ppa, and continuous abstinence measured at each follow-up. Intervention satisfaction in both conditions will be measured with items about overall satisfaction and whether they would recommend it to a friend (scale from 0-10). Satisfaction with frequency of text messages will be measured.[28] To assess perceived message relevance, participants will be asked whether text messages "were written personally for you"[29] and "were directed at you personally".[30]

Data Analysis Plan

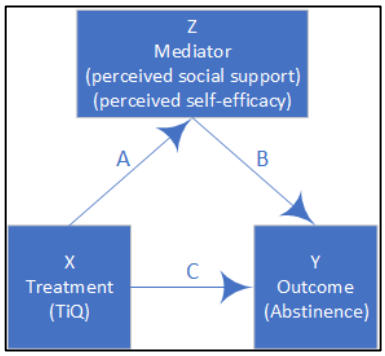
Primary Analysis. Point-prevalence abstinence (ppa) at 7-months post-randomization will be compared across the treatment and control groups using logistic regression. All estimates will be adjusted for baseline confounders of the intervention-outcome relationship. We will identify potential moderators (e.g., age, gender, baseline motivation to quit) by analyzing interactions between treatment and selected variables. For

all moderators found to be associated with the primary outcome, we will examine the effects of treatment/moderator interaction terms on outcomes after entering main effects.

Secondary Analyses. Additional outcomes related to abstinence and treatment engagement will also be analyzed with logistic regression as secondary analyses. These include likelihood of making a quit attempt, likelihood of reducing e-cigarette use, and changes in confidence and self-efficacy in quitting e-cigarettes.

Missing Data. Missing data will be handled in two ways. First, we will conduct an intent-to-treat (ITT) analysis in which participants who have been lost to follow up are assumed to be treatment failures (i.e., vaping). This analysis will be conducted because ITT analyses are common in the smoking cessation literature, despite simulations demonstrating that the approach is neither conservative nor anti-conservative but rather biased in favor of whichever condition contains less missingness.[31] Second, we will supplement the ITT analyses with an analysis that uses a multiple imputation (MI) procedure to minimize bias in estimates and standard errors, under the assumption that outcomes are not missing at random (NMAR) but rather more likely to be missing for treatment failures (i.e., vaping) than treatment successes (i.e. abstinence). Since the magnitude of actual response bias is unknown, we will conduct a sensitivity analysis to evaluate the treatment effect on outcomes under a range of magnitudes, from equal odds of missing (OR=1) to five times more likely to be missing (OR=5).

Mediator Analysis. Our conceptual model is that treatment increases the odds of abstinence by increasing perceived social support and perceived self-efficacy for quitting. Those two constructs will be measured at baseline, 1-month and 7-months post-treatment. Change in those constructs from baseline will be evaluated with separate mediation analyses as presented in Figure 1. Specifically, we hypothesize that the effect of treatment on abstinence will be mediated by perceived social support and perceived self-efficacy, such that: (1) a significant effect A is found associating X with Z ; (2) a significant effect B is found associating Z with Y; (3) a significant effect C is found associating X with Y; and (4) the effect of C is significantly attenuated when A and B are simultaneously included in the model.



PROTECTION OF HUMAN SUBJECTS

Human Subjects Involvement, Characteristics, and Design

Participants will be 1,800 e-cigarette users aged 13-17 who respond to online advertising about a research study and who complete enrollment into a text message program based on random allocation. Study enrollment is conducted entirely online and is fully automated. Randomization occurs after participants have provided informed consent, passed the decisional capacity check, and completed the baseline survey. Study enrollment will not be considered complete until the participant responds to the initial system-generated text message.

We will be recruiting adolescent participants under the age of 18 and we are requesting a waiver of parental consent. This approach is based on published research with adolescents engaging in high-risk behavior as well as the American Psychological Association Resolution on Support for the Expansion of Mature Minors' Ability to Participant in Research.[32] Parents are often unaware of their adolescent's use of e-cigarettes and many adolescents hide their e-cigarette use from their parents for fear of punishment and disapproval, making parental consent a significant barrier to studying e-cigarette use and treatment among teens. As noted in the APA resolution, requiring parental consent in adolescent research may lead to biased samples, causing researchers to overestimate or underestimate the scope of health problems in at-risk populations and leading to findings that is not generalizable to the population of adolescent vapers who want to quit vaping. Research supports that children as young as 14 years old can provide valid informed consent similarly to adults when information is presented at developmentally appropriate levels and the

consent process is conducted under minimal stress. Adolescents that meet study eligibility criteria will be provided information about the study at a 5th grade reading level and required to complete a series of questions showing decisional capacity before they continue with study enrollment.

Sources of Materials

Sources of research material include the following: 1) screening data, 2) text message utilization data, and 3) baseline and follow-up assessments. The baseline assessment will be conducted online with the survey hosted on a secure server. Mixed-mode follow-up (online, phone, text message) will be employed. Phone surveys will be conducted by research staff blind to treatment condition.

Materials Access

For all data, the Principal Investigator (Dr. Amanda Graham), Data Analysts (Dr. Michael Amato, Anna Funsten), Project Managers (Sarah Cha, Megan Jacobs), and research assistant (Giselle Edwards) will have access to individually identifiable information about human subjects. Electronic data files with identifiable information will be maintained separately from other data files and will only be used for administrative purposes (e.g., tracking follow-up completion, managing subject payment). All personnel already have or will have received certification in human subjects protection prior to beginning work on this project.

POTENTIAL RISKS TO SUBJECTS

The overall risk is judged to be very low. Study participants who attempt to quit e-cigarette use will likely experience some nicotine withdrawal symptoms that may include anxiety, restlessness, anger, irritability, sadness, and problems concentrating. There is no reason to believe that participation in this study would worsen nicotine withdrawal symptoms or that symptoms would differ based on randomization assignment.

ADEQUACY OF PROTECTION AGAINST RISKS

Exposure to evidence-based information and support for e-cigarette cessation in the intervention arm is expected to attenuate withdrawal symptoms associated with e-cigarette cessation that may occur. The following steps will be taken to ensure adequate understanding of study procedures and full consent.

Step 1 (Study information): Potential participants who click on an online ad for e-cigarette users who are interested in quitting and willing to participate in a research study will be directed to a website that provide additional details about the study. This webpage will provide information on who is behind the study, what participation entails, and who may be eligible for the study. **Step 2 (Eligibility screening):** Individuals who are interested in participating will complete a short survey to confirm eligibility for study participation. Those who are eligible will be asked to provide contact information (e-mail address to send links to surveys and mobile number for text message sign up). **Step 3 (E-mail confirmation):** An email message is sent to the participant with a distinct URL (Web address) containing the baseline survey and instructions to complete the survey within 24 hours to complete study enrollment. This process ensures that enrolled participants have a valid email address where they can receive study-related correspondence. **Step 4 (Informed consent):** When the participant clicks on the URL in the email, it will open up an online baseline survey. On the first page of the baseline survey, the Informed Consent text will be provided, including a) each study condition; b) financial incentives for participating; c) the process of randomization and the equal chance of being assigned to one of three treatment conditions; d) protection of confidentiality and the right to withdraw at any time; and e) expectations regarding follow-up data collection, including compensation for time required to complete follow-up assessments (regardless of e-cigarette use status). Users will be required to select "Yes, I would like to continue" as active affirmation that they are providing consent for study participation. Contact information for the study and the Institutional Review Board where IRB approval has been obtained will be included in the Informed Consent form. All information about the study will be written at a 5th grade reading level to ensure adequate comprehension. **Step 5 (Decisional capacity confirmation):** After reading the informed consent, they will be asked to complete an assessment of decisional capacity and understanding of the informed consent by answering the following 7 questions:

What is the purpose of this study?; Do you have to be in this study?; Can you tell me what will happen if you agree to take part in this study?; How might this study not help you or even hurt you?; How might this study help you?; What would you do if you wanted to leave the study?; What will happen if you decide not to be in the study? Correct answers will be required for all 7 questions in order for the potential participant to move onto the Baseline assessment. **Step 6 (Baseline assessment):** Users who respond correctly to the decisional capacity questions will move onto the baseline assessment. **Step 7 (Randomization):** Randomization will only occur after an eligible study participant has completed the online enrollment process (confirmed eligibility, indicated informed consent, passed decisional capacity confirmation, and completed baseline survey). **Step 8 (Text message sign-up):** Users will be randomized at the conclusion of the baseline assessment and provided with a keyword to text based on their assignment. Users must text their assigned keyword to the provided phone number and reply to the welcome text message to confirm text message enrollment and finalize their study enrollment. Those who are willing to provide additional contact methods will be asked to add their social media handle for private messaging at this step (optional).

POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO HUMAN SUBJECTS AND OTHERS

Subjects may benefit from participation in this research in several ways. By participating in an e-cigarette cessation treatment program, subjects may increase the likelihood that they will attempt to quit e-cigarette use and be successful. Alternatively, participants will gain a greater understanding of their e-cigarette use behavior that may help them to quit successfully in the future. Finally, although this is not a direct benefit, all participants will be involved in a project to evaluate innovative treatments for e-cigarette cessation that may ultimately produce an enormous public health impact. We believe the substantial potential benefits significantly outweigh the minimal potential risks to research participants.

Payment for participation

There is no payment for study enrollment or completion of the baseline assessment. All participants are asked to complete follow-up surveys at 1- month and 7-months post-randomization. Participants will be paid $20 for completing each follow-up survey via the Internet or by phone with a telephone interviewer. Participants who respond within 24 hours of receiving the initial survey invitation will receive an additional $10. Participants in the intervention and assessment-only control arms will also be compensated $5 for each text message assessment (7 total) they respond to, for a total compensation of up to $95 for their entire study participation. Payment for completing the surveys and the text message assessments will be delivered via Rybbon, a company specializing in digital gift management for marketing and research. Rybbon is fully integrated with Qualtrics. When a participant completes an assessment, Rybbon will generate a unique link for gift card redemption and will email it to the participant. Rybbon has no access to any other identifying information other than email and no access to assessment data. Participants can redeem their Rybbon gift card from a variety of gift card options.

IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

This is Quitting is the first text message intervention for e-cigarette cessation designed specifically for young people. We have seen a high volume of enrollment since the program launched in January 2019 with only earned media and organic marketing efforts to date. We have been flooded with interest from youth-serving organizations looking for a proven quit vaping program to offer to their young people. To our knowledge, this study will be the first to rigorously evaluate a scalable, cost-efficient, market-tested quit vaping program among adolescents. These data are urgently needed.

DATA AND SAFETY MONITORING PLAN / DATA & SAFETY MONITORING BOARD

Confidentiality will be protected at all times and potential risks will be minimized systematically. The following measures will be taken specifically to ensure data safety and monitoring.

Youth Advisory Board

Prior to any recruitment of research participant occurs, we will review all of our materials (recruitment ads, assessments) with adolescents with similar characteristics to our eligible populations (aged 13-17, U.S. residents, current or former vapers). The members of this youth advisory board will be recruited from our community partners who work directly with adolescents. No identifying information will be collected from these youth advisory board members, and they will not receive any intervention. Their role is to provide feedback on recruitment strategies and data collection procedures.

Data Safety

Respondents will fill out computer-based surveys. All survey data will be stored in a secure Qualtrics database online. All research studies and their related non-public materials are confidential information. This includes, but is not limited to, the study title, study questions that are responded to, provided as part of a study, and any concepts related to those materials. Respondent information will remain confidential.

All data used specifically for this project will be maintained in a manner consistent with NIH standards. The Principal Investigator (Dr. Amanda Graham), Data Analyst (Dr. Michael Amato), Project Managers (Sarah Cha, Megan Jacobs), and research assistant (Giselle Edwards) will have access to participants' identifying information. All study staff will have received certification in human subjects protection from the NIH Office of Human Subjects Research. Confidentiality of data will be maintained by numerically coding all data, by disguising identifying information, and by keeping all data electronically protected. Electronic data files with identifiable information will be maintained separately from other data files and will only be used for administrative purposes. Identifying information will not be reported. The list of participant phone numbers, content of text message responses, and documentation of incoming and outgoing messages will be accessible to study staff through a password protected administrative web page available only over an encrypted connection (SSL).

Adverse Event Reporting

HHS definition for "adverse events" will be used for this study (https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html#AA). Adverse event is defined as any untoward or unfavorable medical occurrence in a participant, including any abnormal sign, symptom, or disease temporally associated with participation in the research. A serious adverse event is defined as any adverse event temporally associated with the subject's participation in research that: 1) results in death; 2) is life-threatening; 3) requires inpatient hospitalization or prolongation of existing hospitalization; 4) results in a persistent or significant disability/incapacity; 5) results in congenital anomaly/birth defect; or 6) any other adverse event that may jeopardize the participant's health and may require medical or surgical intervention to prevent one of the other outcomes listed above. Unanticipated problem includes any incident, experience, or outcomes that is: 1) unexpected given the research procedures and the characteristics of the subject population being studied; 2) related or possibly related to a subject's participation in the research; and 3) suggest that research places subjects or others at a greater risk of harm related to the research than was previously known or recognized.

Adverse events, serious adverse events, and unanticipated problems are unlikely in this sociobehavioral only intervention, but any potential events will be reported immediately upon discovery by study staff to the Principal Investigator who will notify the IRB within 24 hours.

Data and Safety Monitoring Board

A data safety and monitory board (DSMB) has been established prior the submission of this protocol for IRB review. Members of the Data and Safety Monitoring Board (DSMB) are invited by Truth Initiative to reflect the disciplines necessary to interpret data from the trial. All members of the DSMB are required to be completely independent of the study and all members are required to sign a DSMB Conflict of Interest and Confidentiality statement.

The DSMB is responsible for safeguarding the interests of study participants, assessing the safety and efficacy of study procedures, and for monitoring the overall conduct of the study. The DSMB is an independent advisory group to Truth Initiative, and is expected to provide recommendations about starting, continuing, and stopping the study. In addition, the DSMB is asked to make recommendations, as appropriate, to Truth Initiative about:

- Selection, recruitment, and retention of participants
- Completeness, quality, and analysis of measurements
- Participant safety
- Adherence to protocol requirements
- Efficacy of the study intervention
- Benefit/risk ratio of procedures and participant burden, and
- Amendments to the study protocol and consent forms

DSMB meetings will be held via remote connections. The purpose of the first meeting is to review and discuss the DSMB Charter, to provide an overview of study activities, to review and make recommendations about the protocol, and to determine the frequency of interim analyses and whether data will or will not be masked to identity of randomized groups. Enrollment in the study will not begin until the DSMB's Charter has been accepted by the DSMB members, and IRB approval has been obtained.

Meetings will be held approximately once a month prior to study launch, with additional meetings or conference calls scheduled as needed. Before each meeting, when the agenda is sent out, Truth Initiative staff will ask all DSMB members to state whether they have developed any new conflicts of interest since the last meeting. If a new conflict is reported, the Chair and other members will determine if the conflict limits the ability of the DSMB member to participate in the discussion. The DSMB also will review adverse event data, other safety data, enrollment data, and quality and completeness of study data at each meeting to ensure proper trial conduct. At intervals, as noted above, the DSMB will also review formal interim analyses of the primary end point. It is expected that all DSMB members will attend every meeting and call. However, it is recognized that this may not always be possible. Quorum for voting is considered to be half the number of standing members plus one. The Board may wish to decide if particular expertise is needed within the quorum for the meeting to be valid. All standing Monitoring Board members are voting members. A quorum of this DSMB is considered to be: Three (3).

Communication with DSMB members will be primarily through the principal investigator (PI, Amanda Graham, PhD) and the research director (Sarah Cha, MSPH). We will use project management software (Basecamp) and cloud-based file storage (Dropbox) to facilitate communications, track feedback, circulate meeting agendas, and document meeting minutes. The DSMB will have a Chair who will lead the discussion at each meeting. Truth Initiative staff will prepare summary of DSMB meeting minutes for review by full DSMB board following each meeting.

At the first meeting, review of the study protocol will include review of the statistical analysis plan. The DSMB should discuss the adequacy of that plan. The final plan, whether part of a research protocol or separate document, will be maintained as an appendix to this charter. The DSMB should discuss the statistical monitoring procedures they propose to follow to guide their recommendations about termination or continuation of the trial. These procedures could include guidelines for early termination for benefit, termination for futility, and termination for safety reasons.

Regulatory and Ethical Considerations

This study targets health topic that is currently receiving significant media and regulatory attention (e-cigarette use). We do not anticipate any regulatory changes that may occur during the study period to impact study conduct as our study is aimed at evaluating a cessation program for a product that may become less

available and fits well into the currently developing regulatory environment.

The assessment-only arm was selected as the most ethical control group for the current study that allows for evaluation of the intervention while keeping control arm participants engaged. We are also adding a Waitlist control to evaluate the impact of regular assessment on outcome. Both control groups will have access to the program at the conclusion of the study if they are interested.

Our payment structure was developed to incentivize participants for their time and increase retention while not creating any coercion. Thus, the incentives are nominal amounts, but provides choices for participants that we hypothesize will lead to great retention.

The current study is a low risk, sociobehavioral only intervention and we do not anticipate any other ethical considerations.

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Summary of Changes to the Original Protocol

1. Assessment Revisions

The following measures were added to the baseline assessment: Roberts Loneliness Scale, PEARLS (IRB approval received 10/13/2021); Questions about vaping behavior, including preferred flavors (IRB approval received 11/16/2021).

2. Updates to Decisional Capacity Questionnaire

We revised the Decisional Capacity Questionnaire to simplify the response options (limited to True/False or Yes/No). We also included a second set of decisional capacity questions for those who failed the first set to provide users with a second opportunity to confirm their understanding of study participation (IRB approval received 12/7/2021)

3. Additional Fraud Prevention Strategies

We added language to the Informed Consent to indicate that participants may be withdrawn from the study if survey responses were flagged as potentially fraudulent. We also added attention checks to the assessments to capture potentially fraudulent responses. A description of additional steps taken to prevent fraudulent enrollment was added to the protocol in the "Potential Problems and Solutions" section. (IRB approval received 9/8/2022 and 9/14/2022).