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A Randomized Controlled Trial of a Smoking Cessation Self-Help Intervention for Dual Users of Tobacco Cigarettes and E-Cigarettes: Intervention Development and Research Design

Lauren R. Meltzer^a, Vani N. Simmons^{a,b}, Steven K. Sutton^{a,b}, David J. Drobes^{a,b}, Gwendolyn P. Quinn^a, Cathy D. Meade^{a,b}, Marina Unrod^a, Karen O. Brandon^a, Paul T. Harrell^c, Thomas Eissenberg^d, Christopher R. Bullen^e, and Thomas H. Brandon^{a,b,*}

^aH. Lee Moffitt Cancer Center & Research Institute, 12902 USF Magnolia Drive, Tampa, FL 33612, United States ^bUniversity of South Florida, 4202 E. Fowler Avenue, Tampa, FL 33620, United States ^cEastern Virginia Medical School, 700 W Olney Rd, Norfolk, VA 23507 ^dVirginia Commonwealth University, Box 980205, Richmond, VA 23298 ^eUniversity of Auckland, Auckland 1010, New Zealand

Abstract

Electronic Nicotine Delivery Systems, also called electronic cigarettes or e-cigarettes, have been available for over a decade and use has been increasing dramatically. The primary reported reasons for use are to aid smoking cessation or reduction, yet a significant proportion appear to be long-term users of both products (“dual users”). Dual users may be motivated to quit smoking and might benefit from a behavioral intervention for smoking cessation. This paper describes the intervention development, as well as the design, methods, and data analysis plans for an ongoing randomized controlled trial (RCT). Formative research and learner verification were conducted to create a usable, understandable, and acceptable self-help intervention targeting dual users. The efficacy is being tested in an RCT with current dual users (N=2900) recruited nationally and randomized to one of three conditions. The Assessment Only (ASSESS) group only completes assessments. The Generic Self-Help (GENERIC) group receives non-targeted smoking cessation booklets and supplemental materials sent monthly over 18 months. The e-cigarette Targeted Self-Help (eTARGET) group receives the newly developed intervention (targeted booklets and supplemental materials) sent over the same period. All participants complete self-report surveys every 3 months over 2 years. The primary study outcome is self-reported 7-day point prevalence abstinence. Cost-effectiveness metrics for the GENERIC and eTARGET interventions will also be calculated.

*Corresponding author.

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Keywords

smoking; self-help; randomized controlled trial; e-cigarettes; dual-use

Introduction

Research on electronic nicotine delivery systems, also called electronic cigarettes or e-cigarettes (ECIGs), is still in the nascent stage with open questions about their health consequences, addiction liability, and smoking cessation potential [1, 2]. To date, there have been few longitudinal studies [3, 4] and the behavior of ECIG users over time remains unclear. ECIGs cannot be overtly marketed as pharmacotherapy for treating tobacco dependence, yet survey research indicates that the primary motivations for their use are to aid smoking cessation or smoking reduction [5–7]. Evidence regarding the smoking cessation benefits of ECIGs is inconclusive; [8] one hypothesis is that they function similar to traditional forms of nicotine replacement therapy (NRT). The efficacy of NRT is greatly improved when combined with minimal behavioral interventions. Although millions of smokers are simultaneously using ECIGs [9, 10], for the purpose of quitting smoking, they usually do so without receiving any behavioral assistance. In addition, although more likely to make a quit attempt than smokers alone, they are not significantly more likely to actually quit [11]. Thus, an opportunity exists to facilitate smoking cessation among the large population of “dual users” who have demonstrated initial action toward smoking cessation by initiating ECIGs and are primed to benefit from a minimal intervention to enhance their chances of tobacco abstinence.

To capitalize upon this circumstance, we adapted our cost-effective, previously validated self-help smoking cessation intervention, *Forever Free®: Stop Smoking for Good* [12], for dual users. That self-help intervention was developed to assist smokers with cessation, and it demonstrated efficacy in a recent randomized controlled trial (RCT) [12]. It was designed to capture key content from empirically supported cognitive-behavioral interventions [13] and to provide it over an extended period of time.

The present study applies this efficacious intervention approach (extended self-help) to the rapidly changing landscape of tobacco use marked by dramatic increases in the dual use of ECIGs and conventional, combustible cigarettes. Reported rates of dual use range from approximately 10% to 35% among current cigarette smokers [14–16]. On the one hand, there is cause for public concern because chronic dual use maintains the multiple health risks associated with smoking while potentially adding yet unknown risks of ECIGs. On the other hand, dual use may offer an opportunity to transform dual users' ECIG use from maintaining tobacco smoking to promoting smoking cessation, with the ultimate goal of complete nicotine cessation, given other potential risks [17–20].

This paper describes the intervention adaptation for dual users, as well as the design, methods, and data analysis plans for the ongoing RCT. The primary aim is to develop and test a minimal self-help smoking-cessation intervention for current dual-users of tobacco cigarettes and ECIGs. Given that small improvements in cessation may not be justified if they require substantially greater cost, we will also compare the interventions on cost-

effectiveness (cost per incremental cessation and expected life-years gained). A secondary surveillance aim will assess the dynamic process of tobacco smoking and ECIG use longitudinally, to capture the natural progression of dual use.

2. Methods

2.1 Study I: Intervention development

The intervention developed in this study is based on the original *Forever Free*® booklets [21, 22], initially designed to prevent smoking relapse. Brandon and colleagues later modified the *Forever Free*® booklets to include instruction on smoking cessation, creating a new version titled, *Forever Free*®: *Stop Smoking for Good* [12]. The first booklet in the series provides a general overview about quitting smoking, and each of the remaining nine booklets includes more extensive information on a topic related to maintaining abstinence: *Smoking Urges*; *Smoking and Weight*; *What if You Have a Cigarette?*; *Your Health*; *Smoking, Stress, and Mood*; *Lifestyle Balance*; *Life without Cigarettes*, *The Benefits of Quitting Smoking*, and *The Road Ahead*. The content of these booklets was based on cognitive-behavioral theory [23, 24] and empirical evidence regarding the nature of tobacco dependence, cessation, and relapse [25]. They were designed originally as a means of translating the cognitive-behavioral counseling that occurs in a smoking cessation clinic into a written format that would be more accessible to a larger population of smokers. In addition, perceived social support appears to benefit smoking cessation [26, 27]. Thus, new motivational pamphlets were added to the intervention to provide a social support analog via tri-fold color pamphlets (*How I Quit Smoking*) that reinforce key messages about quitting smoking (e.g., dealing with stress, keeping weight gain in perspective, finding other forms of positive reinforcement). To further induce a sense of social support, the message is communicated via a first-person narrative from a former smoker, incorporating photographs of the purported smoker.

A systematic approach was used to adapt and refine the *Stop Smoking for Good* booklets and the *How I Quit Smoking* motivational pamphlets for dual users [28]. First, in-depth interviews ($N=28$) were conducted to identify and explore new content topics for inclusion that would be relevant for dual users. Two trained doctoral level interviewers conducted all in-depth interviews with participants. Each interview lasted approximately 60 minutes and participants were provided \$30 compensation. Participants represented four subgroups: (1) current dual users without interest in quitting smoking; (2) current dual users who had attempted, unsuccessfully, to quit smoking; (3) current ECIG users who had successfully quit smoking; and (4) former dual users who had quit both products. These subgroups were selected to obtain a wide range of smoking and e-cigarette experiences and perspectives from individuals across the continuum of dual use, from those unmotivated to quit smoking to those who were successful in quitting both products. The participant sample was 48% female, 79% Caucasian, with 15% identifying as Hispanic. The average age was 48.8 (SD = 14.2), and 48% reported annual household income above \$50,000. Current and former smokers smoked a median of 16–20 cigarettes per day and vaped a median of 15–19 times a day.

Verbatim transcripts were coded using an inductive content analysis and the constant comparative method [29]. The constant comparative method is a process in which newly collected data are compared to previous data. The process is used to extrapolate and identify emergent themes related to the study aims, and enables coders to identify when and if saturation has occurred.

Based on these findings, as well as existing and emerging research and theory regarding both ECIGs and the use of NRT for smoking cessation, deeper content (i.e., specific advice for quitting smoking for dual users) modifications regarding quitting smoking using ECIGs were incorporated. Examples include: gradually reducing nicotine levels; switching from a tobacco flavor to an alternative flavor; and limiting ECIG use to places one would normally use tobacco cigarettes (i.e., not expanding use). In addition, language that reflects the current preferences of the target population was used throughout the materials. For example, ECIG use is referred to as “vaping” and the ECIGs themselves are often called “personal vaporizers.”

The existing tri-fold color pamphlets (*How I Quit Smoking*) were also revised to enhance relevance for dual users. To attain a high level of face validity, the pamphlets will include language, photos, and graphics that incorporate ECIGs. Additionally, the illustrative vignettes in the booklets and the personal stories in the pamphlets were replaced or modified based on testimonials from the interviews. For example, one of the pamphlets was modified to describe a smoker’s experience using tobacco-flavoring early on to ease the transition to ECIGs, and then switching to other flavors to reduce the association with smoking. During the interviews, we also gathered feedback about the existing *Stop Smoking for Good* booklets in terms of tone and other important elements of smoking cessation message design for this audience. Participants responded favorably to the booklets and provided suggestions on how to best incorporate information about quitting smoking using ECIGs. For example, participants felt that ECIGs should be presented separately from traditional forms of nicotine replacement therapy (NRT) as a quit aid. In addition, participants indicated mixed opinions regarding the value of ECIGs for coping with stress. Therefore, new content sought to clarify and reinforce the use of an ECIG over a traditional cigarette during times of stress. Furthermore, because the long-term health consequences of ECIG use remain unknown, we elected to include progressively stronger and more specific advice to discontinue ECIG use following smoking cessation. However, because during the interviews the majority of participants felt it would be off-putting to include these messages early on in the series, we introduced these messages in the latter half of the booklet series. Finally, two initial brochures, one for each intervention condition, were developed to provide participants with an introduction to the *If You Vape* booklets and the *Stop Smoking for Good* booklets, respectively, and the goal of using ECIGs to quit smoking.

Next, learner verification interviews ($N=20$ dual users) were conducted to assess the suitability of the revisions. This methodology allows investigators to assess the suitability of the educational materials for the intended audience with respect to attraction, cultural acceptability, understanding (literacy), efficacy, and persuasion, in an effort to reduce miscommunication of messages [30–32]. A sample of 10 participants is generally considered sufficient when conducting learner verification; therefore, 10 newly recruited

participants were recruited for each of the two iterations [31]. The participant sample was 57% female, 53% Caucasian, with 27% identifying as Hispanic. The average age was 42.6 (SD = 15.9), and only 12% reported an annual household income above \$50,000. The sample was similar to the earlier sample with respect to smoking and vaping patterns. Interviews lasted approximately 30–60 minutes and participants were compensated \$30.

Although the majority responded favorably to the revisions, suggestions included broadening the visual appeal for a younger demographic, adding more tips for quitting smoking using ECIGs, and utilizing a variety of terms for ECIG devices. All of these suggestions were incorporated into the final materials. All materials were written at the 5th–6th grade reading level to maximize their accessibility to a wide range of smokers [33, 34].

2.2 Study II: The RCT

There are three arms of the RCT. The e-cigarette Targeted Self-Help (eTARGET) group receives the intervention created as the product of Study I. The Generic Self-Help (GENERIC) group receives the extended self-help intervention that was previously validated [12]. The Assessment Only (ASSESS) group does not receive any intervention materials, but they complete all assessments. An overview of the intervention and assessment schedule is summarized in Figure 1.

The primary outcome is self-reported 7-day point prevalence tobacco abstinence at 3-month intervals up to 24 months. We hypothesize that the recipients of our targeted *If You Vape* intervention (eTARGET) will show higher rates of smoking abstinence than either comparison condition. A secondary hypothesis is that the targeted intervention will also produce higher rates of abstinence from ECIGs. As noted earlier, cost-effectiveness indices will also be calculated for the interventions, with the ASSESS group as the referent.

2.2.1 Participants—Participants will be 2900 newly recruited dual users (580 ASSESS, 1160 GENERIC, and 1160 eTARGET) recruited throughout the United States (see below). We initially planned to recruit 500, 1000, and 1000 individuals to the ASSESS, GENERIC, and eTARGET conditions respectively, in expectation of 17% attrition after baseline assessment (i.e., participants who complete no follow-up assessments), as observed in our previous self-help study [12]. Based on return rates of the 3-month survey for the first 575 study participants, we now estimate 27.5% attrition after baseline. Consequently, we increased our target sample sizes to 580, 1060, and 1060 for the three conditions.

To maximize generalizability, we have minimal inclusion criteria: (1) Cigarette use at least once per week over the past year; (2) ECIG use at least once per week over the past month; (3) age ≥ 18 years; (4) not currently enrolled in a face-to-face smoking cessation program; and (5) able to speak and read English. In addition, no more than one participant per street address will be enrolled.

2.2.2 Procedures—This study was reviewed and approved by the Chesapeake Institutional Review Board. It is registered on clinicaltrials.gov (NCT02416011). Enrollment to the RCT began on July 18, 2016. The target enrollment of 2900 participants (580 in ASSESS and 1160 each in GENERIC and eTARGET; see below) is expected to be achieved

over an 18-month period via multimedia advertisements, including social media, ECIG forums, cable TV, radio, and newspapers. Recruitment ads state that we are conducting a nationwide study to measure behaviors and attitudes regarding cigarettes and ECIGs. During the first telephone contact after a dual user responds to an advertisement or other recruitment efforts, research staff collect basic demographic information, a brief tobacco and ECIG history, and screen for the inclusion criteria.

Dual users who meet inclusion criteria and provide initial verbal consent over the telephone are sent the baseline assessment by postal mail or via a link that is sent by email. Participants who return a completed baseline assessment and still meet the smoking and vaping criteria are formally enrolled into the RCT. They are randomized to one of the three study arms using balanced-permuted block randomization [35] with a block size of 10 (2–4), and sent the appropriate intervention materials if randomized to the GENERIC or eTARGET conditions. All participants are sent the intervention materials via postal mail, and participants who elect to receive them electronically are also sent a link to access the booklets online.

Follow-up assessments occur at 3-month intervals after the date of enrollment, through 24 months. Participants are provided the option of completing the assessments online or via postal mail, and they receive \$20 for completing the baseline assessment, \$10 for each completed abbreviated follow-up, \$20 for each completed full follow-up, and a state lottery ticket if they return the assessment within one week of receipt. They will also receive bonuses of \$40 or \$60 for completing at least 7 or all 9 of the assessments, respectively. In addition, local participants are paid \$20 for completing the biochemical verification interview and \$15 for providing the biochemical samples.

2.2.3 Intervention Conditions

2.2.3.1 Assessment Only (ASSESS): Participants in this condition do not receive intervention materials. This comparison condition controls for repeated assessments and allows for the most meaningful evaluation of the efficacy and the cost-effectiveness of the eTARGET intervention. This condition is the primary source of data for the secondary surveillance aim to capture naturalistic changes in smoking and ECIG use over time.

2.2.3.2 Generic Self-Help (GENERIC): Participants receive the generic smoking cessation materials that recently were found efficacious in a national RCT [12]. Materials include the introductory *Stop Smoking for Good* brochure, the 10 *Stop Smoking for Good* didactic booklets, and 9 *How I Quit Smoking* pamphlets. The initial brochure and the first booklet are mailed upon receipt of the baseline assessment (randomization). The remaining booklets are mailed at 1, 2, 3, 5, 7, 9, 12, 15, and 18 months. The pamphlets are mailed at 4, 6, 8, 10, 11, 13, 14, 16, and 17 months.

2.2.3.3 Targeted Self-Help (eTARGET): Participants receive the newly developed *If You Vape: A Guide to Quitting Smoking* intervention, designed specifically for dual users. This includes the introductory *If You Vape* brochure, a series of 10 *If You Vape: Guide to Quitting Smoking* booklets, and 9 supportive *My Story* pamphlets. These materials are mailed on the same schedule as the Generic materials.

2.2.4 Measures

2.2.4.1 Baseline assessment: Dual users who meet inclusion criteria and provide initial verbal consent over the telephone are mailed a single booklet of baseline questionnaires or provided with an email link to an online survey, depending on the participant's preference. This survey has 3 primary sections: (1) demographic characteristics, (2) tobacco cigarettes, and (3) e-cigarettes. The tobacco cigarette section has items covering smoking history, current use, nicotine dependence (using the Fagerström Test for Nicotine Dependence (FTND) [36]), intention to quit, motivation to quit, and use of cessation aids. Motivation to quit tobacco cigarettes is assessed using the Stages of Change Algorithm [37], and a continuous measure of readiness to quit, the Contemplation Ladder [38]. We also assess three other motivation-related constructs: a situation-specific abstinence self-efficacy scale [39]; a measure of abstinence-related motivational engagement (ARME) [40]; and a measure of tobacco cigarette expectancies that we developed for the previous survey. Finally, there will be single items to assess overall "commitment" to, and "confidence" about, being smoke-free, as well as craving for cigarettes.

The e-cigarette section was developed to parallel the tobacco cigarette sections as closely as possible. There are items addressing current and past ECIG use (using a questionnaire developed in a previous ECIG survey [41]), dependence (modified version of the FTND), and intention to quit, motivation to quit, expectancies, and cravings.

2.2.4.2 Follow-up assessments: Participants are sent follow-up assessments (by mail or email link) at 3-month intervals through 24 months, as indicated in Figure 1. We deliberately keep each followup assessment brief to minimize participant burden and attrition. Participants receive full follow-ups at 6, 12, 18, and 24 months, and abbreviated follow-ups at 3, 9, 15, and 21 months. The abbreviated follow-ups include assessment of the use of tobacco cigarettes, ECIGs, pharmacotherapies, and other tobacco cessation aides or services. These data will be sufficient for calculating the primary treatment outcome as well as for the longitudinal tracking of cigarette and ECIG usage for the secondary aim. The full follow-ups are comparable to the baseline assessment for smoking and vaping, however there are additional items to evaluate the intervention (Client Satisfaction Questionnaire) [42] and use of the intervention materials (e.g., how much they read, how often they refer back, whether they helped them to quit smoking).

Breath carbon monoxide (CO) and saliva samples (for cotinine analysis) are collected at the 12-and 24-month follow-up points for participants who report abstinence and reside within 100 miles of the home institution. The breath sample is collected with a portable CO monitor (Micro CO™ by Micro Direct, Inc.), and the saliva sample is collected in a 2ml tube for immediate cotinine analysis using the NicAlert™ dipstick (Nymox Pharmaceutical Corporation, Hasbrouck Heights, NJ). Cut-offs of 8 ppm for CO and 10 ng/ml for cotinine are used to determine abstinence [43]. We will use the disconfirmation rates from this sample to estimate adjusted smoking rates for the full sample.

2.2.5 Data analyses plan

2.6.2 Analysis overview: The first aim is to evaluate the efficacy of the *If You Vape* intervention (eTARGET) in producing higher rates of smoking abstinence than both comparison conditions (ASSESS and GENERIC). The primary analyses of 7-day point prevalence abstinence will be performed using generalized estimating equations (GEE, [44]) to evaluate condition, time (months from baseline), and the condition $\times$ time interaction. Each of 3 paired comparison (e.g., eTARGET versus ASSESS) will be performed with adjusted alphas following Holm [45]. A significant main effect for condition or condition $\times$ time interaction will be evidence for condition-based differences in abstinence rates. Any potential confounding variable (e.g., a demographic or smoking history variable) that is significantly different across conditions despite randomization will be included. Pair-wise condition (e.g., eTARGET versus ASSESS) and time interval (e.g., 6 months versus 18 months) comparisons will be tested using the generalized score statistics from the GEE models.

In separate models, prospective moderators (e.g., gender, nicotine dependence, intention to quit tobacco cigarettes, use patterns) will be explored via interactions with condition and condition $\times$ time. Mechanisms of change associated with treatment (e.g., self-reported motivation, intervention usage, ECIG usage) will be explored via mediation analyses [46]. We will further extend our analyses to lapse/recovery models and explore proportional shifts in cigarette vs. ECIG use. Specifically, we will use the Kaplan-Meier method with log-rank test for the stratified sub-groups (e.g., lapsed and recovered groups) to test the effect of intervention condition, with Cox PH models controlling potential confounding variables. To capture proportional shifts in cigarette vs. e-cigarette use, we will create a response variable with multiple levels for each follow-up assessment, reflecting the relative level of e-cigarette to cigarette use, referenced against baseline use of each product. The multi-level outcome variable will be fitted using a logistic analysis on the generalized logits to test if the interventions have a significant impact on these shifts.

To manage missing data, multiple imputation under the Missing at Random assumption will be applied using a Markov Chain Monte Carlo method [47] via PROC MI in SAS, given the expected large number of non-monotonic missing data patterns. Preliminary analyses will determine auxiliary variables (e.g., baseline measures that predict smoking status at follow-up) to be used. A post hoc approach [48] will address the influence of Missing Not at Random (MNAR) on smoking status (i.e., missing is due to smoking). Sensitivity analyses will be performed to assess the extent of MNAR influences. A comparable set of analyses will be performed to assess cessation of e-cigarette use.

A secondary aim is to describe the patterns of cigarette smoking and ECIG use among initial dual users at 3-month intervals for 2 years. This process will occur relatively naturalistically in the ASSESS condition. The primary analysis will be completed using a growth mixture model [49]. We aim to (1) describe the trajectories for tobacco cigarette and e-cigarette use, and (2) identify distinct subgroups of trajectories over time.

2.2.5.2 Sample size estimation: The primary statistical analyses will assess 7-day point prevalence for abstinence over time using GEE with a binary outcome and a logit link

function. Based on Bullen et al. [50], data from our cessation study [12], and considering that the sample will not be limited to treatment-seekers, we estimated no greater than 15% abstinence by 18 months for ASSESS, 20% for GENERIC, and 25% for eTARGET. GEESIZE version 3.1 [51] was used to estimate sample size with the following options selected: an AR(1) working correlation structure and coefficient of 0.7; adjusted alphas of .017 (ASSESS vs. eTARGET), .025 (ASSESS vs. GENERIC), and .05 (GENERIC vs. eTARGET) following Holm's procedure [45]; and abstinence rates that increase from 6 to 18 months, then remain stable through 30 months. Randomizing 2065 participants (413 to ASSESS, 826 to GENERIC and to eTARGET) will ensure 80% power for each contrast. In expectation of 17% attrition after baseline assessment, as observed in our prior study [12], we planned to recruit 2500 participants. However, as noted earlier, we recently increased the target sample size to 2900 in response to an initial pattern of higher than expected rates of missing data for the first follow-up assessment.

2.6.3. Cost-Effectiveness Analysis—Because stakeholders, including health care systems, the insurance industry, government agencies, and policy makers, must balance the benefits of proposed interventions against the costs associated with them, efficacy alone is often insufficient justification for implementation. Therefore, efficacy data derived from this study will be incorporated into cost-effectiveness analyses to generate economic statistics of value to stakeholders.

The relative effectiveness and costs of the intervention compared to an assessment only condition will be measured based on the health care system perspective; that is, focusing on costs and outcomes associated with the health care system rather than society as a whole. Using the trial endpoint results, effectiveness will be predicted in terms of smoking cessation and translated into life years and quality adjusted life years (QALY) based on published associations between smoking cessation and long-term health outcomes [52, 53]. Costs include the intervention costs, collected prospectively, and lifetime costs of reduced medical expenditures attributable to smoking-related morbidity, that will be modeled using published estimates [54–59]. No out-of-pocket costs or transfer payments (i.e., increased social security payout due to longer lifespans after quitting smoking) will be incorporated into the analysis, because they do not fall within the system perspective. In addition, costs associated only with research (e.g., mailing of assessments) will be excluded. Monetary values will be inflation adjusted, and all outcomes will be presented in discounted and undiscounted values.

The effectiveness and cost results will also be presented as incremental cost-effectiveness ratios, specifically cost per quitter, cost per life year, and QALY. We will assess the robustness of incremental results between the three study arms using probabilistic sensitivity analysis.

3. Discussion

There is little direct evidence about the efficacy of ECIGs for promoting smoking cessation. Although ECIG manufacturers cannot market their products as pharmacotherapy for smoking cessation in the United States, it is clear from surveys that ECIG users are

purchasing them for this purpose [7, 10]. For example, 77% of ECIG users surveyed reported initiating use to quit smoking or prevent smoking relapse [60, 61]. In our own survey [41], 84% reported that smoking cessation was a reason for initiating ECIG use, and 56% listed it as their primary reason. Population-based surveys of adults have consistently found the highest prevalence of ECIG use among current smokers (i.e., dual users), followed by former smokers and nonsmokers [14, 62]. Longitudinal studies of dual users find that the vast majority (e.g., 89%) [63] remain dual users a year later, and the association between ECIG use and smoking cessation has been weak [3, 4]. However, a large British retrospective study found that among those who attempted to quit smoking in the previous year, ECIG users were more likely to have quit than those who used NRT or no aid (20.0%, 10.1%, 15.4%, respectively) [64]. Furthermore, recent data indicate that smokers with greater frequency, intensity, and long-term use of ECIGs have higher smoking-cessation rates, often surpassing rates from those using traditional forms of NRT [65–67].

To our knowledge, this study represents the first RCT of an intervention to facilitate smoking cessation among dual users of tobacco cigarettes and ECIGs. Aside from cessation and cost-effectiveness outcomes, the study will provide long-term, prospective, longitudinal data on dual use in a community-based sample. The intervention is based on the successful *Forever Free*® series for former smokers [21], and recently-validated series (i.e., *Forever Free*®: *Stop Smoking for Good*) for current smokers [12], both of which drew on empirical and theoretical work in cessation and relapse prevention. As a surveillance study, we will be able to track changes in the use of both products over time and examine predictors of cessation. We will also be able to examine whether provision of the self-help intervention alters either the patterns of use or cessation predictors. While we await more RCTs testing ECIGs as a smoking cessation aid, the present study capitalizes on the growing population of smokers who have already initiated ECIG use, and it tests whether a self-help intervention is sufficient to improve their smoking cessation success, and eventually the cessation of all nicotine products.

This study has several strengths. This is the first RCT to test a self-help intervention targeted to dual users of tobacco cigarettes and e-cigarettes. The intervention content was largely informed by our formative work with the target population. In addition, the large sample size ($N = 2900$) should provide statistical power to test both mediating and moderating variables, including demographic variables as well as smoking and ECIG characteristics. This study also includes a true no-treatment control condition, which will also be the source of data for the secondary surveillance aim regarding naturalistic changes in smoking and e-cigarette use over time. Moreover, the GENERIC arm will allow us to test whether tailoring the intervention specifically for dual users is necessary, or if basic smoking cessation information is sufficient. Furthermore, recruiting a wide range of dual users, rather than solely those who are seeking smoking cessation treatment, provides several advantages, including: 1) the ability to test whether the intervention motivates attempts to quit smoking among non-treatment seeking, non-cessation-motivated dual users; 2) the modeling of likely dissemination approaches for a low-cost self-help intervention; and 3) the avoidance of apparent promotion of ECIGs as a cessation tool for current smokers.

Finally, based on previous findings indicating dual users' interest in receiving interventions delivered either via booklet or the internet [68], the proposed intervention is offered via mail, as well as with an internet option. The internet option provides participants with a personalized link to the appropriate booklets and to all earlier booklets in the series. Data will be collected regarding the use of the internet-based materials, namely how many times the link was accessed, and whether the electronic booklet(s) were downloaded, which will allow us to document their use and acceptability. We will also collect evaluations and preferences regarding internet distribution at follow-up to test as potential moderators or mediators of treatment effects. Distribution via the internet also increases the reach of the intervention and lowers cost [69].

A few limitations to the study should be noted. Biochemical verification of smoking cessation status will be completed by a sub-sample of participants (i.e., those residing within 100 miles of the institution) due to logistical considerations, as participants are being recruited from throughout the United States. In general, low contact interventions such as the one described above tend not to benefit from bio-verification, and trials should avoid assessments that might cause reactivity, a threat to generalizability. Considering the low-contact nature of the intervention, potential for reactivity, and little expected differential in social-desirability demand across conditions, we concluded that bio-verification of the *full* subject sample was not warranted [43, 70].

Generalizability of the findings may be limited due to potential sampling bias that may occur based on the primary sources used for recruitment (e.g., social media). To ensure greater representativeness of dual users in general, we are able to assess demographics at various time points during data collection and adjust recruitment methods as needed. For example, during the early recruitment period, we observed a lower than expected proportion of female participants. Therefore, we modified the targeting parameters of our social media campaign to increase the number of women reached and enrolled.

We recognize the ECIG marketplace is rapidly changing with the entrance of the traditional tobacco industry. This process is expected to consolidate the market as well as lead to a more consistent product and more sophisticated product marketing. Another ongoing change is the regulation of ECIGs by the FDA as well as the passage of state-level restrictions. Meanwhile, ECIG technology will continue to evolve. These trends suggest that the landscape of ECIGs and dual use will be different by the end of the study than it is today. However, the rapid growth of ECIGs and dual usage necessitates immediate research; the opportunity costs incurred by postponing research to an unknown time when ECIG usage and development stabilizes would be considerable. Nevertheless, we have concentrated our accrual to an 18-month period so as to produce relevant findings as rapidly as possible.

Finally, we are sensitive to the risk that either our intervention or the study itself could be construed as promoting ECIGs as a cessation tool. Given insufficient evidence regarding the safety or efficacy of ECIGs, we do not wish to promote their use, and we took several actions to minimize such a perception: (1) We do not recommend or provide ECIGs to participants; (2) We only recruit dual users—smokers who are already using ECIGs; (3) Reflecting the first two points, our intervention materials are titled, *If You Vape: A Guide to*

Quitting Smoking; (4) Our public recruitment materials do not mention smoking cessation, but rather only surveillance of dual users; and (5) Our intervention recommends—and assists with—cessation of ECIGs following smoking cessation.

In summary, this project tests whether the high-risk behavior of dual use can be capitalized upon to facilitate smoking cessation and, ultimately, cessation of all nicotine products. This study will have high public health significance if it demonstrates the novel self-help intervention to be clinically effective and cost effective at promoting smoking cessation among dual users via a modality with potentially wide reach due to ease of dissemination and implementation.

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Figure 1.
Flow Chart of Study Design: Interventions and Assessments