Official Title: Enhanced E-cigarette Coaching Intervention for Dual Users of Cigarettes and E-cigarettes

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2. Research Strategy

2.1 Significance

More than a third of current smokers have tried ENDS,[6] often as part of an attempt to quit smoking.[8,10,26-34] **Whether ENDS help people quit smoking is largely unknown due to limited well-designed research.[12,16,23] However, some recent data suggest promise for a role of ENDS in harm reduction and as a pathway to cessation.[17,20,35-38]** Only two randomized trials examining ENDS and smoking cessation have been conducted. A New Zealand study found no significant differences in 6-month quit rates or adverse events for ENDS compared to patch, although quit rates in both groups were low.[39] Combining data from the New Zealand study and the ECLAT randomized trial in Italy, a 2016 Cochrane Review concluded that ENDS with nicotine were more effective as quit aids than no nicotine ENDS.[12,16,39,40] The numerous observational studies in this area have been summarized,[15,41] but, as Pearson demonstrated, there are limitations with these studies that can lead to differing results depending on available control data and analytic techniques.[14] In addition, few observational studies have focused only on smokers using ENDS as a quitting aid,[14,17,42] and the majority have not even focused on smokers interesting in quitting.[15,41] In our longitudinal study of commercial quitline (QL) callers, those not using ENDS specifically for quitting were significantly less likely to be cigarette abstinent at 6 months compared to non-ENDS users and those using ENDS to quit.[3]

Regardless of whether ENDS help people quit smoking, treatment providers need to know the best way to address ENDS during smoking cessation treatment among current dual users of cigarettes and ENDS. State funded QLs in the United States provide free, evidence-based, cost-effective tobacco cessation treatment, including phone counseling and NRT.[22,43-47] Over 10% of QL callers report current ENDS use at registration, translating to 40,000 dual users entering treatment each year.[11] Alere Wellbeing, Inc. (AWI), the provider of QL services in the proposed study, has a general approach to addressing ENDS: (1) the QL's primary goal is to help cigarette and traditional tobacco users quit, but it will also help with quitting ENDS, (2) Quit Coaches (QCs) are trained to educate that ENDS are not regulated by the FDA as a cessation aid, their long-term safety is unknown, and they are not empirically supported cessation aids, and (3) to not promote ENDS for cessation, but also not to discourage smokers switching to ENDS to quit.[48] We conducted one-month post-registration qualitative interviews with 40 QL callers (i.e., *after* most program calls had been completed) who used ENDS and wanted to quit smoking at registration. ENDS often were not discussed or only briefly discussed on calls and callers perceived a range of ENDS-related messages from QCs (top four: discouraged use, encouraged use, much unknown about, not regulated; see manuscript in Appendix B).[3] The existing protocol and/or deficits in coach confidence in addressing ENDS may lead to variable delivery or limited focus on ENDS. Expert recommendations for addressing ENDS during smoking cessation include recommending empirically supported medications as the first-line treatment, educating about the importance of completely quitting combustible tobacco and what is known about the safety and efficacy of ENDS for quitting smoking, and, for smokers who have failed first-line treatments or are insistent on using ENDS for quitting, to support their quit attempt.[2,13,19,23,24,26,49-51] Some recommendations are more extensive, noting the superiority of nicotine-containing ENDS, better nicotine delivery and craving reduction with later generation models, use of ENDS with other pharmacotherapies (i.e., combination therapy), use duration, handling and storing of devices, and other safety precautions.[19] **The best way to operationalize these recommendations and help smokers who use ENDS make decisions about their quit plan (QP) has not been examined in previous research.**

The proposed study will address this gap by developing and pilot testing an enhanced ENDS coaching intervention for dual users calling tobacco QLs with three key components: education, tailored behavioral support, and shared decision making (SDM) QP development. In our qualitative interviews described above, we identified five potentially adaptive and four maladaptive quit strategies using ENDS.[3] Adaptive strategies included (1) using NRT and ENDS as combination therapy, (2) using patches and no nicotine ENDS to stop smoking and wean off nicotine-containing ENDS, (3) stepping down nicotine mgs in ENDS liquid to wean off nicotine after quitting smoking, (4) using ENDS to cut down or completely quit smoking and then using NRT to quit ENDS and maintain cigarette abstinence, and (5) gradual or complete substitution of ENDS for cigarettes ending in complete abstinence. Maladaptive strategies included behaviors more likely to establish a separate ENDS habit and/or unlikely to result in complete smoking abstinence based on behavior change principles and previous research[52,53] such as (1) using ENDS where they did not previously smoke, (2) frequent, automatic use, (3) continued cigarette smoking in high craving situations, and (4) cutting down to quit with no plan or schedule.[3,11] **This research suggested that some ENDS users identify effective ways to use ENDS at least for short-term cigarette abstinence, while other ENDS users would benefit from behavioral support and education.[3]** In fact, studies have noted concerns that smokers who use ENDS often

have more complex quit histories,[10,14,35] that intermittent ENDS use has been negatively associated with quit motivation,[35] and that ENDS use in itself could signal a need for more intensive quitting support for some.

Research has also identified knowledge gaps and incorrect beliefs about ENDS and the relative harm of ENDS compared to cigarettes and FDA-approved cessation medications, suggesting a need for clear education during treatment.[3,11,54-59] U.S. data show that the proportion of smokers who believed ENDS are less harmful than cigarettes decreased from 85% in 2010 to 65% in 2012.[55-57] National surveys have also revealed misperceptions about the safety and efficacy of NRT (e.g., two-thirds had concerns about NRT safety or believed NRT is just as harmful as cigarettes), which may impact use and compliance.[60] Our research identified misinformation among dual users at QL registration, including that ENDS and the aerosol it produces are completely safe, ENDS are safer than NRT, patches have unsafe constituents such as tar, and concerns about nicotine in ENDS and NRT despite continued smoking.[3,11] Most participants also reported either support for or confusion about the safety of long-term ENDS use and requested more information about ENDS.[3]

Concerns about ENDS use include safety and, until recently, no manufacturing standards or regulation. **Reviews of safety data and expert consensus have concluded that short-term ENDS use has not resulted in serious adverse events**,[12,16,36] **and is safer than combustible tobacco**.[9,19,51,61] One study found ENDS had substantially (9-450 times) lower levels of toxic substances than cigarettes and levels were similar to the nicotine inhaler.[9] Research is not yet available on the safety of long-term ENDS use; however, given the known impacts of smoking, long-term ENDS use is likely preferable to relapsing to cigarettes.[19] U.S. government oversite of ENDS constituents and manufacturing by the FDA began on August 8, 2016; however, it may take 2-3 years for manufacturers to submit new tobacco product applications and for the FDA to review these applications. The start of FDA regulation of ENDS products does not change the fact that treatment providers still need evidence-based methods for addressing ENDS during smoking cessation treatment. **There is no reason to wait to conduct this research until FDA regulation of ENDS has progressed further, and if anything, waiting would be a disservice to dual users trying to quit smoking now.**

Individual differences in use experiences with ENDS and NRT and past quit experiences suggest that a tailored assessment and QP development approach, involving education and SDM, could increase success. SDM is a patient-centered approach to decision making recommended in healthcare situations where there is more than one reasonable treatment option.[25,62] Elywn et al. have detailed a 3-step model for implementing SDM in practice: (1) introducing choice, (2) describing options including education, discussion, and decision aids, and (3) discussing preferences and making an informed decision. Patient-centered techniques such as SDM have been associated with improved health self-management, adherence, and outcomes.[63,64] Given the potential for misinformation about ENDS and cessation medications, and that, although efficacious on average, the majority of NRT users do not successfully quit smoking,[2] **the SDM paradigm is a good fit for systematically addressing options, offering education, and supporting an informed decision about QP development among smokers already using ENDS.** Our qualitative research found that, based on their personal quitting experiences, approximately equal numbers of dual users preferred NRT only, ENDS only, or using NRT and ENDS in combination for quitting smoking.[3] SDM may also decrease the likelihood that ENDS will be used instead of empirically supported treatments by users likely to benefit from first-line therapies, a commonly noted concern about the potential negative impact of ENDS on public health.

2.1a Summary. The quality of evidence about ENDS as a smoking cessation aid is low due to the limited well-designed research in this area. Despite this lack of research, many smokers use ENDS during their cessation process. There are no empirically tested interventions for dual users of cigarettes and ENDS. Research is needed to develop and test the best way to address ENDS during smoking cessation treatment in a way that maximizes smoking cessation outcomes and engagement with treatment. Knowledge gaps suggest that education and tailored behavioral support are necessary components, and a SDM model for QP development, effectively used in other areas of healthcare decision making, could lead to creating a QP a smoker is committed to, and to better outcomes for smokers using ENDS during their quit process.

2.2 Innovation: The proposed research is highly innovative in the following ways: **1) There are no empirically supported behavioral smoking cessation interventions addressing ENDS use; expert recommendations need translation and testing.** Standard QL treatment does not systematically address how and why ENDS are being used. Smokers are using ENDS during their quit process regardless of research progress or government regulation; it is pragmatic and necessary to research how best to address ENDS during cessation treatment, particularly given correlational data that some smokers who choose to use ENDS may have worse cessation outcomes.[65] **2) Diary data to inform mechanisms of success vs. failure.** Previous ENDS studies are limited in assessment of how, when, and why smokers are using ENDS, and whether and how ENDS are used in conjunction with cessation medications.[14,35] By providing behavioral

support and tracking product use details via diary methods, we will have valuable data to understand potential mechanisms of successful vs. unsuccessful abstinence, even regardless of the EEC intervention success. **3) Findings will benefit cessation studies with NIDA's research ENDS device (expected in 2017).** Our intervention and educational material development, diary, and outcome findings can inform study design in future RCTs examining the efficacy of ENDS as a cessation device. **4) Real-world, low SES sample.** Our ability to recruit dual users seeking treatment may result in a more generalizable sample with findings that will benefit treatment providers in other settings. Studies that seek dual users through ads may recruit a more limited subgroup of ENDS users (e.g., committed users wanting to discuss devices). In addition, our population is predominately low education/income, and Medicaid-insured or uninsured—a priority population for outreach.

2.3 Approach

Overview and Timeline. We will develop and test a novel smoking cessation treatment for state QL enrollees using cigarettes and ENDS, which will include education, SDM, and behavioral support. Phase 1 will include treatment development and refinement through delivery of the EEC to 10 dual users. In Phase 2, we will conduct a randomized controlled pilot study with 100 dual users randomized to EEC or QL treatment as usual (TAU). We will analyze results, identify further improvements, and determine if the EEC warrants a future RCT.

Task	*2017*		*2018*				*2019*	
	Q3	*Q4*	*Q1*	*Q2*	*Q3*	*Q4*	*Q1*	*Q2*
Phase 1: Treatment development and training	X	X	X					
Application development, Quality Assurance[1]	X	X	X					
Phase 2: Recruitment				X	X			
Phase 2: Intervention				X	X	X		
Phase 2: 3-month follow-up					X	X	X	
Analysis and dissemination							X	X

[1]Application development is required to change existing electronic systems used to deliver QL treatment to include: (1) eligibility questions, study offer, and consent scripting and (2) EEC intervention delivery support and data elements to be collected on each call.

2.3a Team: Dr. Vickerman has completed extensive analyses on ENDS use among QL callers, identified education gaps and adaptive and maladaptive behavioral strategies for using ENDS, and collected focus group data on ENDS-related messages.[3,10,11,66] Dr. Wagener has considerable ENDS knowledge and has been invited to write ENDS reviews and commentaries by leading journals.[67-69] He has developed treatments to encourage smokers to completely switch to ENDS,[18,67,70] and has published studies on the impact of ENDS on smoking behaviors and beliefs.[18,71-73] Dr. Brandon is creating self-help booklets for smokers who vape as part of a separate ongoing R01, has a successful history of developing effective self-help materials, and has extensive treatment development experience.[50,74-76] Dr. Carpenter has expertise in developing brief, phone-based treatments and training QCs in numerous studies. Dr. Gillapsy is the Director of the Oklahoma Tobacco Helpline, and has extensive experience in tobacco cessation and training healthcare providers in motivational interviewing, which overlaps with tenets of SDM.[62] Finally, Dr. Javitz, a senior biostatistician who has published extensively on tobacco and QLs, will oversee analyses and provide input on study design.

2.3b Phase 1: EEC treatment development and preliminary acceptability testing. *Theory.* Intervention development will follow behavior change program development best practices[77,78] and will be based in social cognitive theory,[79] self-determination theory,[80,81] and the theory of reasoned action.[82-84] Social cognitive theory is the basis for the existing QL coaching program and recognizes the reciprocal relationships of social environment, cognitions or personal factors, and behaviors.[79] The theories of self-determination and reasoned action work well in the context of social cognitive theory and underlie the specific components chosen for the EEC: education, SDM, and tailored behavioral support. The theory of reasoned action highlights the need to change beliefs (e.g., misconceptions about ENDS or NRT) prior to changing behavioral intention or behavior and acknowledges the strength of norms or others' viewpoints on behavior change,[82-84] whereas self-determination theory is an underpinning of SDM and patient-centered care which asserts that a participant's natural inclinations towards motivation, engagement and growth can be supported or thwarted based on their experiences within a social context, particularly with regard to autonomy, competence, and relatedness.[82-84] *4 Key Treatment Development Components.* (1) A treatment manual will be developed including educational material, the SDM paradigm for QP development (tailoring Elwyn's model for applying SDM in clinical practice,[25] and ENDS behavioral support guidelines (e.g., adaptive strategies to consider, maladaptive strategies to avoid). (2) Two educational booklets will be developed to be impactful, concise, and understandable at a 4th grade reading level on common indices.[85-87] (3) QC training protocol and materials (see Training QCs below). (4) Treatment fidelity monitoring measures and enhancement methods will be developed, including design, training, delivery, receipt of treatment assessment, and use of skills assessment best practice strategies as described by Borrelli and colleagues.[88,89] *Process.* The following resources will be utilized to

develop treatment components: (1) findings from Dr. Brandon's R01 to develop self-help materials for dual users, (2) published fact sheets and expert treatment recommendations,[2,13,19,23,24,26,49-51,90] (3) needs assessment findings from Dr. Vickerman's qualitative work and focus groups,[3,66] (4) empirical literature, and (5) clinical and research experience, particularly from Drs. Wagener and Brandon's previous work with this population. QL calls are not scripted. Instead, talking points are provided to guide QCs in treatment delivery and ensure fidelity, while allowing flexibility for clinical decision making, individualized care, and rapport development. Dr. Vickerman will create initial drafts of all components and work with Drs. Brandon, Carpenter, and Wagener through an iterative feedback process to prepare Phase 1 materials. Materials will then be reviewed by focus groups of experts and treatment delivery stakeholders at AWI, including QC trainers with expertise in adult learning, QC supervisors, and QCs as a means of preliminary acceptability testing; improvements will be made prior to QC training. Finally, the team will monitor ENDS-related media, research, practice guidelines, and regulations to revise educational materials as needed and prepare coaches to educate and respond to questions from participants. **Training QCs.** Four bachelors-level QL counselors ("QCs") will be trained on the EEC intervention (15 training hours plus ongoing feedback and booster content). Training will include (1) ENDS product, safety, and regulation education, (2) participant education materials, (3) SDM model for QP development, (4) examples of potentially adaptive and maladaptive ENDS use strategies, and (4) session by session content and tailored behavioral support strategies. QCs have already received over 240 hours of tobacco cessation treatment training and receive ongoing supervision (see Resources section). EEC skill acquisition will be assessed via written pre-post tests of knowledge and skills and through simulated call role plays where process (helpfulness, warmth, empathy) and content adherence will be rated. Coaches will be trained to complete a checklist of all EEC components delivered on each call. **Phase 1 Procedures (*n*=10).** *Recruitment, Study Offer, and Consent.* New OKHL registrants who are dual users will be contacted by study staff who will screen, consent, and complete baseline measures by phone. In Phase 1, some participants may complete the initial intervention call prior to consent; this method of identifying participants reduces start up time and increases flexibility for treatment refinement. *Inclusion Criteria.* Participants must be eligible for a 5-call QL program, smoke any CPD (dual users may have already replaced some cigarettes with ENDS), report ENDS use in the past 30 days at registration, be willing to set a cigarette quit date in next 30 days, speak and read English, be non-pregnant and not planning pregnancy during study, ≥18 years of age, and willing to complete diaries. We will recruit equal numbers of males and females. *Intervention & Data Collection.* Phase 1 participants will then complete the EEC Assessment & Planning call. ENDS use will be assessed, education provided, and their QP developed or revisited using SDM. Calls will then proceed as shown in Table 1. Participants will complete diaries (described below) for a total of 5 weeks (first two weeks and the 7 days prior to 1-month, 2-months, and 3-months post-consent). Non-responders to the diary assessments (i.e., less than 5 of 7 days completed) will be contacted by a RA to complete a TLFB[91,92] interview by phone. At the end of treatment (approx. 2 months post-registration), participants will complete the multimodal Outcomes Survey and a qualitative interview. Participants will receive

Table 1. Call content: QL TAU and EEC Intervention

Call Number	QL TAU (control)	Enhanced ENDS Coaching (EEC) Intervention
Addressed in every call	**Intervention grounded in social cognitive theory[79] and US PHS clinical guidelines.[2]** Assessment of current status and challenges. Modify medications or set new quit date if needed.	**All EEC calls will include key QL TAU components *PLUS*** behavioral support and education regarding ENDS use (if currently using). EEC educational booklets will be referenced. Additional call-specific components noted below.
1: *Assessment & Planning*	Program overview, assessment and planning with focus on setting a quit date, cessation medications, urge management, tobacco proofing and support. Quit Guide mailed.	(1) Assessment of ENDS use and intentions for use, (2) ENDS education, and (3) SDM on use of ENDS and FDA-approved cessation medications in QP. Tailored EEC educational booklet #1 mailed to participant.
2: *Pre-quit date*	Motivational enhancement, reinforce QP.	Reinforce QP including use of ENDS and/or medications.
3: *Quit date*	ACE model (avoid, cope, escape), social support, tobacco proofing.	Tailored EEC educational booklet #2 mailed to participant.
4: *Quit date follow-up*	Relapse prevention (RP), ACE.	If current using ENDS: (1) RP addressing plans for ENDS use, (2) address intentions for long-term use of ENDS.
5: *Ongoing*	RP, ACE, summarize and wrap up program.	Same additional content as call 4.
NRT provision	Same for both groups. All are eligible for 2-8 weeks of NRT (depending on insurance status) if they medically qualify and/or return a medical override letter from their doctor (see Human Subjects/Risks of NRT for more detail).	
NRT dosing	Typically based on CPD prior to start of dual use, but also utilizes QC judgement guided by an established dosing protocol. Strongly encourages stopping all non-NRT forms of nicotine (including ENDS) on quit date.	Participants will work with coaches using SDM to determine plans for ENDS and NRT use while quitting. NRT dosing will be adjusted if participants plan to continue ENDS use. QCs will assess potential side effects and QP adherence on every call and make needed adjustments to the QP or NRT dosing.

$20 for completing the baseline, $5/week for diaries with 5/7 days completed (or TLFB interview completed) plus a $30 bonus for completing all 5 weeks, $50 for final survey, and $50 for qualitative interview (potential total: $175). **Fidelity.** The research team will review all call recordings, code for treatment fidelity and collaborate with QC supervisors to review standard call quality metrics. Feedback will be provided to coaches. **Feedback from QCs.** Feedback from QCs on challenges with the EEC and recommendations for improvement, which will be used to refine the EEC prior to Phase 2. **Measures. (**Table 2.) *Baseline.* Standard QL registration includes demographic and tobacco use questions. Prior to randomization, participants will complete additional measures on ENDS and cessation medication use, knowledge and beliefs (questions from the empirical literature or developed to assess key misconceptions targeted by EEC education), and brief assessments of psychosocial functioning (depression, stress, anxiety). *Treatment Adherence/ Engagement.* Call completion, call minutes, and NRT sent from the QL are standardly captured data. *Daily diaries.* Participants will complete brief diary assessments on their use of ENDS, cessation medications, and traditional tobacco products, as well as cravings and an open-ended question on quit challenges (1-5 minutes to complete; procedures will be refined to facilitate completion during Phase 1 Pilot). Diaries can be completed (1) online via emailed mobile-optimized survey links or (2) via paper measures that will be returned by mail weekly. RAs will provide orientation to diary completion, and will closely track online completion and mailed surveys to provide reminders. Nonresponders (<5/7 days completed) will be contacted by a RA to complete a brief TLFB interview by phone. *Multimodal Outcome Survey.* The outcome survey will include measures used at Baseline (see Table 2) plus: (1) Program Satisfaction and Acceptability: assessed via a 10 Likert-rated item questionnaire (e.g., Would you recommend this to a friend?) and, for the EEC group only, several open-ended questions (e.g., what would you change about this program?) developed based on the methodology outlined by Dumas and Redish;[93] (2) Treatment Adherence: questions will assess use of EEC educational materials (EEC only) and use of print materials (both groups); (3) SDM: the 3-item Collaborate scale will assess coach effort in helping participants understand quitting options, eliciting participant preferences, and integrating preferences in QP decision making,[94] and (4) adverse events during treatment and specifically during ENDS or cessation medication use. Surveys will be emailed with a link for online completion, followed by multiple attempts to complete by phone, and finally a truncated paper survey will be mailed. *Qualitative Interviews.* After program completion, trained interviewers will conduct an interview to assess: (1) ENDS, NRT, and nicotine beliefs (relative harm, safety, long-term use), (2) quit strategies used and how and why ENDS were used during the program, (3) reactions to SDM model for QP development, and confidence in and adherence to QP, (4) use of and reactions to EEC print materials, (5) reactions to coaching calls and education from QCs, (6) why/why not callers would recommend the program and recommendations for improvement, and (7) diary completion experiences. Findings will be used to augment other data to determine readiness for Phase 2, as well as to refine the treatment and measures. **Criteria for Proceeding to Phase 2.** 8/10 participants would recommend the EEC to other ENDS users. 7/10 report improved knowledge about ENDS and NRT. 7/10 articulate QPs that include adaptive, but not maladaptive strategies. Iterative changes will be made to the EEC; if benchmarks are not met, we will recruit for Phase 1 until the EEC is ready.

Table 2. Study Measures

Questionnaire	Baseline	Diary assessments	Outcome Survey[b]
Demographics (age, gender, race/ethnicity, education, chronic conditions, etc)	X[a]		
Smoking/Tobacco use details (time to first use, cigarettes per day, types of tobacco, last use, tobacco users at home/work)	X[a]	X (selected items)	X
ENDS use details (type of ENDS product, frequency of use, last use, reasons for use, nicotine content, ENDS users at home/work)	X	X (selected items)	X
Penn State E-cigarette Dependence Questionnaire[30]	X		X
Use of FDA-approved cessation medications	X	X	X
Knowledge and Beliefs about ENDS and FDA-approved cessation aids	X		X
Psychosocial functioning: PHQ-2 (depression),[95] GAD-2 (anxiety),[96] PSS (Stress)[97,98]	X		X
Cravings, open-ended questions on quit challenges		X	X
Program Satisfaction and Acceptability			X
Collaborate, 3-items[c] (SDM assessment)[94]			X
Engagement data (call completion, call minutes, NRT sent through QL)	Recorded by coaching application		
Adverse events (any serious adverse events are also recorded on coaching calls)		1x/ wk	X

[a]Standardly collected at QL enrollment. [b]Multimodal Outcome Survey at end of treatment (approx. 2-months post-registration) in Phase 1 and at 3 months post registration in Phase 2. [c]"Health issue" terminology will be edited to increase specificity to quitting smoking.

2.3c Phase 2: Randomized pilot to test feasibility and acceptability, and explore preliminary efficacy. Design. Pilot study with 100 ENDS and cigarette dual users randomized (1:1) to EEC intervention or QL TAU. Phase 2 will use the same EEC intervention and procedures described and refined in Phase 1 with several

exceptions described below. **Procedures.** *Recruitment, Study Offer, and Consent.* Participants who meet eligibility criteria based on standard registration questions will be asked if they would like to participate. Interested dual users will then be asked if they are willing and able to complete short daily questionnaires. Those who respond yes will be called back by a QC to complete consent, baseline measures, and be randomized to TAU or EEC. Randomization will be stratified by gender to ensure equal representation of males and females in each group. Participants will then immediately receive their first coaching call. *Inclusion Criteria.* Same as Phase 1. On average, 140 OKHL callers report ENDS use each month. Based on previously conducted studies, we estimate 40% (56) will meet other eligibility criteria, from which we expect to be able to recruit 80% (44) per month, allowing us to easily reach our *N*=100 goal over 6 months. *EEC Intervention Protocol.* The EEC intervention will be developed and refined as described in Phase 1 and will follow the call schedule in Table 1. *QL TAU (Control).* The QL program (described in Table 1) has been proven effective and cost-effective in numerous clinical trials and evaluations for the general population of smokers.[22,43-47] AWI's general approach for addressing ENDS during coaching calls was described above;[48] however, our qualitative work suggested ENDS are often not discussed or only discussed briefly on calls.[3] **Fidelity.** The research team will review call recordings and complete fidelity coding for 20% of EEC and TAU calls. Feedback will be provided to coaches weekly. Other fidelity domains will be reviewed and rated per procedures outlined by Borrelli and colleagues.[88,89] **Measures.** All measures and compensation are as described in Phase 1 with three exceptions: (1) additional measures or measure changes needed based on Phase 1 work, (2) Outcomes Survey will be completed at 3-months post-registration in Phase 2 (in Phase 1, outcomes will be assessed at end of treatment), and (3) Qualitative interviews will be completed with 10 EEC participants total. In line with published recommendations,[99] we are not including biochemical abstinence verification due to no face-to-face contact and no expectation for systematic reporting bias across groups. Moreover, the primary goal of the EEC is smoking cessation at 3 months. Participants may or may not be using ENDS at that time. ENDS use can result in salivary cotinine levels similar to cigarette smoking and that exceed standard biomarker thresholds, which limits utility for assessing smoking abstinence in this study.[99,100] **Strategies to Minimize Attrition.** Our team has obtained outcome survey response rates of 80% using multiple modalities (phone, email, mail), incentives, and alternative contacts provided at baseline. Dr. Wagener's team has achieved diary completion rates of 59% in weeks 1 and 2 of an adaptive intervention study including ENDS devices; we aim to improve these rates with additional incentives, monitoring and reminder protocols. We will use participant retention and education strategies addressing research participation and engagement in consent materials.[101] Call completion will be monitored and improvements made (e.g., increasing attempts) if needed.

2.4d Statistical Analysis. Participant baseline characteristics and program engagement will be summarized using proportions (with 95% confidence intervals (CIs)) and means (with SEs). We will use regression (and non-parametric rank sum tests) to examine primary hypotheses that, at 3-months, EEC participants will (1) have completed as many or more calls, (2) have satisfaction rates at least as high and rate QP development experiences more positively, and (3) report more accurate beliefs about ENDS, smoking, and quit medications, compared to TAU. Secondary outcome analyses will examine rates of 7-day point prevalence smoking abstinence and of ENDS and cigarette dual use. The control and EEC groups will be compared using logistic regression for binary outcomes or ANCOVA for continuous outcomes, while controlling for relevant baseline data (caller characteristics, nicotine dependence, smoking history). Diary data will be reviewed to categorize frequency and characteristics of ENDS, cessation medication, and cigarette use. We will explore correlates of outcomes based on product use reported on diaries to examine potential mechanisms that lead to smoking cessation or continued dual use of cigarettes and ENDS. Finally, we will explore potential group differences or moderators of treatment engagement and outcomes (e.g., gender, age, race/ethnicity, reasons for ENDS use).

We will address missing values multiple ways: 1) analyzing existing data (responders), 2) assuming worst case (smoking) for missing, 3) using multiple imputation, and 4) conducting sensitivity analyses with different non-responder relapse probabilities to determine how extreme values would need to be to invalidate results. For all aims, preliminary analyses will include summary statistics, cross tabulations of outcomes and baseline variables by group, and correlations. Standard regression diagnostics will be performed.

Sample Size/Power. Assuming 30% loss-to-follow-up, we will have 3-month outcomes for 35 per group, which aligns with Pilot/Stage I study recommendations.[70, 92] While this feasibility study is not powered to identify significant differences at the 5% alpha level, examination of CIs can identify outcomes or moderators worth investigation in a larger trial and inform treatment refinement, while avoiding over interpretation of effects.

This study will test the first behavioral cessation treatment tailored to ENDS and cigarette dual users and provide currently unavailable ENDS and NRT use pattern data in relation to smoking outcomes.