

Article

Pilot Study of Electronic Nicotine Delivery Systems (ENDS) Cessation Methods

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Abstract: Currently 7.6% of the U.S. young adults aged 18-24 years old currently use e-cigarettes. This study piloted three methods of ENDS cessation by measuring cessation rates, motivational techniques that contributed to cessation success, and participants' changes after decreasing vape use. Participants were randomized into three study arms [nicotine replacement therapy (NRT) + behavioral support, vape-taper + behavioral support, self-guided] in a 1:1:1 ratio. All participants were invited to attend 9 in-person or phone appointments over the 6 month study period. At 12 weeks, 3 of 7 (42.9%) participants in the NRT + behavioral support arm, 6 of 8 (75%) vape-taper + behavioral support arm, and 7 of 9 (77.8%) self-guided arm self-reported being vape- and nicotine-free. At 6 months, 3 of 7 (42.9%) participants in the NRT + behavioral support arm, 6 of 8 (75%) vape-taper + behavioral support arm, 4 of 9 (44.4%) self-guided arm self-reported being vape- and nicotine-free. A challenge to quitting and remain quit is social pressures, but participants identified self-control and establishing new habits to be the best methods to overcome the desire to vape. Participants who received behavioral support and a vape-taper plan from pharmacists were more likely to be vape- and nicotine-free at 6 months.

Keywords: Electronic nicotine delivery systems, vaping, cessation, nicotine addiction

1. Introduction

Electronic nicotine delivery systems (ENDS), commonly referred to as vapes or e-cigarettes, have gained popularity in recent years, especially among teens and young adults [1]. The most recent U.S. data reports 7.6% of 18-24 year olds use electronic cigarettes [2]. Many adolescents try flavored ENDS products because of social pressures without knowing they contain nicotine, which can lead to nicotine addiction, increased use, and use of marijuana [3-6]. Adolescents are also more likely to transition to traditional cigarettes after trying ENDS; 30.7% of ENDS users reported recent use of at least one combustible tobacco product at a six month follow up, compared to 8.1% of participants who had never used ENDS [7].

While many people believe ENDS to be safer than combustible cigarettes, research has shown that ENDS users obtain plasma nicotine concentrations similar to combustible products and have been linked to many health issues [8-13]. Since 2019, e-cigarette or vaping product use associated lung injury (EVALI) has been diagnosed in over 2,800 patients and the cause of sixty-eight deaths [9].

Many health care providers are unsure of how to help their patients quit ENDS due to lack of research [10-13]. National Cancer Institute and the Truth Initiative each sponsor a tobacco quit service that utilizes text messaging for behavioral support [14,15]. The Truth Initiative's BecomeAnEx program had 46% of participants report reduced ENDS use and 16% report ENDS cessation in two weeks. Most enrollees indicated a desire for additional and longer support in their quit attempt [16]. This research shows that behavioral support and frequent touchpoints are important components of quitting ENDS, but neither program assesses pharmacotherapy. The use of

nicotine replacement therapy (NRT) has been well established in smoking cessation for traditional cigarettes, but currently there is only one case report for using NRT in the cessation of ENDS, giving limited information on how to appropriately dose patients [17]. Additional literature to support clinicians to help ENDS users to quit is a case study using a vape-taper and another case study using varenicline [18,19].

The objectives of this study were to pilot three methodologies of ENDS cessation by measuring cessation success rates, motivational techniques that contributed to cessation success, and participants' changes after decreasing vape use.

2. Materials and Methods

Adults who currently vape were recruited to enroll in the study through informational fliers posted in town and emails sent through a university's listserv to employees and students. The enrollment goal was 30 total participants, 10 in each arm. Researchers recruited from May 2019-January 2020 and enrolled participants on a rolling basis.

Inclusion criteria for the study population included adults who used ENDS at least 4 days a week and were motivated to quit within 2 weeks. Exclusion criteria included the following: participants who were pregnant or plan to become pregnant, have had a heart attack or stroke in the past 2 weeks, or have poorly controlled COPD or asthma.

The framework of the study design was based off of smoking cessation research using a 12 week timeframe, high touch points with participants, and healthcare professionals offering support and guidance [20,21].

Block randomization was used to place eligible participants in 1 of 3 arms [NRT (nicotine patch +/- nicotine lozenge or gum) + behavioral support, vape-taper + behavioral support, or self-guided quit] in a 1:1:1 ratio. Due to the nature of the intervention, blinding was not done for the researcher or participant.

Arm 1: Participants in the NRT group were provided behavioral support and nicotine patches and/or either nicotine gum or lozenges based on their personal preference. NRT quit plan was determined based on their Fagerstrom Test for Nicotine Dependence score modified for vaping [24,26].

Arm 2: Participants in the vape-taper group used their own ENDS and e-juice. They received both behavioral support from a pharmacist as well as a recommended nicotine vape-taper plan (Figure 1) based on their current e-juice nicotine concentration and vaping habits.

Arm 3: Participants in the self-guided group served as the control group, and were asked to become vape and nicotine free within 12 weeks. They did not receive behavioral support from the research team, but were asked at each call and in-person appointment to discuss their quit attempt to help the researchers identify additional cessation methods for future studies.

Behavioral support provided to Arm 1 and Arm 2 was provided by the pharmacist after probing questions (Supplemental Table 1) to identify the patient's motivating factors, challenges, and strategies for success. The pharmacist would provide some tips on strategies for success if the patient was unable to identify any. This time provided opportunity for open dialog between the patient and pharmacist.

Each participant received a \$20 gift card at 4, 8, and 12 week appointments. Participants in the self-guided group and vape-taper group were expected to purchase their own vaping supplies so they received an additional \$40 gift card at enrollment, 4, and 8 weeks to cover out-of-pocket expenses.

All participants had the same appointment and phone call schedule and were referred to the Michigan Tobacco Quitline [22].

Prospective data collection occurred over the 6-month study period. Baseline data was collected from each participant at enrollment during the initial in-person appointment. Additional data was collected at phone calls at 3-7 days, 2 weeks, 6 weeks, 10 weeks, and 6 months. Participants were asked to attend in-person appointments at 4 weeks, 8 weeks, and 12 weeks to collect data, vitals, and receive NRT, if applicable. The Fagerstrom Test for Nicotine Dependence (FTND) was modified by

the researchers (referred to as mFTND) to quantify nicotine addiction related to vaping habits. The mFTND was used on all participants to track dependence over the study time period. Participants were asked a series of open-response questions related to withdrawal symptoms and other health effects related to the study.

Participant demographics, tobacco use, and quit-method perceptions were summarized. Relative effectiveness of the three arms were measured by comparing the participant outcomes of successful vape and nicotine cessation at 12 weeks and 6 months. The percentage of participants quitting at their 12 week appointment was compared between groups using the chi-squared test. For each group, changes in mFTND score and biometric measures (blood pressure, heart rate, and body weight) from baseline to 12-week appointment were compared using the Wilcoxon sign rank test and the paired t-test, respectively. When determining the status of quitting, any participant that was vaping or using nicotine products or were lost to follow-up was assumed to still be vaping. For other variables, missing data resulting from lost to follow-up or refusal to answer were excluded from the analysis of that variable. Test results with p-values less than 0.05 were considered significant. Open-response questions were coded and then classified using a sentiment analysis to decipher positive and negative effects. One researcher did the initial work that was then reviewed by another researcher. Disagreements were discussed by a third researcher to come to a final conclusion.

The study was approved by the Ferris State University Institutional Review Board, project identification code FY18-19-27. All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki.

3. Results

Twenty-nine individuals set-up initial appointments, but initial data was only collected for twenty-four participants due to failure to attend the initial appointment (Supplemental Figure 1). Of the twenty-four participants who were assigned to one of the study arms, eight participants were lost to follow-up during the 6 month study period. The NRT arm lost the highest percentage of participants compared to the other arms. Twelve week data was collected on 20 participants. The majority of our participants were male (71%) and white (79%). The average age of all study participants was 19.8 years \pm 2.1. Mean age, sex, and vape history of each group are shown in Table 1. No statistical significance was seen in baseline demographics between groups. Participants in the NRT arm reported a lower concentration of nicotine e-juice and shorter duration of vaping. However, the NRT group reported more time spent vaping and consumed more milliliters of e-juice a day compared to the vape-taper and self-guided arms; these differences were not statistically significant (Table 1). The NRT arm had a lower average mFTND at baseline compared to the other arms (Table 1).

At baseline, the majority of our study participants had systolic blood pressures that were above the normal pressure of <120 mmHg (Table 1). The self-guided arm average systolic blood pressure decreased over 12 weeks, while the NRT and vape-taper groups had a modest increase in systolic blood pressure (Supplemental Table 2). At baseline, participants' heart rates were within normal range (60-100 bpm), and decreases were seen in the majority of participants in the NRT and vape-taper groups (Supplemental Table 2). Increases in weight were seen in all arms, with the NRT arm having the largest average increase compared to the vape-taper and self-guided groups (Supplemental Table 2). No significant differences were found between groups for any vitals collected over the study period (Table 2).

Our primary endpoint was number of participants to self-report being vape- and nicotine-free at 12 weeks and 6 months. The self-guided arm had the highest percent of successful attempts with 77.8% of participants reporting vape- and nicotine-free at 12 weeks, but this number dropped to 44.4% at 6 months. The vape taper arm showed favorable results of 75% quit at 12 weeks and 6 months. The NRT arm had the lowest success rate with 42.9% (Table 2).

3.1. Figures and Tables

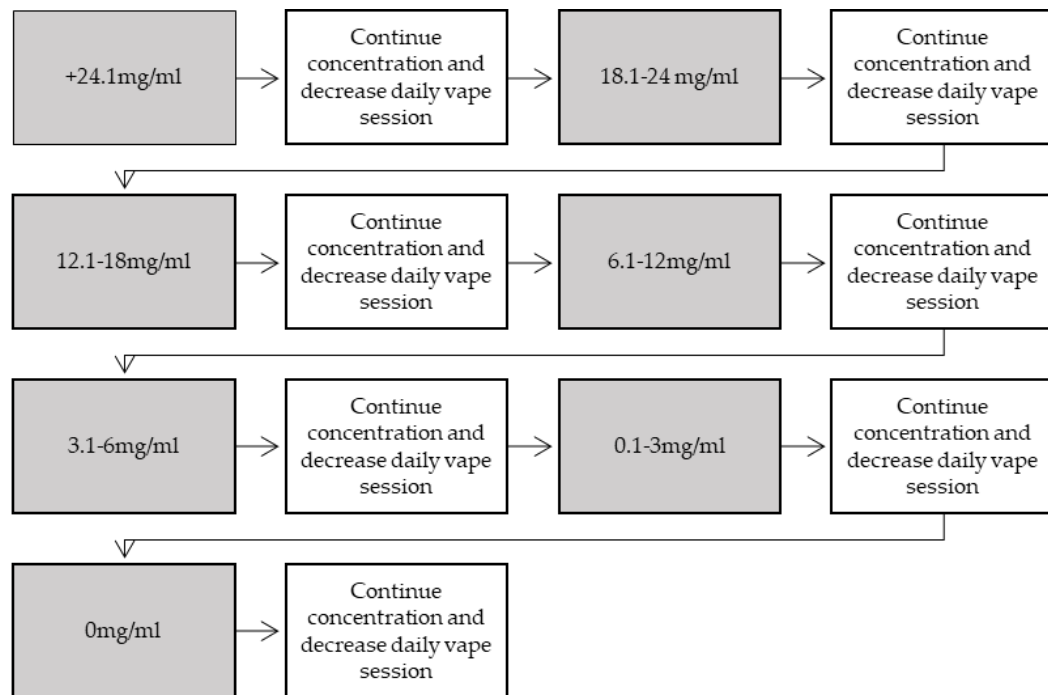


Figure 1. Taper schedule used for vape-taper arm. Vape taper will aim to decrease amount of nicotine consumed by reducing concentration and frequency over time. Start at the participant's current nicotine concentration of vape liquid. The first week the participant will decrease vape exposure by one session per day or decrease duration of sessions (~10-15% of time spent vaping), and the second week the participant will decrease nicotine concentration of vape as shown in the diagram above or by ~20-25%, depending on available products. If unable to complete the step then repeat the same step until successful before moving on. Steps will be followed until participant is vape and nicotine free.

Table 1: Demographics and Baseline Data by Study Arm

	Nicotine Replacement Therapy + Behavioral support (n=7)	Vape-taper + Behavioral support (n=8)	Self-guided (n=9)
Mean Age (SD), y	22.6 (7.3)	20 (2.3)	19.4 (1.5)
Male, n (%)	5 (71.4)	7 (87.5)	5 (55.6)
Mean e-juice nicotine concentration (SD), mg/mL	40.14 (18.17)	43.13 (16.4)	49.11 (8.55)
Mean e-juice daily consumption (SD), mL/day	3.56 (6.33)	1.08 (0.5)	1.21 (0.91)
Mean time spent vaping (SD), hr/day	2.64 (2.59)	0.95 (0.96)	1.3 (1.1)
Mean duration of vape history (SD), y	1.74 (1.31)	2.75 (1.28)	2.8 (2.33)
Mean past quit attempts (SD)	2.7 (1.1)	3.9 (3.5)	3 (1.3)
Mean mFTND score (SD)	4.57 (3.1)	5.38 (2.62)	6.11 (1.69)

mFTND= modified Fagerstrom Test for Nicotine Dependence

Table 2: Selected Results during Study Period by Each Study Arm

	Nicotine Replacement Therapy + Behavioral support (n=7)	Vape-Taper + Behavioral support (n=8)	Self-guided (n=9)	P-value
Quit at 12 weeks ¹ , n (%)	3 (42.9)	6 (75)	7 (77.8)	0.280
Quit at 6 months ¹ , n (%)	3 (42.9)	6 (75)	4 (44.4)	0.350
Continuous quit at 6 months ^{1,2} , n (%)	2 (28.6)	3 (37.5)	1 (11.1)	0.440
Mean mFTND score: 4 weeks (SD)	0.80 (1.79)	2.88 (1.86)	3.67 (2.78)	0.109
Mean mFTND score: 8 weeks (SD)	0.00 (0.00)	1.29 (1.60)	1.33 (1.41)	0.077
Mean mFTND score: 12 weeks (SD)	1.00 (1.41)	0.33 (0.82)	1.11 (2.26)	0.703
Mean mFTND score: 6 months (SD)	1.00 (2.00)	0.00 (0.00)	0.83 (1.60)	0.349
Mean e-juice daily consumption at 4 weeks (SD), mL/day	0.002 (0.004)	2.02 (3.27)	2.37 (2.50)	0.015
Mean e-juice daily consumption at 8 weeks (SD), mL/day	0.00 (0.00)	0.92 (1.40)	0.26 (0.59)	0.037
Mean e-juice daily consumption at 12 weeks (SD), mL/day	0.9 (1.75)	0.00 (0.00)	0.32 (0.71)	0.277
Mean e-juice daily consumption at 6 months (SD), mL/day	0.18 (0.35)	0.00 (0.00)	0.25 (0.52)	0.341
Mean Systolic blood pressure: 12 weeks (SD), mmHg	136.20 (13.04)	129.33 (13.16)	127.88 (6.94)	0.404
Mean heart rate: 12 weeks (SD), bpm	71.40 (17.60)	71.83 (12.83)	75.63 (19.62)	0.884
Mean Weight:12 weeks (SD), lbs	205.80 (46.86)	185.00 (31.73)	171.88 (38.81)	0.338

¹ Current use of ENDS or tobacco or lost-to-follow up were analyzed as not quit

² Patients have not vaped or used any tobacco since original quit date

mFTND= modified Fagerstrom Test for Nicotine Dependence

The mFTND score decreased within all study arms from baseline (Table S1). The drop in scores is clinically significant to show that as vape users consume lower concentrations and vape less, they become less dependent on the habit of vaping and nicotine contained in the e-juice. No participants used the Michigan Tobacco Quitline or any additional quit services during the study period.

Participants in all groups experienced positive and negative effects during the first 12 weeks while quitting. Table S2 categorizes the effects into positive or negative themes. The most commonly reported positive effects were improved concentration and focus (20), improved sleeping (20), more energy (9), and better breathing and exercise tolerance (8). Participants reported withdrawal symptoms to improve over time and had fewer cravings to vape or less satisfaction while vaping.

The highest frequency of negative effects occurred in the first four weeks of the study, and were seen most frequently in the self-guided arm (Supplemental Table 3).

NRT-specific adverse effects that were noted were itching and rash with the patch (1) and worse heartburn with the gum (1).

At 6 months, 56% of participants reported the greatest challenge to quitting and remain quit was social pressures. Participants reported using self-control (31%) and establishing new habits (25%) as key techniques to overcome the pressures to vape. Participants reported the greatest benefit to quitting was saving money (44%) and feeling healthier (31%).

4. Discussion

This study had a small sample size and was designed to be a pilot project to explore various methods of helping ENDS users to quit. This study was not powered to determine which method is superior or to set an ENDS cessation protocol, but it shows that all methods are possibly effective options.

With smoking cessation research, it is usual for quit-success rates being low and usually <25% [23]. In this small sample size, quit rates at 12 weeks were seen at higher percentages of 42-77%, and quit attempts lasted for an additional 3 months in 42-75% of participants. Many participants experienced minor slips or relapses during the 3 month observation period of the study, but this is very normal with smoking cessation and showed that the participants had the skills to get back to being quit. All arms had the same appointment schedule, similar data collection from the researchers, and were motivated to quit within 2 weeks of enrollment. This study is in alignment with Graham's results supporting that the structure of a quit program is very important [16].

Participants of the study had more positive health benefits than anticipated. One benefit that is not in current literature, is skin improvement, specifically eczema clearing up for one participant. This may be an added benefit for users who are able to quit using ENDS. The majority of the other positive health benefits were improved sleeping, improved concentration, and breathing better. Positive benefits were seen most frequently in the vape-taper arm compared to the other two arms. Personal benefits that many of the users experienced included saving money, breaking dependence to nicotine, and pride in their accomplishment to quit. Negative health effects that were seen were expected issues with withdrawal symptoms and known adverse events of NRT. The self-guided arm experienced more negative effects compared to the arms with behavioral support from a pharmacist indicating that support from a healthcare provider can make for a smoother quit attempt.

Some of the barriers identified in this study included mindless use of ENDS, poor adherence to NRT, and social pressures. Participants found it challenging to quantify ENDS use by amount (mL/day), time (hr/day), and even triggers because it was such a subconscious activity. Participants noted that after enrolling in the study, they were much more cognizant of when they were vaping which allowed them to work on reducing their consumption. The NRT arm participants typically used less NRT than what was recommended by the pharmacist. This could have been a reason for why a smaller percentage of the NRT arm was successful in quitting. The other large barrier with ENDS use is social factors and pressures. This is a huge issue with young adults including our study population. Additional education is needed to change the perceptions and use of ENDS by taking away its "cool" persona.

This study population does not correlate to all ENDS users since it was conducted on a college campus and only students enrolled. Of the adult population, the age range with the highest percentage of ENDS users are 18-24 years old which does fall in line with our study population. The majority of the study population was white males which is also supported as a group with the highest prevalence of e-cigarette use compared to females and other races [24].

While this study demonstrated that multiple methods may contribute to ENDS cessation success, and that pharmacist-led behavioral support is associated with ENDS cessation success, further research is warranted to better elucidate behavioral support strategies and pharmacotherapy that offer greatest efficacy. Research should also focus on quantifying use and dependence in order to appropriately pair NRT. Some studies have been done to do this, but there are still many

confounding factors with ENDS such as nicotine concentration, lack of regulation on manufacturing and quality, quantifying use, device differences, and e-juice variances [27-29].

5. Conclusions

This study has shown ENDS users to be successful at quitting within 12 weeks of starting a quit-program. Participants who received behavioral support and a vape-taper from pharmacists were more likely to be vape- and nicotine-free at 6 months. This study shows that frequent touchpoints and program structure may be important pieces to helping motivated users to quit, but more robust assistance and behavioral support from pharmacists can provide a more positive quit attempt with fewer negative effects and a more lasting quit attempt.

Supplementary Materials: Figure S1: Participant Flow Chart, Table S1: Behavioral Support Question Prompts Administered to Study Participants by Pharmacists, Table S2: Pre-post Comparison of Dependence and Vitals within Study Arms, Table S3: Frequencies of Participant-Perceived Effects and Withdrawals by Study Arm.

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