The Effect of Electronic Nicotine Delivery System Use on Combustible Cigarette Smoking: Findings from a Randomized Trial

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Research Objective

Smoking is still the leading cause of preventable death and disease, contributing to half a million deaths per year in the U.S. alone.

Electronic Nicotine Delivery Systems (ENDS) are alternative products for adult smokers who seek to switch away from combustible cigarettes. These products are a non-combustible alternative that deliver nicotine through vapor. They are designed and intended to compete with cigarettes, but without the smoke from burning tobacco.

Many prior studies suggest that using ENDS can reduce cigarette smoking[1][2][3]. However, many of these studies utilize retrospective data from smokers who purchased ENDS, and this group may be systematically different in behavior than the average smoker in the population. One approach to reduce this type of selection bias and understand the switching potential of ENDS is prospective random assignment.

We sought to understand the impact of making ENDS products available to daily smokers, by conducting one of the first real-world studies that examine the impact of random assignment of ENDS products on cigarette smoking.

Population Studied

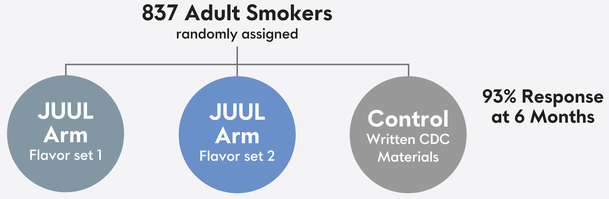
Participants were selected from the U.S. general population through probabilistic address-based sampling to recruit a nationally representative sample.

Enrolled study sample included 837 adult daily smokers who were age-verified to be over 21, smoked at least 10 cigarettes/day (as verified by self-report at two baseline measurements), had not used ENDS products in the past month, and were willing to try ENDS products.

Participants were not recruited based on expressed interest in quitting smoking; fewer than 3% indicated that they planned to quit smoking in the next 30 days at baseline.

Study Design

Figure 1. Study Design and Random Assignment



Participants were randomly assigned to 1 of 3 study arms (**Figure 1**); two intervention arms received ENDS products over the course of the study (JUUL device and a variety of cartridges), with different flavor sets available to each group (one set included a starter pack variety of 4 flavors, while the other included tobacco flavored cartridges). Respondents were also free to purchase other cartridges on their own externally throughout the study, and many respondents reported doing so in both intervention arms. As such, differences in outcomes between both arms related to assignment to flavor set can not be assessed. In the control arm, participants were given written materials developed by the CDC on approved means of smoking cessation.

Participants were given a baseline survey to assess basic demographics and smoking behavior and history, and then followed longitudinally. Follow-up assessments were conducted at 6 months to understand changes in smoking behavior. Analyses were conducted separately for all three arms, and also with the pooled data for the intervention arms as compared to the control arm.

Key outcomes assessed at follow-up included switching (reporting not smoking at all, not even a puff, for at least 30 days) and reductions in cigarette consumption among those that continued to smoke. Analyses were conducted for those who provided full baseline data and smoking status at the 6-month follow-up point. All data were self-reported.

This study was authorized by the ethical review committee of the Advarra Institutional Review Board (Columbia, MD, USA).

Principal Findings

A response rate of 93% was achieved across study arms at the 6-month follow-up point.

Key Outcomes (Table 1):

In the control arm (received printed materials), 4.3% of respondents reported that they had not smoked a cigarette in the past month at the 6-month follow-up arm. In the intervention arms (received ENDS products), 20.8% of pooled respondents reported not smoking for 30 or more days at 6 months. The rate of no longer smoking was significantly higher in the intervention arm than the control arm ($p<0.001$).

Similarly, a significantly higher percentage of those in the intervention arms (8.6% pooled) than the control arm (3.6%) reported reducing their daily smoking to 10 or fewer days in the past month at follow-up but did not stop smoking entirely ($p<0.001$).

There was a 52.1% average reduction in total cigarettes smoked per day at follow-up in the intervention (ENDS) arms, vs. 23.2% in the control arm ($p<0.001$).

Differences in cigarette smoking reduction and switching (no longer smoking) rate were not statistically significant between both intervention arms. Findings reported above were consistent when comparing each intervention arm separately to the control arm.

Stratified analyses (**Table 2**) showed that among those in the intervention arms, there were no statistically significant differences in reported rates of switching (no longer smoking) by baseline demographic characteristics such as gender, age, employment status, or a proxy measure for socioeconomic status (usually purchasing high cost vs. low cost cigarettes, relative to median cigarette cost).

Binomial and logistic regression models (**Table 3**) demonstrated that after controlling for demographic characteristics and smoking history, participants in the intervention arms had significantly higher odds of reporting no longer smoking, and significantly lower rates of daily cigarette consumption, as compared to those in the control arm (all adjusted Odds Ratios and Relative Rate Ratios $p<0.001$).

Table 1. Six Month Follow-Up Outcomes Among Baseline Daily Smokers Randomly Assigned to Intervention and Control Arms (Sample: Respondents at Baseline and 6 Months)

	Pooled Intervention Arms (ENDS)	Control Arm (Printed Materials)	P value
No smoking, not even a puff, for at least 30 days	20.8%	4.3%	<0.001
Substantial Reduction: Smoking 1-10 days in past 30 days	8.6%	3.6%	<0.001
Average Reduction in Daily Cigarette Consumption	52.1%	23.3%	<0.001

*Note: As a sensitivity analysis, we also calculated switching rates among the enrolled sample, where we assumed that those who dropped out at 6 months continued to smoke. Given the low dropout rate, these rates were not drastically different. Switching rates with this approach were 16.1% to 18.5% in the two intervention arms (once again, not significantly different from each other), and 3.7% in the control arm.

Table 2. Stratified Rates of Switching (Reporting No Longer Smoking in Past 30 Days at 6 Month Follow-Up) by Key Demographic Variables, Pooled Across Intervention Arms

Baseline Demographic Characteristic	Switching Rate - Characteristic Level 1	Switching Rate - Characteristic Level 2	P value (between group comparison)
Gender	*Male* 18.7%	*Female* 23.2%	0.202
Age	*Adults aged 21-30* 25.4%	*Adults aged 30+* 20.4%	0.361
Employment Status	*Employed* 21.7%	*Not Employed* 21.7%	0.987
Proxy Socioeconomic Status Measure [Cost per Pack of Usual Cigarettes Purchased lower or higher than Median]	*Purchase High Cost Cigarettes* 19.7%	*Purchase Low Cost Cigarettes* 23.8%	0.291

Table 3. Binomial and Logistic Regression Modeling of 6 Month Follow-Up Smoking Status and Cigarette Consumption Between Intervention and Control Arms

	Intervention Arm 1 vs. Control (Reference)	Intervention Arm 2 vs. Control (Reference)	Intervention Arm 1 (Reference) vs. Intervention Arm 2
Unadjusted Logistic Regression- Odds of No Longer Smoking for at least 30 Days at 6-Month Follow-Up	5.02*** [2.48 -10.18]	5.93*** [2.94 -11.93]	1.18 [0.76 -1.82]
Adjusted Logistic Regression^- Odds of No Longer Smoking for at least 30 Days at 6-Month Follow-Up	6.91*** [3.18 - 15.01]	6.64*** [3.17 - 13.89]	0.88 [0.56 - 1.38]
Adjusted Binomial Regression^- Relative Rate of Cigarettes Smoked Per Day at 6-Month Follow-Up	0.69*** [0.59 -0.82]	0.65*** [0.55 -0.76]	0.93 [0.79 -1.10]

***p<0.01

Implications for Policy or Practice

This work provides strong evidence that the availability of ENDS products can help adult smokers with switching away from smoking combustible cigarettes. Policy makers should consider the potential impact of making alternative products available to smokers when designing harm reduction policies.

Conclusion

Similar to prior studies of ENDS use, this study demonstrated significant reductions in cigarette smoking and level of cigarette consumption among adult smokers randomized to receive ENDS products as compared to a control arm.

These findings are particularly important as the study included daily smokers, the majority (97%) of whom did not plan on quitting smoking in the next 30 days at baseline. This group of smokers may have difficulty switching from cigarettes.

Further research is needed on long-term switching among adult smokers using ENDS, as well as the long-term impact of ENDS use.

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[2]Russell, Christopher, Farhana Haseen, and Neil McKeganey. "Factors associated with past 30-day abstinence from cigarette smoking in a non-probabilistic sample of 15,456 adult established current smokers in the United States who used JUUL vapor products for three months." Harm reduction journal 16.1 (2019): 22.
[3]Prakash, S., Wissmann, R., Vose, J., Russell, C., McKeganey, N., Augustson, E. (2019, May). Identifying Predictive Attributes of Adult Smokers Who Cease Combustible Smoking using the JUUL Electronic Nicotine Delivery System (ENDS) via Logistic Regression and CART. Poster presented in Mental Health Research Session. International Society for Pharmacoeconomics and Outcomes Research, New Orleans, LA.

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