Published on *The National Law Review* https://www.natlawreview.com

Largest U.S. E-Cigarette Clinical Trial Confirms Role in Smoking Cessation

Article By:

Azim Chowdhury

Neelam Gill

A new study published this month in The Lancet's *eClinical Medicine* – the largest electronic cigarette (e-cigarette) clinical trial in the U.S. to date – confirms the role of e-cigarettes in smoking cessation. Specifically, the new research supports that e-cigarettes can be a viable means of quitting or reducing more harmful combustible cigarette use for adult smokers (21+). This study, significant because it supports the role that e-cigarettes play on cigarette reduction or quitting *in the real-world setting* (i.e., without detailed instructions or additional cessation support), was conducted using 639 adult smokers across 11 U.S. cities over a span of four years. Previous studies supporting the smoking cessation benefit of e-cigarettes have been far more structured and included smokers wanting to quit. Many have criticized the application of these types of studies to the real-world setting, contending that such studies do not reflect how adult smokers actually initiate and use e-cigarettes.

To address this concern, researchers in the recent study employed a predominantly naturalistic or "hands-off" approach by providing a group of random adult smokers (regardless of motivation to quit) with NJOY closed-tank e-cigarettes pre-filled with 3 mL of flavored e-liquid containing 15 mg/mL of nicotine. These participants were given little instructions on use, no cessation support, and broad discretion of whether and how much to use the study product. The other control group of adult smokers, on the other hand, did not receive any study product.

The NJOY e-cigarette was selected for this study given its status as the National Institute on Drug Abuse (NIDA) Standardized Research E-Cigarette (SREC) for research purposes, which means that it is now a standardized product that will be used in other lab-based studies. For this study, however, the product was provided in its original packaging to more closely approximate real-world use. Study participants could choose up to two flavors among five of the top-selling flavors offered: tobacco, menthol, blue/blackberry (one flavor), apple melon, or iced fruit, and could change selection at the second shipment. These top five selling flavors were offered to more closely represent a real-world scenario of e-cigarette uptake and use. The study aims, however, did not specifically address the role of these flavors in measuring naturalistic uptake, patterns of use, combustible cigarette reduction or cessation behavior, or other assessments such as biomarkers and adverse events.

When compared to the control group, the study found that, across the board, the e-cigarette group

was more likely to self-report a reduction of cigarettes consumed per day, more quit attempts, and complete abstinence from combustible cigarettes:

As a whole and with few exceptions, cessation and smoking reduction outcomes favored the e-cigarette group, even among smokers who expressed little interest in quitting at study outset. Smokers in the e-cigarette group showed declines in cigarette dependence and increased motivation and confidence to quit smoking, with minimal reported adverse events compared to the no-product control group.[1]

This finding is key, particularly given that the study specifically included smokers with little to no interest in quitting. At all time points, researchers found that e-cigarette dependence was significantly lower than combustible cigarette dependence based on the Penn State Nicotine Dependence Index. The results suggest that unguided e-cigarette use can lead to smoking cessation and address the criticism that causal effects of e-cigarettes on cessation are not reflective of the real-world scenario of self-determined use.

One limitation of the study was that the data relied on participants' self-reports of their smoking behavior in the absence of biochemical verification of smoking cessation or reduction. Although the research team initially attempted to verify participants beginning with a subsample from one of the 11 cities (Charleston, SC) by inviting these participants into the research lab to provide biochemical verification of smoking behavior, this was not completed due to COVID-19-related shutdowns and challenges. Nevertheless, self-reporting is generally considered to be a reliable way of assessing behavior and behavioral intentions[2] and, coupled with the strengths of the study – i.e., the large, randomized (removing selection bias), and largely naturalistic design – the results of this significant new study provide additional evidence that e-cigarettes have the potential to benefit public health for current smokers who try e-cigarettes by reducing smoking and promoting cessation.

[1] *See* https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370%2823%2900319-X/fulltext#%20.

[2] *See* U.S. Food & Drug Admin., Guidance for Industry: Tobacco Products: Principles for Designing and Conducting Tobacco Product Perception and Intention Studies (August 2022) at 11 (available at https://www.fda.gov/media/143322/download) (FDA acknowledging that "[s]elf-reported intentions to use tobacco products are considered proximal predictors of behavior, and can help inform FDA's evaluation of [an] application, for example, by providing information relevant to evaluating how [the tobacco] product could affect the likelihood of use among different groups.")

National Law Review, Volumess XIII, Number 242