



Is Nicotine Reduction in Cigarettes Enough?

David B Abrams, PhD; Caitlin Notley, PhD

In July 2017, the US Food and Drug Administration (FDA) announced a proposal to limit all cigarettes to those with very low nicotine content (VLNC) as a key part of the comprehensive plan for nicotine regulation. The objectives of that plan are to promote smoking cessation in existing adult smokers and to help keep those who are experimenting, especially young people, from progressing to persistent smoking.¹ For more than a decade, the FDA has funded research on the use of VLNC cigarettes among the general population of smokers. Higgins et al² examined the changes in consumption of VLNC cigarettes in 3 groups drawn from vulnerable populations: individuals with affective disorders, those with opioid use disorder, and women with socioeconomic disadvantage. These populations have disproportionately high rates of smoking and low rates of cessation and warrant special attention as a matter of social justice as well as health. Paid volunteers were randomized to receive experimental cigarettes with normal nicotine content or cigarettes with 2 levels of VLNC. After a week of smoking to establish a baseline, participants were given their assigned cigarettes for 12 weeks. Participants received twice the number of baseline cigarettes used to allow for the possibility they might smoke more. However, participants in the VLNC groups often used their own brand of cigarettes, despite instructions not to do so, complicating interpretation of results. The primary outcome was that those in the 2 VLNC groups smoked about 5 to 7 cigarettes less per day than control participants. There were small decreases in carbon monoxide and nicotine dependence in the VLNC groups, but, importantly, there was no difference in smoking cessation. The suggested conclusion of the study by Higgins et al² is that “reducing nicotine content of cigarettes to low levels has the potential to benefit populations that are vulnerable to tobacco use, addiction, and smoking-attributable morbidity and mortality.”

Is this strong policy statement warranted by the findings in this study? We think not. The main finding—a modest within-trial reduction in cigarette consumption—does not support the objectives of the comprehensive plan for nicotine regulation at a national level. The ability of the VLNC intervention to promote smoking cessation was specifically tested at week 12 when participants were offered \$100 to abstain from smoking for 24 hours, a modest goal given that most smokers who abstain for 24 hours relapse, and smokers do not get such offers in real life. The VLNC intervention did not result in smoking cessation.² This raises serious questions about the conclusion that a VLNC cigarette policy alone would promote smoking cessation or reduce morbidity and mortality. The health benefits of VLNC cigarettes remain unclear. Reductions in the level of NNAL (4-[methylnitrosamino]-1-[3-pyridyl]-1-butanol), a biomarker for tobacco smoke carcinogens, were small, and 1 group (opioid users) experienced an increase in the level of NNAL.²

To effectively support policy change, research that considers the broad context of the whole FDA strategic plan is required.¹ Areas to be considered include evidence from implementation studies of real-world use rather than ideal conditions, unintended negative consequences associated with VLNC cigarettes, complex market forces, evolving safer nicotine products, complex user behaviors, and even black markets. Consideration of black markets is particularly useful when attempting to make nicotine, which is an avidly sought-after commodity for over 30 million smokers in the US and 1 billion smokers worldwide, so much harder to obtain in legitimate cigarette products.³

Any VLNC cigarette policy needs to be considered—as the FDA intended—as just 1 part of a broader initiative to move nicotine seekers completely away from smoking deadly combusted cigarettes. Cigarettes with VLNC are at best half of the policy. The FDA put it plainly the “new tobacco strategy has two primary parts: reducing the addictiveness of combustible cigarettes while

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recognizing and clarifying the role that potentially less harmful tobacco products could play in improving public health."^{1(p1112)}

The second part of the FDA's comprehensive nicotine plan is making available substantially less harmful products by which nicotine can be delivered without the toxic effects of tobacco smoke. The most common way of using nicotine without smoke, indeed without tobacco, is nicotine vaping (e-cigarettes), which decreases exposure to harmful chemicals,^{3,4} emits no carbon monoxide, may facilitate the switch from cigarettes to medicinal nicotine or nicotine products without smoke,^{3,4} can complement the use of VLNC cigarettes,⁵ and may accelerate saving smoker's lives.^{3,4} It is encouraging to note that the FDA has recently authorized a modified-risk marketing order for a product that heats but does not burn tobacco and will be reviewing the safety of other nicotine vaping products in the near future, allowing for clearer communication to the public that smokeless nicotine product use may be associated with lower exposure to harmful chemicals. In terms of smoking behavior, to encourage more smokers to switch from deadly cigarettes to medicinal nicotine or nicotine products without smoke, it is essential to correct misperceptions among the public, health care clinicians, and policy makers who believe that nicotine is the most harmful component of smoking. The FDA has stated that "Nicotine, though not benign, is not directly responsible for the tobacco-caused cancer, lung disease and heart disease that kill hundreds of thousands of Americans each year."^{1(p1112)}

Embodied in FDA's modeling study,⁶ which predicted that 8.5 million smokers' lives could be saved by reducing the levels of nicotine in cigarettes, is the need to implement both parts of the comprehensive nicotine regulation plan. Harm reduction keeps the focus squarely where it should be: on reducing the severe disease burden and mortality associated with smoking.^{1,3-6} The FDA plan accepts that many smokers may not want or be able to achieve complete nicotine abstinence, but they do not have to die from the method of nicotine delivery. The perfect public health outcome would be for people who are already using any form of nicotine to stop all use and abstain for their lifetime or, better still, never to start. But a pragmatic public health approach requires that realistic alternatives to de facto nicotine prohibition be considered.³ Cigarettes are by far the most popular yet deadly route of nicotine administration. Safer alternatives are now available along the FDA nicotine harm continuum.^{1,3,4} Years of robust evidence are available for the use of nicotine replacement therapy (NRT) as a safe way to deliver clean nicotine. But after more than 25 years, NRT has not become a viable vehicle for displacing smoking at a scale to impact the population, partly because of inadequate nicotine delivery and its unattractive and expensive medicinal positioning in the market. Far more smokers try to quit by vaping nicotine than with NRT.^{3,4} Many former smokers enjoy vaping nicotine and report its advantages.^{7,8} They find vaping nicotine to be a reasonable and safer substitute for smoking.^{4,9} Informed by rigorous evidence reviews, the United Kingdom endorses harm reduction (including vaped nicotine e-cigarettes) as part of a comprehensive tobacco control plan.⁴

Whereas other fields have accepted that continued safer use of a psychoactive drug may help avoid more serious harm (eg, methadone maintenance in people dependent on opiates) the tobacco control field is not quite there yet. The combination of VLNC in deadly combusted cigarettes with the availability of adequate alternative nicotine delivery products holds promise to rapidly reduce smoking, which remains the leading cause of premature death in the US.¹⁰ The time has come to rethink nicotine use. The lives of 1 billion smokers worldwide are at stake.

ARTICLE INFORMATION

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Corresponding Author: David B. Abrams, PhD, School of Global Public Health, New York University, 715 Broadway, 12th Floor, New York, NY 10003 (da94@nyu.edu).

Author Affiliations: Department of Social and Behavioral Sciences, School of Global Public Health, New York University, New York, New York (Abrams); Norwich Medical School, Faculty of Medicine and Health Sciences, University of East Anglia, Norwich, United Kingdom (Notley).

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