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Another Study Shows Electronic Cigarettes Harm Lungs: It Is Time for Researchers to Move from the Tobacco Playbook to a Tobacco Endgame

Electronic cigarette (e-cigarette) use is common among adolescents and young adults. An entry to nicotine addiction, e-cigarettes are casually associated with future combustible cigarette and dual-use among young people and with significant harm to cardiovascular and respiratory health in adults. In this issue of the *Journal*, Xie and colleagues (pp. 1320–1329) report on the association of electronic cigarette use with respiratory symptom development among young adults in the United States using data from the PATH (Population Assessment of Tobacco and Health) study (1). They present longitudinal data from PATH Waves two through five, reflecting survey data from 2014 to 2019, demonstrating that both former and current e-cigarette use is associated with the development of respiratory symptoms and wheezing in 18- to 24-year-old young adults who otherwise had no respiratory disease or symptoms at baseline. The associations were seen whether or not subjects reported ever smoking combustible cigarettes.

As the authors note, "e-cigarettes have gained immense popularity," including high rates of current e-cigarette use among youth who have never smoked combustible cigarettes. This state of affairs has come about through deliberate and effective targeting of youth through investments in marketing and promotion by the tobacco industry. Abundant evidence shows that e-cigarettes contain toxic chemicals with inflammatory and carcinogenic effects; while concentrations are often lower than those found in combustible cigarettes, this is relevant to their potential harm-reduction benefit and not to addiction of new users.

This paper reports important and significant findings contributing to our understanding of the harms of e-cigarette products. The analysis uses all available PATH data and appropriately excludes participants with preexisting respiratory disease. Young people with asthma, for example, are likely to have very different patterns of use and exposure and to have been nonusers of any nicotine products because of potential symptom exacerbation. Xie and colleagues cite two other longitudinal studies using PATH data to explore the association between e-cigarettes and wheezing. One, using longitudinal data, reported similar odds of wheezing in 12- to 17-year-old adolescents who used e-cigarettes (2). The other, using the same data and similar design, found dual use of e-cigarettes and combustible cigarettes, but not e-cigarettes alone, associated with more respiratory symptoms in those aged 12 or older (3). Another research group is constructing summary measures to define "'functionally important respiratory symptoms" with regard to self-reported health status, using PATH data (4).

The important underlying questions, however, are not whether symptoms are casually proven if one includes the few 12- to 14-year-olds who vape in samples or whether young people develop wheezing, cough, or both symptoms from e-cigarette exposure. Nor is it appropriate to conclude that more research is needed to understand what damage these products might cause. Rather, the question that must be asked is whether these competing analyses continue to undermine and delay effective action to protect the public's health. Throughout its history, the tobacco industry has used multipronged efforts to distort and promote disagreement over the scientific evidence, and uses these controversies to delay effective regulatory action (5). The "tobacco playbook" is increasingly recognized in other industries, and its effects are clearly seen in the

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deadly inroads made by Juul and other e-cigarette manufacturers in their addiction of the current generation of youth (6). But does PATH data help counter the industry's efforts to addict youth and avoid regulation, or not?

PATH is an annual longitudinal survey of large nationally representative samples of adults and youth, funded by NIH and the U.S. Food and Drug Administration (FDA) to inform the FDA's regulatory decisions and actions under the 2009 Family Smoking Prevention and Control Act (7). The act empowers the FDA to implement standards for tobacco products, requires warnings to protect public health, and mandates that the FDA act to prevent addiction of youth. Sadly, evidence-based actions that could help protect youth are stalled or delayed, allowing the promotion of e-cigarettes to continue unchecked. The age of legal tobacco product purchase in many states is now 21, and thus the vast majority of young adult and all adolescent users are doing so illegally. Many papers from PATH avoid discussion about the addictive nature and toxicity of nicotine or the implications of their findings on the FDA's efforts to prevent youth addiction and protect young people. By side-stepping the strong evidence for causality, these studies avoid discussing the implications of their data for a "tobacco endgame" (8) and risk being used out of context to feed the "controversy" over the evidence.

This variation in interpretation of the evidence about e-cigarettes is not unique to studies of their health effects. Another obvious example is the interpretation of evidence for whether these products are useful in cessation. Here, too, conflicting conclusions arise from the same data. The Cochrane collaborative meta-analysis concluded that "nicotine e-cigarettes probably do help people to stop smoking for at least 6 months," noting moderate-certainty evidence that e-cigarettes with nicotine increase quit rates compared with nicotine replacement therapy (9). In contrast, Wang and colleagues, in meta-analyses of the same literature, found that as consumer products in observational studies, e-cigarettes were not associated with increased smoking cessation, but that in randomized clinical trials, provision of e-cigarettes as a therapeutic intervention was associated with increased cessation (10). This latter framing provides a specific and relevant finding to the FDA and to others seeking to limit or reduce smoking and tobacco-related diseases. But many who advocate for the promise of e-cigarettes for harm reduction ignore or minimize the impact of unrestricted marketing of these products.

It is time for all tobacco control researchers to call on our professional colleagues and the NIH and FDA to keep new findings grounded in an "endgame", a framework for ending the tobacco epidemic. The "tobacco endgame" reorients tobacco "control" toward plans for ending the tobacco epidemic and envisions a tobacco-free future (11). The idea of an endgame has been discussed by the CDC, the Surgeon General (12), and the World Health Organization Framework Convention on Tobacco Control (13); and, in 2021, the state of California formally adopted an endgame policy initiative, with a commitment toward ending the commercial tobacco epidemic in California by 2035 (14). The FDA, the entire Public Health Service, and the whole of U.S. Government should endorse and support tobacco endgame goals; and tobacco control researchers should consistently recognize and frame our research findings in alignment with endgame policies to prevent new addiction and end the tobacco epidemic. ■

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