POLICY FORUM

PUBLIC HEALTH

Evidence, alarm, and the debate over e-cigarettes

Prohibitionist measures threaten public health

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This is a moment for legitimate alarm at the intersection of two distressing but distinct epidemiological patterns involving e-cigarettes ("vaping"): an increase in vaping among youth and a sudden outbreak of acute lung injuries and deaths in the United States, associated most strongly with vaping tetrahydrocannabinol (THC), the main psychoactive compound in cannabis. Discussions of vaping, however, often neglect distinctions between nicotine and THC; between adults and youth; and between products obtained through the retail and black markets. As we move to confront these challenges, we face the danger that justifiable alarm will turn alarmist, short-circuiting careful analysis of the full range of evidence and focusing attention on the most frightening, thus enhancing the prospect of adopting counterproductive policy. We suggest that the evidence warns against prohibitionist measures. Restricting access and appeal among less harmful vaping products out of an abundance of caution while leaving deadly combustible products on the market does not protect public health. It threatens to derail a trend that could hasten the demise of cigarettes, poised to take a billion lives this century.

For years, some leaders in the public health community observed with concern the rise in the number of U.S. adolescents who are vaping flavored liquids. Debate centered on whether vaping devices, which do not burn tobacco but rather heat liquids containing some combination of flavors and/or nicotine and/or THC, should be viewed as an intolerable threat to nonsmoking youth, or whether they can be managed with reasonable regulations that give adult smokers access to less hazardous alternatives to deadly combustible cigarettes (*1*, *2*).

This summer, the tone of the debate shifted markedly. The U.S. Centers for Disease Control and Prevention (CDC) reported sudden clusters of serious and sometimes fatal respiratory injuries. As of 4 December 2019, the CDC reported 2291 cases and 48 deaths. The CDC and the U.S. Food and Drug Administration (FDA) warned consumers not to vape THC or any liquids obtained off the streets or from unknown sources (*3*). In the ongoing investigation to determine the causes of illness and death, the CDC identified vitamin E acetate, a THC product additive, as "a chemical of concern." Nicotine or flavored vaping liquids have not yet been implicated.

Even as the investigation was under way, interest in prohibitionist measures swelled. Massachusetts banned retail and online sale of all nicotine vaping products until January 2020. San Francisco will ban all nicotine vaping products in early 2020. Michigan has banned all flavors (except tobacco flavor, meant to make a vaping liquid taste like a traditional combustible cigarette) for nicotine products, but not for THC. Ohio may ban menthol and mint flavors in e-cigarettes while still allowing them in more harmful cigarettes and little cigars. The American Medical Association called for a total ban on all vaping products. New York City is poised to become the largest jurisdiction to ban all flavored nicotine vapes including menthol, although it chose not to enact a menthol ban for combustible products. As a measure of the magnitude of the urge to weigh in, even the White House has offered policy pronouncements, including a potential ban on all nicotine vape flavors except tobacco, from which it recently backed off. Such sweeping measures have been adopted in the face of continuing debate over the public health impact of such interventions.

THE CONTESTED HISTORY OF HARM REDUCTION

There has been a long debate in the United States about harm reduction as an evidence-based approach to reduce harms associated with life-threatening behaviors by providing safer, although not totally safe, alternatives. For example, despite strong, albeit always imperfect, evidence demonstrating the effectiveness of needle exchange programs in countering the spread of HIV infection, it took decades to overcome reluctance to providing sterile needles to people who inject drugs. Battles over needle exchange persisted long after the evidence was clear, and programs suffered under on-again, off-again federal funding.

For those addicted to combustible tobacco, harm reduction is a pragmatic approach (*4*). From the 1950s through the early 1980s, public health officials saw great promise in so-called "safer" combusted tobacco. Interest died with the emergence of damning evidence about mass deception on the part of the tobacco industry over light and low-tar cigarettes. In the 1990s, nico-

Although not safe, vaping nicotine represents a safer alternative to combustible cigarettes for adult smokers who cannot or will not quit smoking.

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tine replacement therapies (NRTs) became widely available over the counter. NRTs were framed both as medicinal treatment and as a harm reduction approach, and the public health and medical communities were prepared to tolerate lifelong use of nicotine if necessary (*5*).

When vaped nicotine products first came on the scene, the harm reduction debate reignited. In the early years, the scientific evidence for this new technology was sparse (*4*). Some saw in them promise for adults who smoked, but most assumed a precautionary posture, arguing that we first required certainty about safety and efficacy.

Even as scientific studies emerged, many who were skeptical of vaping nicotine wanted stronger proof that such products were safe, effective, would not lead to greater net population harm than benefit, and would not renormalize smoking, in advance of allowing them to be sold. As time went on, although uncertainties remained, those open to harm reduction became more willing to act to provide alternatives. They believed the emerging science was sufficiently strong and the global toll of preventable smoking deaths remained so massive and urgent that benefits outweighed harms (*4*, *6*).

Vaping nicotine grew in popularity as products delivered nicotine in ways that were more appealing (e.g., flavored e-liquids) or more efficient (e.g., nicotine absorption began to mimic the effect of combustible products). In parallel, systematic reviews of the science accumulated, demonstrating that although such products were not safe, they were safer than combustible products. They became more popular and more effective than medicinal NRTs at helping smokers quit.

The U.S. FDA and the United Kingdom's (UK) Public Health England (PHE), which carefully tracked the evidence, showed openness to harm reduction, describing the importance of recognizing a continuum of risk, with combustible products at the far end of that continuum. Even some early skeptics of nicotine vaping changed their minds and began to attend to the scientific evidence that increasingly addressed the uncertainties when it came to a harm reduction approach. Yet there was also a wide spectrum of what counted as harm reduction. For example, some proposals suggested taxing nicotine vaped products at the same rate as combustible products (described by some as harm reduction in name only). Others suggested leaving vape products untaxed while doubling the tax on combustibles to incentivize smokers to switch. Nonetheless, with different degrees of enthusiasm and intent, harm reduction was the new lingua franca by 2017 (*7*).

VEXING TENSIONS

In the United States, broad comfort with using harm reduction as a kind of policy language evaporated in the face of evidence that both the promise and peril of safer nicotine delivery alternatives to combusted tobacco that we have imagined for more than half a century materialized at the intersection of the twin phenomena of increased youth vaping and acute lung injuries and deaths.

In the case of youth who would not likely otherwise smoke or use nicotine in any form, vaping offers no benefits and introduces potential harms of nicotine dependence and a possible transition to combustible products (*1*, *4*, *8*–*10*). U.S. surveys confirm a large increase in the proportion of high schoolers who reported any vaping in the past 30 days, from 11.7% in 2017 to 27.5% in 2019. As expected, the majority of vaping is infrequent (experimental) and there is a positive association between vaping and smoking, but the public health impact remains unknown, nor is there a consensus on whether such an association constitutes a causal pathway (*4*, *6*, *8*–*10*). The majority who vape (about 60% of those who experiment, about 89% of regular vapers) are also smokers or former smokers. The calculus is complex: In a policy landscape in which, in virtually all locales, vaped nicotine products and all types of tobacco (smokeless and combusted) can be legally purchased at age 18, large numbers of 12th graders who vape do so legally (*1*, *2*, *4*, *8*, *9*). Contemporaneously, population youth smoking rates dropped much faster in the years vaping surged the most (2013–2019) than in prior years, reaching record lows during that same period (*2*, *9*), which suggests that nicotine vape use may be replacing smoking more than promoting it (*1*, *4*, *6*, *8*, *9*).

"...the evidence warns against prohibitionist measures."

We share strong concern about the large surge in youth vaping (some call it an epidemic and point to studies of a possible but unproven causal gateway into smoking) and we promote harm minimization and management. Yet we suggest that careful analysis of all the data in context indicates that the net benefits of vaped nicotine products outweigh the feared harms to youth (*4*, *6*, *8*).

Complicating the question of the relative harms of youth vaping are data showing that some youth only vape flavored products (without nicotine or THC), and 41.8% of vaping youth report vaping THC. Some U.S. states have legalized cannabis for adults. In others it remains illegal. The impact of the black market, a source of contaminated THC-based oils, has been devastating. Although the carrier liquids and additives in THC oils are different and more hazardous than those used safely for a decade in commercial nicotine products or flavors alone, there are unknown risks from unregulated and illegally obtained products. Addressing the rapid rise in teen use of vaping is imperative. But public health measures must not neglect distinctions between nicotine and THC as well as between products obtained through the retail and black markets. The illegal marketplace provides access to both THC and nicotine-based products at costs lower than over the counter. Users can obtain products not available over the counter. In a black market, age is no barrier to access. Further, there is evidence that in the face of bans, adolescent vapers switch to smoking (*11*). Regulation inevitably produces the possibility of the black market, but the approach to regulation can make the black market more or less attractive and more or less harmful to users, be they youth or adults.

In the case of adult smokers, there is solid scientific evidence that vaping nicotine is much safer than smoking. In a 2018 report by the U.S. National Academies of Sciences, Engineering, and Medicine (NASEM), commissioned by the FDA, an expert panel systematically reviewed the scientific evidence. It determined, "There is conclusive evidence that completely substituting vaping nicotine for combustible tobacco cigarettes reduces users' exposure to numerous toxicants and carcinogens present in combustible tobacco cigarettes" (*10*), consistent with other major evidence and systematic reviews (*4*, *6*, *12*).

But what this NASEM determination of less harm meant for overall public health impact was another question. Concerned with uncertainties, particularly involving presumed high risks to youth, some of the NASEM report authors made clear that their findings should not be construed as blanket support for harm reduction. A contemporaneous systematic review conducted by PHE came to a different conclusion about the promise of nicotine vaping as a safer alternative to smoking by weighing concerns about youth differently (*4*, *6*, *8*–*10*).

Although it may be decades before we fully understand the long-term consequences of vaping nicotine without smoke, many argue that we know enough and stress that too many smokers die every day we delay taking reasonable and rational action based on the science to date. Evidence from multiple strong observational studies and randomized trials suggests that vaping nicotine is more appealing and more effective than NRT at displacing smoking (*4*, *6*, *8*, *13*). Vaping flavors with or without nicotine may appeal to youth, but flavors also appeal to adult smok-

ers and help them switch. Evidence suggests that the vast majority of smokers who successfully switch completely from smoking combustible products to vaping do so—after weeks, months, or years of dual use—by transitioning from vaping tobacco, or menthol-flavored liquids, to other flavors and often to lower nicotine concentrations or even to no nicotine in order to reduce the triggers that remind them of their prior smoking product (*4*, *6*, *13*, *14*).

THE WAY FORWARD

Making policy in the absence of evidentiary certainty must involve trade-offs. Policy action has consequences for those who have never smoked, especially youth. It also has implications for current and future smokers. It is estimated that more than 1 billion smokers will die prematurely across the globe in the 21st century. We believe that the complex calculus of pros and cons warrants finding an optimal balance (*4*, *6*, *8*), thereby making fully regulated nicotine vaping products available to smokers while adopting forceful measures to limit the risks to and use by youth as much as possible. The UK, which embraced nicotine vaping harm reduction as a safer alternative to combustible products, has been able to accomplish appropriate regulation that has managed both youth nicotine uptake and helping adult smokers to quit. The UK, through the Medicines and Healthcare Products Regulatory Agency (MHRA), has a notification system that requires assurance by the maker about the safety and quality of any product on the market. The UK also prohibits sale of THC products. In addition to a system for reporting adverse events, the MHRA maintains a website so users can determine whether products are being legally sold. UK measures reflect regulatory requirements in the European Union.

Although the U.S. health care, advertising, and regulatory systems are different from those in the UK, there are measures we can take short of outright bans. The United States needs a regulatory infrastructure to ensure that products on the market are as safe as possible. The FDA should implement a product monitoring system or require manufacturers to conduct product monitoring under Section 915 of the Tobacco Control Act. Prudent product standards (neither overly burdensome nor too lax) should rapidly be promulgated by the FDA Center for Tobacco Products for vaping nicotine products as a class.

Menthol is the single most critical flavor when it comes to both adult and youth smoking. Despite two FDA-derived reports that recommended a ban on menthol in combustibles, there has been policy paralysis in the face of appalling evidence: 52% of all youth and more than 90% of African American youth initiate smoking with menthol. If we are going to take policy action on flavors, menthol in combustible products must be the first target.

The challenges of nicotine vaping also demand a rigorous system of surveillance that might detect an unanticipated harm early, similar to pharmaceutical post-market surveillance for adverse events. Although the CDC and FDA, through searching and rigorous analyses, are pinpointing the source of the sudden serious and deadly lung injuries (*3*), there is the risk that additional complications will emerge. Vitamin E acetate may not be the only chemical of concern. Ongoing surveillance is the best means of detecting harm in a situation where we may never have absolute certainty about safety.

No youth (for policy purposes, traditionally less than age 21) should use nicotine in any form (regardless of whether it is vaping or more harmful smoking) or use any form of THC. Current U.S. laws restrict purchase of alcohol to those 21 or older. The U.S. Institute of Medicine issued a 2015 report indicating that age 21 restrictions on tobacco sales would reduce teen tobacco uptake and save lives. Failure to promulgate age 21 purchase laws across the United States and enforce restrictions is unacceptable. Taxation has also proved an effective means of pricing products out of the hands of youth. Setting vaping nicotine taxes lower than those on combustible products can help keep products out of the hands of teens but still provide an incentive for adult smokers to switch. Communicating accurately the absolute and relative harms for vaping nicotine compared with smoking is critical so smokers can make informed decisions. Finally, predatory marketing to youth should be prohibited.

But appropriate regulation and strong limits on youth access will only address part of the U.S. problem. Although they are not nicotine or tobacco products, THC vaping products must be addressed nationwide.

THREADING THE NEEDLE

Every day, more than 2500 U.S. teens start smoking, and about 1300 U.S. adults who cannot stop smoking cigarettes die prematurely; 5.6 million U.S. youth alive today will die from smoking, feeding the pipeline of 35 million U.S. adult smokers, more than half of whom will die prematurely, despite efforts to prevent all youth uptake. Sixteen million people in the United States suffer with smoking-related illnesses such as cancer, emphysema, chronic obstructive lung disease, and other debilitating chronic diseases.

The most conservative estimates suggest that were vaping nicotine to replace most smoking over the next 10 years, 1.6 million premature deaths would be avoided and 20.8 million quality adjusted years of life would be saved in the United States alone. The greatest gains would be among younger cohorts (*15*). Across the globe, more than 8 million smokers will die prematurely from smoking cigarettes, not from nicotine itself, in 2019 alone. The potential benefit of appropriately regulated, innovative, noncombusted nicotine modes of delivery could have a tremendous impact globally.

The mounting numbers of acute lung injuries and deaths linked to vaping illicit THC cartridges have understandably fueled a policy impulse to do something. Although blanket bans on all devices, all types of liquids (with or without nicotine or THC), or flavors other than tobacco may provide immediate relief to our collective sense of urgency when it comes to protecting youth, the landscape has changed over the past decade. The calculus is no longer limited to nicotine vaping. Proposed solutions that conflate vaping THC oils with nicotine or with flavors, and that may lose sight of population-wide issues while focusing on subsets of the population (*4*, *6*, *8*, *9*), may do more harm than good.

Whatever specific regulations and policies are promulgated at local, state, national, or international levels, policies or regulations must be risk-proportionate. The most harmful products on the nicotine-harm continuum, combustible products, should be much more aggressively and stringently regulated than less harmful noncombusted nicotine products. Policies that fail to differentiate will fail public health. ■

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