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Commentary
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The Gateway Effect of E-cigarettes: Reflections on Main Criticisms

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Introduction

The recent spread of e-cigarette use has spurred not only enthusiasm about their harm reduction and smoking cessation potential but also concerns about possible risks from long-term use, and stalled cessation through dual use.[1] Another main concern is that e-cigarette use is increasing among tobacco-naive youth[2] than among only adult smokers who are using them for cessation and expectation of risk reduction.[1] With youth smoking at all-time lows in several nations with advanced tobacco control programs,[3–5] there are therefore concerns that e-cigarettes may stall or reverse these declines as youth who were likely to never use any form of nicotine become familiar with it, and start experimenting with other forms of nicotine delivery.

These concerns were strengthened by the recent publication of a meta-analysis of longitudinal studies showing that e-cigarettes can serve as a gateway to later cigarette smoking among nicotine-naive youth.[6] They were also emphasized by the 2018 report of the National Academies of Sciences, Engineering, and Medicine (NASEM),[7] which concluded that such studies "provided "strong evidence of plausibility and specificity of a possible causal effect of e-cigarette use on smoking…" with the Committee "consider[ing] the overall body of evidence of a causal effect of e-cigarette use on risk of transition from never to ever smoking to be substantial" (pp. 16–32).

By contrast, Public Health England concluded, "Despite some experimentation with these devices among never smokers, e-cigarettes are attracting very few young people who have never smoked into regular use".[8]

Given the importance of putative gateway or "catalyst"[9] effects in assessing the population impact of e-cigarettes, proponents of e-cigarettes were quick to criticize such evidence and their underlying gateway hypothesis.[10–13] In the context of this debate, the gateway hypothesis is adapted to denote the use of less harmful forms of nicotine delivery (eg, e-cigarettes), leading to the use of more harmful ones (eg, combustible cigarettes).[7,10–13] We here present and respond to three major criticisms that have been made of e-cigarettes' gateway potential based on currently available evidence.

Downward Trends in Adolescent Smoking Are Incompatible With a Gateway Effect for E-cigarettes

Several prominent harm reduction proponents have argued that the gateway hypothesis is incompatible with population trends in the United States[3] and United Kingdom[4] of declining adolescent smoking. The argument here runs that vaping has been rising while smoking continues to fall, so vaping cannot be causing smoking to any significant degree among adolescents.[13]

In both nations, declining trends of smoking among youth were apparent well before the introduction of e-cigarettes.[14–16] Moreover, associations in population trends are known to be prone to the ecological fallacy; that is, what is true at the population level may not be true at the individual level, especially when other population-level attributes are not considered (eg, effective tobacco control policies). Specifically, the ecological argument relies on an assumption that the population net impact of any putative gateway effect of e-cigarette use would be larger than the combined net impact of all other policies, programs, and factors that are responsible for reducing adolescent smoking prevalence (eg, tobacco tax and retail price, measures of the denormalization of smoking, exposure of children to adult-targeted quit campaigns, retail display bans, health warnings, plain packaging).[17] This is an extremely high bar that gateway critics demand that anyone suggesting gateway effects needs to jump over. The combined impact of such factors in preventing uptake could, thereby, easily mask considerable smoking uptake that might not have occurred in the absence of e-cigarettes.

With smoking prevalence at record lows in the United States, England, and Australia, only adequately powered longitudinal studies, which control for factors known to be associated with smoking uptake, are vital to examining potential gateway effects.[9] Nine such studies were included in a 2017 meta-analysis.[6] Adjusting for demographic, psychosocial, and behavioral risk factors for cigarette smoking the meta-analysis showed that, the odds of subsequent cigarette smoking by nonsmokers who had *any* experience of vaping more than tripled compared with those with no vaping experience.

Common Liability Rather Than Gateway?

One of the main criticisms of the gateway hypothesis lies in the difficulty in excluding other mechanisms for the observed relationship between vaping and later cigarette smoking. The most commonly proposed alternative explanation is based on the "common liability theory,"[18] which emphasizes shared predisposing characteristics among multidrug users. According to this hypothesis, a "propensity" for drug use predicts multidrug use. Interestingly, however, several longitudinal studies have reported the strongest association between e-cigarette use and smoking initiation among youth with the lowest risk of smoking.[19–21] Moreover, recent evidence using national data from the United States shows that a third of youth who start with e-cigarettes have risk profiles that make them unlikely to start with cigarettes.[22]

Rather than being mutually exclusive, the gateway and common liability hypotheses are likely to be complementary. Common factors will explain the use of drugs in general, and specific factors will explain why young people use specific drugs and in what contexts.[23] This dynamic perception is in line with contemporary models of behavioral change being dependent on the balance between intention and ability. Intention implies individual factors including any propensity for drug use. However, such factors are contingent on environmental conditions, such as access and feasibility of drug use for intentions to be materialized.[24]

Indeed, the success of most tobacco control was the result of targeting those potentiating environmental factors rather than some innate propensity to use drugs. The salience of these environmental factors is also evident from societal trends of smoking propagation in response to tobacco industry marketing and obstruction of tobacco control policies, as well as declines in smoking in response to successful implementation of effective population-based policies.[17]

The wide availability and intense marketing of e-cigarettes and their low-risk appeal may coalesce to increasingly make e-cigarette delivered nicotine the likely first drug on a multidrug cascade. But, rather than be alarmed by these developments, e-cigarette proponents use this to argue against a specific temporal sequence needed to establish causality. For example, Etter argues, "The temporal sequence argument would not hold if the ordering of product use was explained solely by the ordering of opportunities to use the products, rather than by some inherent capacity of vaping to cause smoking."[10] In reality, things are far more complicated, and relationships between risks (causes) and outcomes are complex, nonlinear, and multidirectional.[25] For example, obesity leads to joint stress, and joint problems also potentiate obesity through reduced movement. Which of these comes first and how they interact at different stages, ages, and contexts is dynamic rather than static relationship.[25] A recent study applying a prospective design and causal analytical framework found a bidirectional association between e-cigarette use and cigarette smoking among 11–18 year olds in Great Britain, yet the association was stronger from ever e-cigarettes use to cigarettes initiation.[26] So if e-cigarettes are a gateway into or away from other drugs/tobacco in different situations that does not preclude causality in both directions.

A recent *NEJM* review of the molecular basis of nicotine as a gateway drug by the founder of the gateway hypothesis (Denise Kandel) and her husband (Eric Kandel, 2000 Nobel Prize winner in Medicine for neurophysiology) concluded that "nicotine acts as a gateway drug on the brain, and this effect is likely to occur whether the exposure is from smoking tobacco, passive tobacco smoke, or e-cigarettes."[23] Although the biological basis of nicotine's gateway effect on the brain is likely to be consistent across different delivery means, the manifestation of nicotine dependence can vary according to different nicotine delivery methods (eg, sensory cues in e-cigarettes can be different from those of traditional cigarettes).

E-cigarette proponents often assert that vaping is demonstrably a reverse gateway *out of* smoking for those who quit, while being scathing about suggestions that it could ever be a gateway *into* smoking.[27] Soundbites like "kids who will try stuff, will try stuff" and "kids who will smoke, will smoke" have been repeatedly used as debate enders. Any cessation researcher offering the equally trite "smokers who will quit, will quit" as a serious contribution to understanding the complexity of transitioning out of smoking would be rightly pilloried for their primitive understanding of the complex processes that can culminate with permanent smoking cessation. Yet, with e-cigarettes, all that is apparently required to be said about anyone who smokes regularly is that that they had a propensity to do so. If this hard determinism was all that was needed to be invoked in understanding smoking uptake, how then do we explain the dramatic falls in uptake that have been seen in nations that have robust, comprehensive tobacco control programs? What eroded the "propensity" of all those who never took up smoking? Nicotine liability may well be a predisposing factor, but what of the known tractable reinforcing and enabling factors that tobacco control has so successfully identified and addressed over decades?

The Implausibility of Experimental Vaping Transitioning to Smoking?

Another salient argument used by e-cigarette proponents is that studies showing a gateway effect do not differentiate adolescent experimental vaping from more regular use, so "any vaping" is treated the same when the association between vaping and later cigarette smoking is assessed. Etter argued that it is "hardly plausible that a simple puff or a few puffs on an e-cigarette can cause subsequent regular smoking."[10] But of course *every* regular smoker started with a "simple puff," nearly always in adolescence. They then typically progress through more regular use to daily smoking. Birge et al. recently reported that over two thirds of smokers who tried as little as a single puff became, for a time, regular smokers.[28]

Moreover, the assertion about the implausibility of experimental e-cigarette use leading to regular smoking in youth contrasts with an important body of evidence regarding the high susceptibility of children and adolescents to the psychotropic and addictive effects of nicotine. For example, Fidler et al.[29] and others[30] have highlighted that children only require a very minimal exposure to develop an important and identified "sleeper effect": A vulnerability to smoking after trying just a single cigarette, which can lie dormant for 3 years or more: "From a neurobiological viewpoint, neural reward pathways might be changed as a consequence of a single exposure to nicotine,

thus potentially increasing vulnerability to later smoking uptake."[29] Others have referred to an established body of evidence relating to youth nicotine exposure; "Importantly, several studies support that a single drug exposure can lead to changes in synaptic strength that are associated with learning and memory. The high susceptibility of children and youth to the "neurobiological insult" of nicotine was recently been highlighted in the US Surgeon General's report on the potential risks of nicotine and electronic cigarettes to youth.[31] Ultimately, these cellular changes could underlie the long-lasting effects of drugs."[30]

McNeill, who has been persistently critical of gateway effects,[13,32] coauthored two heavily cited articles that noted, "The first symptoms of nicotine dependence can appear within days to weeks of the onset of occasional use, often before the onset of daily smoking."[33] Moreover, in a 30-month follow-up of the same subjects, it was noted, "Symptoms of tobacco dependence commonly develop rapidly after the onset of intermittent smoking, although individuals differ widely in this regard. There does not appear to be a minimum nicotine dose or duration of use as a prerequisite for symptoms to appear. The development of a single symptom strongly predicted continued use, supporting the theory that the loss of autonomy over tobacco use begins with the first symptom of dependence."[34] The clear contrast between the well-established understanding of cigarette smokers' rapid onset of symptoms of nicotine dependence with efforts to trivialize concerns about initial infrequent use of e-cigarettes is therefore noteworthy.

The NASEM report[7] emphasizes that because the e-cigarette phenomenon is relatively recent, "the majority of studies … lack sufficient duration of follow-up to study the naturalistic cigarette smoking progression sequence, which can involve a lengthy period between ever use and reaching daily smoking." Emerging longitudinal data should provide greater clarity on the extent to which "ever" smoking after e-cigarette uptake converts to daily smoking.

Concluding Remarks

Schneider and Diehl in their e-cigarettes as "catalysts" model,[9] given prominent status in the NASEM report, reviewed features of vaping that make it both attractive to adolescents (perceived lower health risks, attractive flavors, lower price, inconspicuous use, higher acceptance among peers and others) and why "increasing familiarity with nicotine could lead to … potential transition to tobacco smoking." They offer several cogent and highly plausible reasons for such transition that gateway opponents seldom consider. These include (1) Accessibility: E-cigarettes and cigarettes are often sold alongside one another. Adolescents who might otherwise never visit a tobacco retailer and be exposed to retail promotions, discount offers, and curiosity push cues would be thus now exposed and (2) Experience: As they state, "Becoming used to the habitual and ritual procedures of smoking such as poise, handling, smoke breaks and body language" may erode negative feelings about smoking in some adolescents and facilitate experimentation with cigarettes. To these we can add the renormalization of the smoking "performance" through e-cigarettes and erosion of indoor clean air policies with e-cigarettes, which might encourage young people, who would not have otherwise done so, to experiment with smoking.[35]

Despite emphatic and repeated claims from transnational tobacco companies over many years that they have no interest in targeting young people to encourage uptake, it would be much in the commercial interests of both the vaping industry and the tobacco industry (where all major companies now sell e-cigarettes) to promote such uptake by youth. A much-quoted 1984 RJ Reynolds tobacco document put this succinctly, "Younger adult smokers are the only source of replacement smokers … If younger adults turn away from smoking, the industry must decline, just as a population which does not give birth will eventually dwindle."[36] With smoking prevalence by youth being at record low levels in an increasing number of nations, the major concern cannot but exist in both the cigarette and vaping industries about the ever-diminishing cohort of young people entering the market. Enticing youth who do not smoke to think of vaping as "safe smoking" may be an essential strategy for long-term survival for both industries, given the major exodus from smoking by youth.

Strategies such as the retail placement of cigarettes with e-cigarettes, retailer incentive promotions to encourage dual use, cross-branding, and promotional activity in poorly regulated environments (especially the Internet) are increasingly used to attract new young customers to e cigarettes. We are probably looking at a fast-emerging picture of broad-based nicotine addiction, with a dominant industry (Big Tobacco) at the helm through mergers and acquisitions providing several product options to suit different sectors of that base. E-cigarettes' availability, low cost, and attractiveness to youth may make them an increasingly likely first step on a possible cascade to other drugs including traditional cigarettes, a concern that has been validated by evidence from a variety of studies. So, rather than being competitive, gateway and common liability are likely complementary (ie, common factors can explain the use of drugs in general, while specific factors can explain why young people use certain drugs and in what sequence).[23]

The NASEM review's[7] categorization of the evidence for the role of e-cigarettes in transitioning to cigarettes as being "strong" and "substantial," together with the undeniable commercial motivations to attract youth into regular nicotine use (including dual use) should be salutary. If Public Health England is correct that the number of children, who have both taken up regular vaping and/or graduated to smoking after first vaping, is currently low, then this may change in response to industry marketing efforts. The public health test of the importance of this if it occurs will be the absolute numbers involved.

The current evidence about this issue is limited by the short time frame of the introduction of e-cigarettes into a market that has other nicotine-based products, to fully understand their effects on these products and their users. It is also limited by the fast evolution of e liquids, and their delivery technology, as well as the scarcity of evidence regarding the potential effects of regulations on the role of these products in the marketplace for nicotine. Notwithstanding, the available evidence provides an unequivocal cause for caution about e-cigarette role as a harm reduction product given the emerging evidence in support of their gateway potential for cigarette smoking.

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References

1. Maziak W. Harm reduction at the crossroads: the case of e-cigarettes. *Am J Prev Med*. 2014;47(4):505–507.

2. Carroll Chapman SL, Wu LT. E-cigarette prevalence and correlates of use among adolescents versus adults: a review and comparison. *J Psychiatr Res*. 2014;54:43–54.
3. Centers for Disease Control and Prevention. Tobacco use among middle and high school students—United States, 2011–2016. *MMWR Morb Mortal Wkly Rep*. 2017;66(23):597–603.
4. Eastwood B, Dockrell MJ, Arnott D, et al. Electronic cigarette use in young people in Great Britain 2013-2014. *Public Health*. 2015;129(9):1150–1156.
5. Greenhalgh EM, Bayly M, Winstanley MH. 1.6 Prevalence of smoking—teenagers. In: Scollo MM, Winstanley MH, eds. *Tobacco in Australia: Facts and Issues*. Melbourne, Australia: Cancer Council Victoria; 2015. http://www.tobaccoinaustralia.org.au/chapter-1-prevalence/1-6-prevalence-of-smoking-teenagers. Accessed January 29, 2018.
6. Soneji S, Barrington-Trimis JL, Wills TA, et al. Association between initial use of e-cigarettes and subsequent cigarette smoking among adolescents and young adults: a systematic review and meta-analysis. *JAMA Pediatr*. 2017;171(8):788–797.
7. National Academies of Sciences, Engineering, and Medicine. 2018. *Public Health Consequences of E-Cigarettes*. Washington, DC: The National Academies Press. doi:10.17226/24952.
8. McNeil A, Brose LS, Calder R, Hitchman SC, Hajek P, McRobbie H. E-cigarettes: an evidence update: a report commissioned by Public Health England. *Public Health England*. 2015;111. http://tobacco.cleartheair.org.hk/wp-content/uploads/2015/08/PHE-e-cig-review-summary-Aug-2015.pdf. Accessed January 29, 2018.
9. Schneider S, Diehl K. Vaping as a catalyst for smoking? An initial model on the initiation of electronic cigarette use and the transition to tobacco smoking among adolescents. *Nicotine Tob Res*. 2016;18(5):647–653.
10. Etter J-F. Gateway effects and electronic cigarettes. *Addiction*. 2017. [Epub ahead of print]. doi:10.1111/add.13924
11. Kozlowski LT, Abrams DB. Obsolete tobacco control themes can be hazardous to public health: the need for updating views on absolute product risks and harm reduction. *BMC Public Health*. 2016;16:432.
12. Kozlowski LT, Warner KE. Adolescents and e-cigarettes: objects of concern may appear larger than they are. *Drug Alcohol Depend*. 2017;174:209–214.
13. Bauld L, MacKintosh AM, Eastwood B, et al. Young people's use of e-cigarettes across the United Kingdom: findings from five surveys 2015–2017. *Int J Environ Res Public Health*. 2017;14(9):973.
14. Johnston L, O'Malley PM, Miech R, Emerson P, Bachman J, Schulenberg J. 2016. *Monitoring the Future National Survey Results on Drug Use, 1975–2015: Overview, Key Findings on Adolescent Drug Use*. Ann Arbor, MI: Institute for Social Research, The University of Michigan.
15. Office on Smoking and Health. Trends in Current Cigarette Smoking. Centers for Disease Control and Prevention; 2016. http://www.cdc.gov/tobacco/data_statistics/tables/trends/cig_smoking/. Accessed July 13, 2017.
16. Health & Social Care Information Center. Statistics on Smoking, England – 2016. https://digital.nhs.uk/catalogue/PUB20781. Accessed January 24, 2018.
17. Pierce JP, White VM, Emery SL. What public health strategies are needed to reduce smoking initiation? *Tob Control*. 2012;21(2):258–264.
18. Vanyukov MM, Tarter RE, Kirillova GP, et al. Common liability to addiction and "gateway hypothesis": theoretical, empirical and evolutionary perspective. *Drug Alcohol Depend*. 2012;123(suppl 1):S3–S17.
19. Barrington-Trimis JL, Urman R, Berhane K, et al. E-cigarettes and future cigarette use. *Pediatrics*. 2016;138(1):1–8.
20. Primack BA, Soneji S, Stoolmiller M, Fine MJ, Sargent JD. Progression to traditional cigarette smoking after electronic cigarette use among US adolescents and young adults. *JAMA Pediatr*. 2015;169(11):1018–1023.
21. Wills TA, Knight R, Sargent JD, Gibbons FX, Pagano I, Williams RJ. Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. *Tob Control*. 2016;1–6. [Epub ahead of print]. doi:10.1136/tobaccocontrol-2015-052705.
22. Dutra L, Glantz S. E-cigarettes and national adolescent cigarette use: 2004–2014. *Pediatrics*. 2017;139(2).
23. Kandel ER, Kandel DB. A molecular basis for nicotine as a gateway drug. *N Engl J Med*. 2014;371(10):932–943.
24. de Vries H, Mudde A, Leijs I, et al. The European Smoking Prevention Framework Approach (EFSA): an example of integral prevention. *Health Educ Res*. 2003;18(5):611–626.
25. Maziak W. Is uncertainty in complex disease epidemiology resolvable? *Emerg Themes Epidemiol*. 2015;12:7.
26. East K, Hitchman SC, Bakolis I, et al. The association between smoking and electronic cigarette use in a cohort of young people. *J Adolesc Health*. 2018. [Epub ahead of print]. doi:10.1016/j.jadohealth.2017.11.301.
27. How Not to Be Duped by Gateway Effect Claims. https://www.clivebates.com/how-not-to-be-duped-by-gateway-effect-claims/. Accessed January 24, 2018.
28. Birge M, Duffy S, Miler JA, Hajek P. What proportion of people who try one cigarette become daily smokers? A meta analysis of representative surveys. *Nicotine Tob Res*. 2017. [Epub ahead of print]. doi:10.1093/ntr/ntx243.
29. Fidler JA, Wardle J, Brodersen NH, Jarvis MJ, West R. Vulnerability to smoking after trying a single cigarette can lie dormant for three years or more. *Tob Control*. 2006;15(3):205–209.
30. Fagen ZM, Mansvelder HD, Keath JR, McGehee DS. Short- and long-term modulation of synaptic inputs to brain reward areas by nicotine. *Ann N Y Acad Sci*. 2003;1003:185–195.
31. U.S. Department of Health and Human Services. *E-Cigarette Use Among Youth and Young Adults*. Altanta, GA: A Report of the Surgeon General, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2016.
32. Bates C, Fagerström K, Jarvis MJ, Kunze M, McNeill A, Ramström L. European Union policy on smokeless tobacco: a statement in favour of evidence based regulation for public health. *Tob Control*. 2003;12(4):360–367.
33. DiFranza JR, Rigotti NA, McNeill AD, et al. Initial symptoms of nicotine dependence in adolescents. *Tob Control*. 2000;9(3):313–319.
34. DiFranza JR, Savageau JA, Rigotti NA, et al. Development of symptoms of tobacco dependence in youths: 30 month follow up data from the DANDY study. *Tob Control*. 2002;11(3):228–235.
35. Dawson CT, Maziak W. Renormalization and regulation of e-cigarettes. *Am J Public Health*. 2016;106(3):569.
36. Burrows DS. *Younger Adult Smokers: Strategies and Opportunities*. Winston-Salem, NC: RJ Reynolds Tobacco Company; 1984. http://legacy.library.ucsf.edu/tid/tqq46b00. Accessed January 29, 2017.