

4th March 2021

Mr. Matthew Cook. Tobacco Products Regulatory Office. Tobacco Control Directorate. Health Canada

RE: Proposal to limit permitted nicotine e-liquid strength to 20mg/ml

We welcome the opportunity to comment on Health Canada's proposal to limit the strength of nicotine e-liquids to 20mg/ml.²

As tobacco and nicotine senior scientists (each with over 40 years in tobacco and nicotine science practice and policy) we do not believe the best and strongest science supports the policy you propose to cap nicotine. Therefore, it is both premature and likely to do much more harm than good to implement such a policy. Our statements are based on what we do know from the best science in full context.

Moreover by way of additional credentials, as a Canadian (Dr. Niaura) and as a former Director of the Office of Behavioral and Social Sciences (OBSSR) for the United States National Institutes of Health (Dr. Abrams) and as the former founding Executive Director and the former Chief Scientist at the Steven Schroeder Institute for Tobacco Research and Policy Studies at the Legacy/Truth Initiative in Washington DC, and as full Professors for many years at Brown University Medical School, at The Johns Hopkins Bloomberg School of Public Health and now as tenured full professors at New York University School of Global Public Health, we (Niaura and Abrams) have also both presented and provided input at previous Health Canada invited conferences related to the specific and complex issues addressed by the disruptive technologies of alternative non combusted nicotine delivery (vape products or e-cigarettes) that have now become established over the last decade. (see about the authors after their signature line for more details below).

We provide in an appendix and in pdf attachments, the scientific backup to our statements herein.

Basically, we have carefully reviewed the statements in the attached appendix (by David Swenor and Clive Bates). We find the appendix to be of the highest scientific quality and integrity. Thus, rather than restate their points we concur with how they have framed and interpreted the science to date. The comprehensive approach has integrity. The big picture involves a complex system of checks and balances and pros and cons that protect the overall health and well-being of the entire population, including youth and also leaves no Canadian or any citizen behind either.

Despite new data about youth uptake and gateways (and some of the Canadian data had to be reinterpreted due to incorrect weightings (By Dr. David Hammond and others) has failed to consider a balanced and careful analysis and the recommendation of many respected experts who have called for more precision in looking at youth use PATTERNS in FULL CONTEXT. Also, our understanding is that Dr. Hammond is testifying against JUUL in a major lawsuit, and thus he has a conflict of interest.

Under the plausible scenarios (and even considering some extreme outlier and dire scenarios with sensitivity analyses), the net deleterious impact of retaining higher nicotine levels is simply not plausible. Moreover, for ANY SMOKER at ANY AGE, the case made by careful analysis of ALL

the science should focus on reducing and eliminating use of the most deadly and lethal combusted smoked tobacco like cigarettes. To do so the retaining of Nicotine Vape removing products must be preserved while protecting youth without removing the most critical factors in Vape products (i.ee. They must be appealing, convenient, much safer and less costly alternative modes of nicotine delivery. **This balance is far more desirable for the population as a whole than for the continued use of deadly combusted (smoked) forms of nicotine delivery. The science backs this up.**

This transition to rapidly make combusted smoking obsolete is the single biggest opportunity the world has ever had in over 100 years. A new disruptive technology has not emerged for less harmful nicotine delivery since the development of the cigarette rolling machine in the 18180's. The new disruptive technology is poised and is already saving lives and improving the quality of life of ALL smokers and also for the majority of youth potential future smokers who would smoke deadly combusted products anyway despite all our best effort to prohibit and prevent their uptake. **Your proposed policy will reverse these trends and drive both youth and adults back to using lethal combusted.**

Reality must take precedence over ideal perfection that is laudable and emotionally appealing but the science shows that it is unrealistic and unattainable. Cherry picking and overweighting some concerning recent youth data ignores the comprehensive overall science in favor of a gateway hypotheses for youth that is misstated and exaggerated and not supported by the science in terms of what has caused the small gateway effect if any at all (see Sweanor and Bates as well as the simulation models and full analysis of the youth uptake data in full context. Such as those by Warner and Mendez and Levy and colleagues). **Models frame a comprehensive plan for nicotine management for public health as a whole They do not support limiting nicotine in Vape products or making them less appealing, quite the opposite.**

This overarching intention to cap nicotine levels in Vaping products has no strong enough scientific rational. In fact, as we have stated in our comprehensive reviews (Abrams Niaura et al. Prev. Med 2018 attached pdf), the new rules prosed by Health Canada deprive unfairly the whole population of the opportunity to make combusted tobacco products obsolete. This can slow the goal to reduce deadly combusted tobacco use more rapidly than ever before possible. This is true even with the uptick in Nicotine Vaping use among some youth in Canada, and in the so-called epidemic in the USA data from 2017 and 2020 that has been debunked as well -- See details in appendix A below and our pdfs attached)

We believe that the most recent scientific information and latest trends, when taken in full context, do not warrant such an extreme policy stance as proposed by Health Canada at this time.

If anything, our comprehensive scientific reviews and the latest scientific information supports and indeed strengthens the frameworks previously proposed for a comprehensive and balanced plan to manage nicotine and tobacco products. What we any may others stated and reviewed in Abrams et al Prev. Medicine 2018 and in Glasser et al 2020) has not in fact changed enough – even with the more concerning patterns in youth uptake or in adult smokers dual use, to warrant a radical change in nicotine management policy.

The evidence is simply not there. Moreover, while the assumed harmful impact on youth is always a concern, in this case the massive change in Canada position is quite surprising. It seems has been strongly driven by one or two individuals and some misinformation, and misinterpretation (ie a distorting the science) cited. Basically, taking some survey data out of context in selected studies. Carefully considering the big picture and more careful analysis of all the contextual forces and systems analysis models are needed place the concerns in a balanced and appropriate science driven perspective.

There is never a good time to implement strong policy especially without strong science. The precautionary principle is often used to defend premature policy (i.e. out of an abundance of caution). However, in a complex system such action is most likely to boomerang with unintended negative consequences and many lives lost that could have been saved. ***It is the opposite of precautionary principle to withhold and undermine a much safer alternative to the most lethal combusted products now on the market. As we and others have shown in our reviews -- as well as in the UK Public Health England latest update, published in March 2021 just weeks ago.***

Based on what we do know to date many smokers would be left behind and many lives will be both prematurely lost and the opportunity lost to attenuate much of the preventable disease burdens, disability and costs due to the massive relative lethality and harms from smoking combusted tobacco products like cigarette smoking. ***This is especially among young adults who are already smoking where disease burdens can be dramatically reduced as early in life as possible well as those among smokers at any age who are unable or do not wish to stop using nicotine and many are at disproportionate risk such as from lower income Canadians.***

Even many underage and at-risk youth will lose out because many will become the next generation of smokers anyway (despite societies best efforts -- youth will try alcohol, cannabis or nicotine and some will progress to a lifetime of lethal cigarette smoking). All of this is clearly articulated in our reviews, other work, and in very recent studies and modeling of the outcomes (see details in the submission of Swenor and Bates (appendix A below) and in our own work that remains very consistent with recent updates of the evidence and is attached in pdfs.)

In short, we believe the 20mg/ml limit obstructs an optimum design mix: products that provide low volumes of high strength liquids have been amazingly successful. Where the nicotine strength is not limited, the product ***can compete*** with much more deadly combusted smoked products ***and displace more rapidly for the whole population, especially at risk youth, most of whom will smoke anyway, and all adults who smoke already, and as we and the science reassures us, with only a small downside risk to some teen who may never have used nicotine.***

Behind the technical-sounding questions and the legitimate concerns about protecting youth while helping save smoker's lives, is a deeper framing issue - how much do you really want non-combustibles to compete with cigarettes and ultimately to render them obsolete? And to do so AS RAPIDLY AS POSSIBLE, thus protecting both future youth who will become smokers or switch back to smoking, as well to adult smokers whose lives can and will be saved if combusted products are made obsolete and made economically less viable and thus become obsolete or rarely used.

This is the biggest prize and opportunity being missed - because of overweighting by far the legitimate concerns about youth gateways into a lifetime of smoking and not finding other ways to manage youth uptake as is done with alcohol and cannabis but without such draconian restrictions on products as is being proposed here for much safer nicotine vape products.

Let us not lose sight of the is ultimate prize here. The data and science has only become stronger since we wrote and testified to the Canada Health issues (fully articulated in our two recent comprehensive reviews in 2018 and updated with recent science as well (see appendix and attachments). By making much less harmful alternatives to deadly and lethal combusted products less effective, less appealing and less able to compete and displace deadly smoked tobacco one is simply helping keep deadly cigarettes dominant in the marketplace and slowing down the saving of lives of most at risk adolescents who will then smoke and also depriving all adults of a much safer nicotine alternative for those who are unwilling or unable to stop using nicotine but who don't want to die from its lethal combusted mode of delivery anymore. Please see the appendix and attached files to back up our statements.

We urge you to stay the original course that Canada was taking. It was largely similar to and supported by the best science that supported harm reduction. In our judgement as senior tobacco and nicotine scientists, the differences in data between Canada, the UK and the USA and New Zealand are not sufficient when examined closely and in full contexts to warrant a major deviation from that original Health Canada course and its comprehensive plan for nicotine and tobacco product management. Respectfully submitted and signed.

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NOTE: Abrams and Niaura declare they have no conflicts of interests, financial or non-financial.

David B. Abrams holds a B.Sc. (Hons.) in Psychology and Computer Science from the University of the Witwatersrand, South Africa and a Ph.D. in Clinical Health Psychology from Rutgers University. Professor Abrams was professor and founding director of the Centers for Behavioral and Preventive Medicine at Brown University Warren Alpern Medical School. He directed the Office of Behavioral and Social Sciences Research (OBSSR), Office of the Director, National Institutes of Health (NIH). He then directed The Schroeder National Institute of Tobacco Research and Policy Studies at Truth Initiative/American Legacy Foundation and was Professor of Health Behavior and Society, The Johns Hopkins Bloomberg School of Public Health. He has published over 300 scholarly articles and been a Principal Investigator on numerous NIH grant awards. He authored with Dr. Ray Niaura *The Tobacco Dependence Treatment Handbook: A Guide to Best Practices*. He received The Joseph Cullen Memorial Award from the American Society for Preventive Oncology for lifetime contributions to tobacco and nicotine use behavior; Research Laureate Award, American Academy of Health Behavior; and the distinguished Alumni Award, Rutgers University. He served on the Board of Scientific Advisors of the National Cancer Institute, NIH; and he was President of the Society for Behavioral Medicine and recipient of their Distinguished Scientist and Mentorship Awards.

Dr. Raymond Niaura is an expert on nicotine and tobacco dependence and treatment, as well as substance use and addiction to alcohol. Dr. Niaura researches the biobehavioral substrates of tobacco dependence, including factors that influence adolescent and early adult tobacco use trajectories. He also evaluates behavioral and pharmacological treatments for tobacco cessation, with a particular interest in cessation in disadvantaged population to address public health disparities in tobacco-related burdens of illness and disability. Dr. Niaura was the Director of Science and Training at the Schroeder Institute (SI) for Tobacco Research and Policy Studies at the [Truth Initiative](#), where he also supervised the pre- and post-doctoral training programs. Dr. Niaura has previously taught and conducted research at Brown University, Johns Hopkins Bloomberg School of Public Health, the Georgetown Medical Center, and the School of Public Health at University of Maryland. He was also a former President of the [Society for Research on Nicotine and Tobacco](#) and was a Deputy Editor of the [Nicotine and Tobacco Research](#). With grants from the National Institutes of Health, numerous foundations, and private industry, Dr. Niaura has published over 400 peer-reviewed articles, commentaries, and book chapters, including the book [The Tobacco Dependence Treatment Handbook: A Guide to Best Practices](#).

Appendix A. next page. and also please see attached pdf files.

Proposal to limit permitted nicotine e-liquid strength to 20mg/ml Comment by Clive Bates and David Swenor

1st March 2021

Tobacco Products Regulatory Office Tobacco Control
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1. We write as public health advocates in favour of the strategy of tobacco harm reduction.¹ We welcome the opportunity to comment on Health Canada's proposal to limit the strength of nicotine e-liquid to 20mg/ml.² There is little evidence to show this measure would have a beneficial public health impact and much to suggest it is a bad idea that will do more harm than good.

Recognise perverse unintended consequences of regulation

2. **Significant perverse consequences are not recognised in the regulatory impact analysis.** It is likely that the effect of a limit on nicotine strengths where these are already popular will: provide regulatory protection to the cigarette trade; inhibit the transition of the consumer nicotine market to far less dangerous non-combustible products; cause more smoking among both adults and adolescents; add to the burden of disease and death caused by tobacco use; prevent or obstruct users from taking action to protect their own health, on their own initiative and at their own expense; stimulate black market activity, user workarounds, home mixing and favour use of devices with higher power combined with higher liquid volume intake, and hence greater toxicant exposure.
3. **No benefits to youth demonstrated.** The analysis does not adequately examine the impact the measure will have on adults and adult smoking. However, the most significant flaw is that the regulatory impact analysis fails to account for the effect on *adolescent smoking* and the likely role that stronger vaping products play in diverting prior tobacco users away from smoking. Evidence from the United States suggests more intensive teenage vapers are likely to be prior tobacco users^{3,4} and that teenage vaping is likely a diversion from teenage smoking.^{5,6} Given that e-cigarettes are an economic substitute for cigarettes,⁷ it is quite possible that teenage vaping has a net positive effect on adolescent health because of its interaction with adolescent smoking.⁸

¹ See [About the authors](#) at the end of this submission

² Government of Canada, Department of Health. Canada Gazette, Part I, Volume 154, Number 51: Concentration of Nicotine in Vaping Products Regulations, 19 December 2020. [\[link\]](#)

³ Tam J, Brouwer AF. Comparison of e-cigarette use prevalence and frequency by smoking status among youth in the United States, 2014–19. *Addiction* 2021 add.15439. [\[link\]](#)

⁴ Jarvis M, Jackson S, West R, Brown J. Epidemic of youth nicotine addiction? What does the National Youth Tobacco Survey 2017–2019 reveal about high school e-cigarette use in the USA? *Qeios* 2020 [\[link\]](#)

⁵ Selya AS, Foxon F. Trends in Electronic Cigarette Use and Conventional Smoking: Quantifying a Possible “Diversion” Effect among U.S. Adolescents. *Addiction* [Internet] 2021 [cited 2021 Jan 11];add.15385. [\[link\]](#)

⁶ Levy DT, Warner KE, Cummings KM, et al. Examining the relationship of vaping to smoking initiation among US youth and young adults: a reality check. *Tob Control* 2019 ;28(6):629–635. [\[link\]](#)

⁷ Pesko MF, Warman C. The Effect of Prices on Youth Cigarette and E-Cigarette Use: Economic Substitutes or Complements? *SSRN Electron J* 2017 [\[link\]](#)

⁸ Friedman AS. How does electronic cigarette access affect adolescent smoking? *J Health Econ* 2015;44:300–308. [\[link\]](#)

4. **Canadian data is consistent with vaping displacing adolescent smoking.** The trends in youth nicotine use in Canada show a sharp decline in smoking as vaping increased, as shown in the figure below:⁹

Figure. Prevalence of Cigarette Smoking, Vaping, and Dual Use Among Youths Aged 16 to 19 Years, 2017 to 2019, by Country

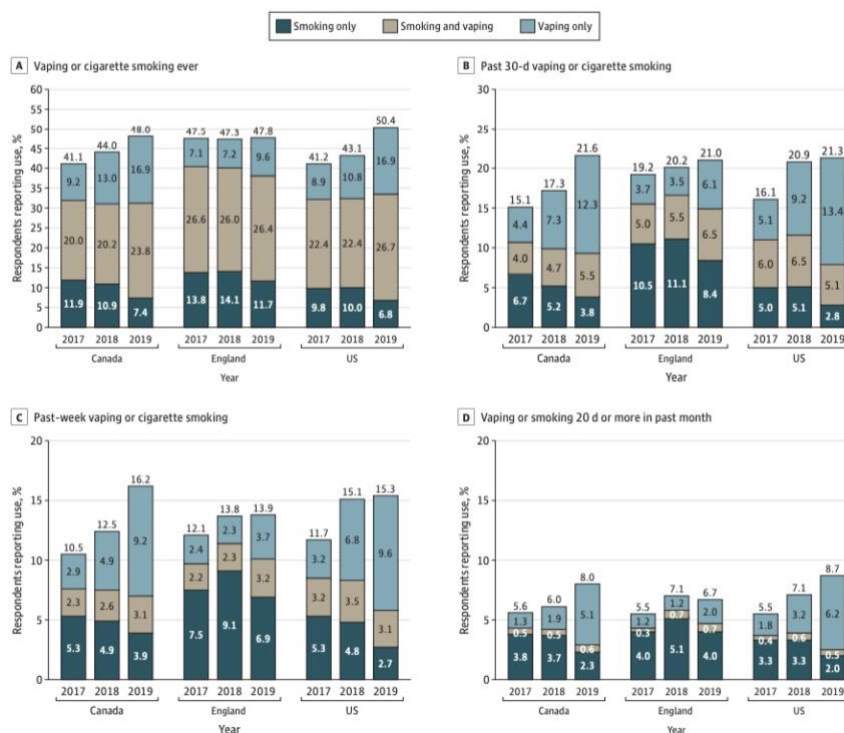


Figure 1: Adolescent smoking and vaping in the UK, the US, and Canada (Hammond et al. 2020)

The United States, which has had a high-pitched moral panic about youth vaping, has a lower adolescent smoking rate than Canada. The UK, which already has the 20mg/ml in place through the European Tobacco Products Directive, has a lower adolescent vaping rate but a higher smoking rate.

5. **Failure to address the interaction of smoking and vaping.** The central problem is how a proposal like this interacts with the smoking and other risk behaviours of adults and adolescents. As the Royal College of Physicians (London) puts it:¹⁰

If [a risk-averse and precautionary] approach also makes e-cigarettes less easily accessible, less palatable or acceptable, more expensive, less consumer-friendly or pharmacologically less effective, or inhibits innovation and development of new and improved products, then it causes harm by perpetuating smoking. Getting this balance right is difficult. (Section 12.10 page 187)

6. **How the 20mg/ml regulation will tilt the balance toward cigarettes.** In terms of the warning in the Royal College of Physicians statement above, the nicotine cap would have three possible harmful effects in favour of cigarettes:

- a. It will make some more compact products pharmacologically less effective than cigarettes and thus grant cigarettes a marketing advantage in the Canadian market, especially for more highly dependent smokers.

⁹ Hammond D, Rynard VL, Reid JL. Changes in prevalence of vaping among youths in the United States, Canada, and England from 2017 to 2019 JAMA Pediatr. 2020 174(8):797–799. [link]

¹⁰ Tobacco Working Group. Royal College of Physicians (London) Nicotine without smoke: tobacco harm reduction 28 April 2016 [link]

- b. It will make many safer products less acceptable by making smaller, more compact devices with adequate nicotine delivery impossible to make. Users will have to use higher power, higher volume devices to achieve satisfactory nicotine delivery or smoke.
 - c. It will be a barrier to pro-health innovation in which new devices draw on stronger liquids to reduce the power inputs and temperatures, reduce the physical size, or improve the pharmacological performance.
7. **No evidence for gateway effects.** It might be worth taking these risks with adult and adolescent health if e-cigarettes functioned as a gateway to smoking or other risk behaviours. But there is no compelling evidence that they do.^{11 12} The alternative explanation for the observed associations between e-cigarette use and smoking relates to the individual's characteristics and their circumstances that incline them to both vaping and smoking. Given the similarities between the two habits (albeit with radically different risk to health), it is not surprising that whatever reasons people have to smoke are also reasons to vape. These common characteristics – genetics, mental health, family, community, delinquency, etc.) are sometimes known as common liabilities, common risk factors or confounders. These provide a more credible explanation for at least part of the observed associations between smoking and vaping.^{13 14} Common liabilities also mean that vaping will tend to be concentrated among those with a propensity to smoke – and therefore likely to be beneficial.
8. **Flawed and implausible cost-benefit analysis.** The cost-benefit analysis presented in the regulatory impact analysis looks sophisticated at first sight, but its main public health finding is predicated on a single simplistic assumption:

The proposed Regulations are expected to primarily benefit youth by contributing to the reduction in the number of young persons who experiment with vaping products, which can lead to exposure to and dependence on nicotine and transition into tobacco use. Long-term benefits would be realized in terms of avoided tobacco- and vaping-related mortality and morbidity, including from exposure to second-hand smoke.

Because the value of life used in such analysis is so high (\$7.9 million in this case), any case will be dominated by the effects of changes in smoking status. The model assumes a gateway effect, implying that a cap on that stronger liquids will prevent net additional smokers resulting in reduced mortality, morbidity and secondhand exposures. Over 90% of the benefit is attributable to *reduced smoking*, which supposedly arises from eliminating a potent *competitor to cigarettes*. This is absurd. All the evidence (and common sense) points the other way: vaping is a low-risk economic substitute and diversion from smoking, and this applies both to adults and adolescents. The likely and foreseeable unintended consequences *of the cap* are increased adult and adolescent smoking and more dual-use. These more realistic consequences have either been ignored or relegated to a break- even or sensitivity analysis. The model findings are an artefact of assumptions about the beneficial impacts of the cap, which, through circular reasoning, inevitably reinforce the modelled case for it.

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- ¹¹ Chan GCK, Stjepanović D, Lim C, et al. Gateway or common liability? A systematic review and meta-analysis of studies of adolescent e-cigarette use and future smoking initiation *Addiction*. 2020;add.15246. [\[link\]](#)
 - ¹² Lee PN, Coombs KJ, Afolalu EF. Considerations related to vaping as a possible gateway into cigarette smoking: an analytical review. *F1000Research* 2019;7:1915. [\[link\]](#)
 - ¹³ Vanyukov MM, Tarter RE, Kirillova GP, et al. Common liability to addiction and “gateway hypothesis”: Theoretical, empirical and evolutionary perspective. *Drug Alcohol Depend* [Internet] 2012;123:S3–S17. [\[link\]](#)
 - ¹⁴ Phillips C V. Gateway effects: Why the cited evidence does not support their existence for low-risk tobacco products (and what evidence would). *Int J Environ Res Public Health* 2015; [\[link\]](#)

Appreciate the valuable role of higher strength liquids in innovation

9. **How high-strength liquids *don't* work – understanding titration and compensation.** Before regulating in this area, it will be helpful to thoroughly understand the role that relatively high nicotine strength plays in the nicotine product market. The most fundamental error is the idea that nicotine strength is somehow a proxy for nicotine exposure or 'addictiveness'. It is not. This is because the users control their exposure to nicotine through a widely understood process known as nicotine titration.¹⁵ This effect has been well documented in smokers for several decades.^{16,17} The user behaviours change to achieve a desired level of nicotine, for example, by puffing more deeply or more often – a process known as 'compensation'. It means that users consume lower volumes of higher strength liquid by adjusting their puffing patterns. But it also means that users will consume higher volumes of lower strength liquid – potentially creating higher exposures to toxicants generated by heating liquids.^{18,19,20} *Lowering the maximum nicotine strength on the market does not necessarily reduce nicotine exposure and may increase toxicant exposure.*
10. **How high-strength liquids *do* work.** The primary function of stronger nicotine liquids is *to enable a satisfactory exposure to nicotine from a compact, low-power device*. Small form factor pod devices, like the Juul, have three synergistic design features: (1) high liquid strength to allow for lower volumes of liquid for a given dose of nicotine; (2) the use of acid additives to form nicotine salts to reduce harshness and improve pharmacokinetics by ensuring more nicotine is delivered via the lung than upper respiratory tract; (3) lower power and operating temperature from smaller batteries to allow a compact device and lower exposure to products of thermal decomposition. These three features combine to make a product that is a powerful competitor to cigarettes – a compact device that is easy to use but has good nicotine delivery and sensory characteristics at vastly reduced risk compared to smoking. It is an ideal entry point for smokers who need a simple but effective transition from smoking to vaping.
11. **Innovation and its enemies.** These compact, high-strength, low-power products have been effective at helping smokers to switch to vaping as an alternative to smoking^{21,22}. The formula of good nicotine delivery combined with convenience has been successful commercially and led Juul to

¹⁵ Dawkins LE, Kimber CF, Doig M, Feyerabend C, Corcoran O. Self-titration by experienced cigarette users: blood nicotine delivery and subjective effects. *Psychopharmacology (Berl)* 2016;233(15–16):2933–2941. [[link](#)]

¹⁶ Benowitz NL, Hall SM, Herning RI, Jacob P, Jones RT, Osman AL. Smokers of Low-Yield Cigarettes Do Not Consume Less Nicotine. *N Engl J Med*. 1983 Jul 21;309(3):139–42. [[link](#)]

¹⁷ Russell MAH, Jarvis M, Iyer R, Feyerabend C. Relation of nicotine yield of cigarettes to blood nicotine concentrations in smokers. *Br Med J*. 1980 Apr 5;280(6219):972–6. [[link](#)]

¹⁸ Kośmider L, Kimber CF, Kurek J, Corcoran O, Dawkins LE. Compensatory Puffing With Lower Nicotine Concentration E-liquids Increases Carbonyl Exposure in E-cigarette Aerosols. *Nicotine Tob Res* 2018 [[link](#)]

¹⁹ Kosmider L, Cox S, Zaciera M, et al. Daily exposure to formaldehyde and acetaldehyde and potential health risk associated with use of high and low nicotine e-liquid concentrations. *Sci Rep* [Internet] 2020;10(1):6546. [[link](#)]

²⁰ Dawkins L, Cox S, Goniewicz M, et al. 'Real-world' compensatory behaviour with low nicotine concentration e-liquid: subjective effects and nicotine, acrolein and formaldehyde exposure. *Addiction* 2018;113(10):1874–1882. [[link](#)]

²¹ Russell C, Haseen F, McKeganey N. Factors associated with past 30-day abstinence from cigarette smoking in adult established smokers who used a JUUL vaporizer for 6 months. *Harm Reduct J* 2019;16(1).

²² Goldenson NI, Le G, Auguston EM. Switching Away from Cigarettes Among Adult Smokers Who Purchased the JUUL System: 12-Month Follow-Up Results from Two Large Longitudinal Studies, Poster 3rd Scientific Summit on Tobacco Harm Reduction 2020 September 25, 2020. Juul Labs Inc. [[link](#)]

dominate the nicotine vaping market in the United States.²³ As e-cigarette use rose rapidly among adults, cigarette sales began an unusually rapid decline. However, a moral panic about a youth vaping epidemic eventually caused a backlash and excessive regulation and hostility that caused the decline in cigarette sales to stall.²⁴ In contrast, the Juul products available in the UK under the European Union nicotine cap of 20mg/ml restrictions are not effective in competition with cigarettes.^{25 26 27} Canada's proposal is essentially to obstruct an innovation that has worked well to liberate smokers from smoking. However, this is based on a paper-thin rationale that does not consider the likely behavioural responses of adults, adolescents, or the marketplace.

Base policy on an understanding of pharmacokinetics

12. **Clarity or confusion over nicotine pharmacokinetics?** The key concept and concern for regulators should be the psychotropic reward of nicotine delivery, not nicotine e-liquid strength. This is a function of the peak level of nicotine reached in the brain and time to achieve this. These characteristics are known as pharmacokinetics (PK). Higher peaks more rapidly are more likely to provide a reward comparable to cigarettes. Many smokers still report that e-cigarettes do not provide a satisfying alternative to cigarettes.²⁸ For any individual, this reward is a function of the user, the device, and the e-liquid. The central question for health agencies like Health Canada is: should these devices compete with cigarettes in nicotine delivery, or should Health Canada use regulation to ensure that cigarettes have a protected market for high-speed, high-peak nicotine pharmacokinetics? The proposed limit puts Health Canada firmly on the side of the cigarette trade.
13. **Other vaping products can achieve high nicotine delivery with weaker liquids.** As explained above, high-strength liquids are tightly linked to the feasibility of compact low-power devices. High power, high volume devices using weaker liquids can achieve an effective nicotine delivery if that is what the user is seeking.^{29 30 31} A ban on higher strength liquids may cause some users to revert to smoking or to quit vaping or never start. It is also likely that young people, driven by curiosity and seeking to emulate adult behaviours, will not simply quit vaping and do something virtuous instead. They may

²³ Huang J, Duan Z, Kwok J, et al. Vaping versus JUULing: how the extraordinary growth and marketing of JUUL transformed the US retail e-cigarette market. *Tob Control* 2019;28(2):146–151. [[link](#)]

²⁴ Jennifer Maloney, Smoking's long decline is over. Wall Street Journal 28 January 2021 [[link](#)]

²⁵ Phillips-Waller A, Przulj D, Smith KM, Pesola F, Hajek P. Nicotine delivery and user reactions to Juul EU (20 mg/ml) compared with Juul US (59 mg/ml), cigarettes and other e-cigarette products. *Psychopharmacology (Berl)* [Internet] 2020 [cited 2020 Dec 5];1–7. [[link](#)]

²⁶ Hajek P, Pittaccio K, Pesola F, Myers Smith K, Phillips-Waller A, Przulj D. Nicotine delivery and users' reactions to Juul compared with cigarettes and other e-cigarette products. *Addiction* 2020;115(6):1141–1148. [[link](#)]

²⁷ Goldenson NI, Fearon IM, Buchhalter AR, Henington JE. An Open-Label, Randomised, Controlled, Crossover Study to Assess Nicotine Pharmacokinetics and Subjective Effects of the JUUL System with Three Nicotine Concentrations Relative to Combustible Cigarettes in Adult Smokers. *Nicotine Tob Res* 2021 [[link](#)]

²⁸ Yong HH, Borland R, Cummings KM, et al. Reasons for regular vaping and for its discontinuation among smokers and recent ex-smokers: findings from the 2016 ITC Four Country Smoking and Vaping Survey. *Addiction* 2019;114(S1):35–48. [[link](#)]

²⁹ Jacobson K, Martinez J, Larroque S, Jones IW, Paschke T. Nicotine pharmacokinetics of electronic cigarettes: A pooled data analysis from the literature. *Toxicol Reports* 2021;8:84–95. [[link](#)]

³⁰ Ramôa CP, Hiler MM, Spindle TR, et al. Electronic cigarette nicotine delivery can exceed that of combustible cigarettes: A preliminary report. *Tob Control* 2016;25(E1):e6–e9. [[link](#)]

³¹ Voos N, Goniewicz ML, Eissenberg T. What is the nicotine delivery profile of electronic cigarettes? [Internet]. *Expert Opin. Drug Deliv.* 2019 [cited 2021 Mar 1];16(11):1193–1203. [[link](#)]

adjust by using larger, higher power devices using higher volumes of lower strength liquids with greater toxicant exposure. This possibility is not addressed in the regulatory impact assessment.

14. **Applying the wrong regulatory paradigm.** To a pharmaceutical regulator, a high nicotine reward would be described negatively as ‘abuse liability’. The regulator would typically aim to attenuate the reward and moderate the pharmacokinetics to prevent dependence. However, most pharmaceuticals are not used in a situation where there is a dominant, widely available incumbent consumer product, the cigarette, that has both high abuse liability and is a cause of severe harm. Several studies wrestle with this contradiction, not always successfully.^{32 33}

Avoid repeating the errors and flawed analysis of the European Union

15. **There is no case to follow the European Union.** It may be reassuring to adopt a rule built into the 2014 European Union Tobacco Products Directive (TPD)³⁴. It should not be. This limit was the outcome of an undignified haggle between member state bureaucrats and owes little to science or reason. The European Commission misunderstood and then misused the available science to justify this measure. Several scientists cited by the Commission to justify its approach pointed out the error when the legislation was crafted.^{35 36 37} It is difficult to know if the Commission’s refusal to acknowledge the deficiencies in its reasoning was cynical and calculated or simply because the negotiations were political and too far advanced for the Commission to admit its error.
16. **The European Union had the right objective but the wrong approach.** The European Union was, in fact, trying to create a non-discriminatory ‘level playing field’ for competition between cigarettes and e-cigarettes. Non-discrimination is a principle of the EU internal market, but it was poorly executed in this case. In recital 38 of the TPD, a roughly appropriate goal is specified:

This concentration [20mg/ml] allows for a delivery of nicotine that is *comparable to the permitted dose of nicotine derived from a standard cigarette* during the time needed to smoke such a cigarette. (emphasis added)

The problem is that the basis for competition is not, in fact, the quantity of nicotine in a device but the *nicotine delivery experience* that can be achieved by a user, a function of its pharmacokinetics.

17. **Tilting the playing field towards cigarettes.** With this limit on vaping technology in place in the European Union, cigarettes can deliver a higher peak of blood-nicotine than vaping products that have been most competitive elsewhere – therefore leaving the most dangerous product with a considerable advantage in the marketplace. The supposedly level playing field was tilted in favour of cigarettes by the Directive. It should have been kept level or tilted towards the safer product.

³² Stiles MF, Campbell LR, Graff DW, Jones BA, Fant R V., Henningfield JE. Pharmacodynamic and pharmacokinetic assessment of electronic cigarettes, combustible cigarettes, and nicotine gum: implications for abuse liability. *Psychopharmacology (Berl)* 2017;234(17):2643–2655. [\[link\]](#)

³³ Shihadeh A, Eissenberg T. Electronic Cigarette Effectiveness and Abuse Liability: Predicting and Regulating Nicotine Flux. *Nicotine Tob Res* [Internet] 2015 [cited 2021 Feb 28];17(2):158–162. [\[link\]](#)

³⁴ European Union Tobacco Products Directive 2014/40/EU, 2014. [\[link\]](#) The nicotine cap is specified at Article 20(3)(b).

³⁵ Farsalinos K. The European Commission has misinterpreted my scientific research on nicotine in e-cigarettes, 10 Jan 2014 [\[link\]](#)

³⁶ Etter, JF and 14 experts, Scientific Errors in the Tobacco Products Directive, A letter sent by scientists to the European Union. 17 January 2014. [\[link\]](#)

³⁷ Dawkins LE. Please Do Not Distort My Words To Justify Your Policy, 13 January 2014. [\[link\]](#)

Summarising the likely adverse consequences of the proposed nicotine cap

18. To conclude, we believe there are several legitimate challenges to the proposal for a nicotine cap that have not been satisfactorily addressed in the regulatory impact analysis.
- 1) **Creates a barrier to stopping smoking for more dependent smokers.** The proposed nicotine cap will deter more dependent smokers from switching in the first place. It will make the consumer transition from smoking to vaping harder for those most at risk.
 - 2) **May cause harm to adolescent smokers.** The impact of the cap will not be neatly divided between the interests of adult smokers and adolescent non-users. The cap could harm adolescents through an adverse effect on their smoking behaviour. Adolescents with a prior smoking habit and higher dependence become more intensive users of e-cigarettes.
 - 3) **Undermines the design of easier-to-use but effective devices that support the early stages of switching.** The cap works against more compact devices that use low volumes of liquid at a higher strength, which do not require refilling or complicated configuring. The larger devices may deter ordinary smokers through initial cost and complexity. The easy-to-use and compact devices are often valued by smokers as they try something unfamiliar, not knowing if it will work.
 - 4) **Obstructs future innovation.** It is also a barrier to new product designs that would use stronger liquids to provide prospective consumers with better or cheaper products to compete with cigarettes and reach smokers who do not currently find e-cigarettes satisfying. Canada would be imposing a constraint that could hold back the endgame for smoking.
 - 5) **Higher consumption of liquid and greater toxic exposure.** It will mean some users will switch devices to consume greater quantities of weaker e-liquids using higher-powered devices with potentially greater toxicant exposure. While these elevated risks remain very low compared to smoking, there is no justification to *increase* them using regulation.
 - 6) **Stimulating a black market.** Bans will promote a black market in the products that are banned. Canada's border with the United States will facilitate illicit trade either because these products are readily available legally or in a black market developed to work around US federal and state regulation. It will also encourage users to mix their own liquids from near-pure imported nicotine – a dangerous substance and risky procedure.
 - 7) **Favouring the cigarette trade.** Limits on ISO or Health Canada Intensive nicotine yield do not materially limit the nicotine delivery of cigarettes to the user. Most smokers can compensate and self-titrate to achieve the nicotine hit they want from cigarettes on the market. In contrast, the 20mg/ml limit is a significant design constraint for the e-cigarette category, especially for the compact and convenient devices that smokers are likely to turn to first.

A better approach – controls on access and marketing

19. We hope we have shown how simple-sounding regulation could easily backfire and cause more harm than it does good. Given the relative risks, the overwhelming focus of tobacco and nicotine policy should be on reducing *smoking* in both adults *and adolescents*. Given vaping is among the least troubling of all adolescent risk behaviours, there is little justification for protecting the cigarette trade from innovative vaping product designs by imposing distorting regulation that works against the interests of smokers. Any regulatory measures to control youth vaping should focus on age-specific controls on access and on marketing or branding targeted at children, but not on modifying a fundamental design parameter of the most advanced products for no demonstrable benefit.

About the authors

Clive D. Bates has had a diverse career in the public, private and not-for-profit sectors. From 1997-2003 he was Director of Action on Smoking and Health (UK), campaigning to reduce the harms caused by tobacco. In 2003, he joined Prime Minister Blair's Strategy Unit as a civil servant and worked in senior roles in the public sector and for the United Nations in Sudan. In 2013, he founded Counterfactual, a consulting and advocacy practise focused on sustainability and public health.

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