

Juul Lab's Submission to the Call for Evidence on the Evaluation of the Legislative Framework for Tobacco Control

Introduction

At Juul Labs, our mission is to transition the world's billion adult smokers away from combustible cigarettes, eliminate their use, and combat underage usage of our products. We do not want any non-nicotine users, especially those underage, to try our products, as they exist only to help transition the world's one billion adult smokers away from combustible cigarettes.

Smoking remains the leading cause of preventable disease and premature death across Europe. Despite progress made to help smokers quit and prevent non-smokers from starting, 23% of Europeans still smoke¹. Half of them will die from a smoking-related disease, resulting in 700,000 deaths each year in Europe². The best way for smokers to reduce their risk would be to quit all tobacco and nicotine. Most, however, will not. Nearly seven in ten smokers want to quit, and about half try each year. But fewer than one in ten will succeed.³

We fully support Europe's Beating Cancer Plan which seeks to create a tobacco free generation by 2040. We believe that e-cigarettes can offer adult smokers a potentially less harmful alternative to combustible cigarettes and, in so doing, reduce the death and disease associated with tobacco use. E-cigarettes are intended to be substitutes for cigarettes for adult smokers. As such, primary health risk assessments should compare e-cigarettes and other alternative nicotine products to cigarettes. While e-cigarettes are not risk-free, a growing body of evidence shows that e-cigarettes are likely significantly less harmful than combustible cigarettes.

The opportunity for tobacco harm reduction cannot come at the cost of underage use. We believe that comprehensive, evidence-based interventions built on limiting appeal, restricting access, and ensuring enforcement are critical tools to address underage use, and as a company we continue to implement such measures and advocate for category-wide adoption. We believe that there are evidence-based approaches that both combat underage use while allowing for tobacco harm reduction for adult smokers.

¹ Eurobarometer "Attitudes of Europeans towards tobacco and electronic cigarettes" 2020

² European Parliament. 700,000 deaths a year: tackling smoking in the EU. [Link](#)

³ Babb S, Malarcher A, Schauer G, Asman K, Jamal A. Quitting Smoking Among Adults - United States, 2000-2015. MMWR Morb Mortal Wkly Rep. Jan 6 2017;65(52):1457-1464. [Link](#)

I. The Relative Risk of E-Cigarettes Compared to Smoking

Cigarette smoking remains the leading cause of preventable disease and premature death across Europe. Cigarettes are the most harmful method of nicotine delivery on the market for consumers. The overwhelming majority of harm associated with smoking comes from combustion. Cigarette smoke contains more than 7,000 identified constituents, 70 of which have been identified by scientists as cancer causing.⁴ The repeated inhalation of toxicants in cigarette smoke – not nicotine – is the primary cause of smoking-related disease.

Delivering nicotine without burning tobacco can significantly reduce the formation of — and users' exposure to — toxicants known to cause smoking-related disease. E-cigarettes can deliver nicotine without burning tobacco and are therefore potentially causing less harm than continued exposure to toxicants through smoking. For those smokers who will not quit using nicotine, switching completely to e-cigarettes can reduce their exposure to toxicants and potentially reduce their risk of smoking-related disease.

While data on the potential long-term health risks associated with e-cigarettes are not yet available, multiple lines of evidence support that e-cigarettes are expected to carry far lower individual health risk than combustible cigarettes.⁵ Thus, public-health authorities have recognized the potential for e-cigarettes products to reduce the significant and established harms of cigarette smoking among adult current users.

The US FDA, in its review of PMTAs (Premarket Tobacco Product Applications) of electronic nicotine delivery systems (ENDS), has stated,

“The currently available evidence indicates that smokers who switch completely to ENDS will have reduced toxic exposures and this likely leads to less risk of tobacco-related diseases.”⁶

Recent studies (summarised below) have found reductions in toxicants known to cause smoking related disease among smokers who switched to e-cigarettes, and evidence for improvements in some physiological and disease-related endpoints. These findings are consistent with the evaluations previously conducted by authoritative public health bodies, including the National Academies of Science, Engineering, and Medicine (NASEM),⁷ the Royal College of Physicians,⁸ and Public Health England,⁹ in support of conclusions that e-cigarettes pose less individual risk than combustible cigarettes.

⁴ Conference of the Parties to the WHO Framework Convention on Tobacco Control. Work in progress in relation to Articles 9 and 10 of the WHO FCTC Report by WHO. [Link](#)

⁵ National Academies of Sciences, Engineering, and Medicine, Public Health Consequences of E-cigarettes (2018). [Link](#)

⁶ US FDA Center for Tobacco Products, “TPL Review of PMTAs: PM0000635, PM0000636, PM0000646, PM0000712, PM0004287, PM0004293”. [Link](#)

⁷ National Academies of Sciences, Engineering, and Medicine, Public Health Consequences of E-cigarettes (2018). [Link](#)

⁸ Royal College of Physicians. Nicotine without smoke: Tobacco harm reduction. London: RCP, 2016. [Link](#)

⁹ McNeill, Ann, et al. "Evidence review of e-cigarettes and heated tobacco products 2018." A report commissioned by public health England. London: Public Health England 6 (2018). [Link](#)

- Hajat et al.

- This was a systematic review of 1,020 publications to “identify, narratively synthesize, assess the strength and quality of evidence and critically appraise studies that have reported disease endpoints associated with the use of ENDS.”
- The authors evaluated evidence of new onset or control of disease end-points. The authors concluded that the evidence to date is supportive of harm reduction associated with switching from cigarettes to e-cigarettes:

“Our review has not demonstrated evidence that ENDS use is causative for any harmful CVD outcomes, and to the contrary, may be beneficial for hypertensive patients. Switching from cigarettes to e-cigarettes resulted in reduced exacerbations of COPD, with no evidence of long-term respiratory harm or deterioration in lung function.”¹⁰

- Cobb et al.

- 520 adult established smokers who were interested in reducing smoking, but not quitting, participated in a study. Researchers randomised the participants to four groups and provided them with substitutes for combustible cigarettes over a 24 week period: Non-aerosol substitute (i.e., no nicotine or produced vapour), e-cigarettes with no nicotine, e-cigarettes with low nicotine (8 mg/ml), and e-cigarettes with higher levels or “cigarette-like” levels of nicotine (36 mg/ml). Participants were instructed to reduce cigarette smoking and were tested at various intervals throughout the study for tobacco-related carcinogens, including the major pulmonary carcinogen NNAL. The study found that the participants using an e-cigarette with the highest level of nicotine reduced their cigarette consumption and had significantly reduced levels of a tobacco-related pulmonary carcinogen (NNAL) at the end of the study compared to baseline. **After 24 weeks, participants using e-cigarettes with a nicotine level of 36 mg/ml had reduced their cigarette smoking by 58% from baseline and saw 46% reductions in NNAL and 23% reductions in exhaled carbon monoxide.¹¹**
- The authors concluded that “*we found that e-cigarettes that delivered a similar amount of nicotine as traditional, combustible cigarettes, helped reduce smoking and exposure to a harmful carcinogen.*”

- Pulvers et al.

- A randomised clinical trial involving JUUL products was conducted by Brown University and published in JAMA Network Open. According to the researchers, this is the world’s first randomised clinical trial of fourth-generation pod e-cigarettes like the JUUL System. 186 adult smokers were divided into two groups and observed over the course of six weeks. Two-thirds of the participants were provided a JUUL Device and JUULpods (5.0%) for six weeks, and the remaining participants continued smoking combustible cigarettes as usual. Some participants who were given JUUL products chose to use both products. **Researchers found that compared**

¹⁰ Hajat et al., “A scoping review of studies on the health impact of electronic nicotine delivery systems”, Internal and Emergency Medicine (2022) 17:241–268. [Link](#)

¹¹ Cobb et al. Effect of an electronic nicotine delivery system with 0, 8, or 36 mg/mL liquid nicotine versus a cigarette substitute on tobacco-related toxicant exposure: a four-arm, parallel-group, randomised, controlled trial. The Lancet Respiratory Medicine. [Link](#)

to continued cigarette smoking, completely switching to the JUUL System among adult smokers led to: ~92% reductions of the lung carcinogen NNAL (a major pulmonary carcinogen), ~80% reductions in carbon monoxide levels, and significantly fewer reports of respiratory symptoms.¹²

- One of the study authors concluded that: *“Switching to pod e-cigarettes significantly reduced exposure to toxins which cause disease, [and] smokers who made a complete switch experienced the greatest reduction in exposure, [while those] who made a partial switch also experienced reduced harm”* — Dr. Kim Pulvers, co-author and Associate Professor of Psychology at California State University San Marcos

Additional evaluations of the differences in health risks in comparison with conventional tobacco products and e-cigarettes should be assessed before making decisions about further legislation.

II. Evaluating the Ability of E-cigarettes to Fully Transition Adult Smokers away from Combustible Cigarettes

Products that present less risk than smoking cannot improve overall public health unless significant numbers of adult smokers switch completely to them. There is a growing body of research that shows that adult smokers are able to switch completely to e-cigarettes. We have highlighted some of the studies below:

- Hartmann-Boyce et al.
 - The Cochrane organisation released a review of studies on e-cigarettes and smoking cessation. Researchers evaluated 50 studies, 26 of which were randomised control trials, which represented 12,430 participants. They evaluated smoking abstinence at 6-months, adverse events (AEs), and serious adverse events (SAEs).
 - Researchers found that: ***“There is moderate-certainty evidence that ECs with nicotine increase quit rates compared to ECs without nicotine and compared to NRT. Evidence comparing nicotine EC with usual care/no treatment also suggests benefit, but is less certain. More studies are needed to confirm the degree of effect, particularly when using modern EC products. Confidence intervals were wide for data on AEs, SAEs and other safety markers. Overall incidence of SAEs was low across all study arms. We did not detect any clear evidence of harm from nicotine EC, but longest follow-up was two years and the overall number of studies was small.”***¹³
- Smith et al.
 - In the study, 135 adult smokers with a history of unsuccessful quitting with stop-smoking medications were randomised to receive either nicotine replacement therapy (NRT) of their choice (including combinations of NRT) or e-cigarettes. Participants reported their smoking

¹² Pulvers K, Nollen NL, Rice M, et al. Effect of Pod e-Cigarettes vs Cigarettes on Carcinogen Exposure Among African American and Latinx Smokers: A Randomized Clinical Trial. JAMA Netw Open. 2020. [Link](#)

¹³ Hartmann-Boyce, Jamie, et al. "Electronic cigarettes for smoking cessation." Cochrane database of systematic reviews. 2021. [Link](#)

behaviour after 6 months, and reports of abstinence or significant reductions (>50%) in smoking were validated with carbon monoxide (CO) testing.

- The study concluded that ***“in smokers unable to quit using conventional methods, e-cigarettes were more effective than nicotine replacement therapy in facilitating validated long-term smoking reduction and smoking cessation, when limited other support was provided.”***¹⁴

- Walton et al.

- This study assessed characteristics and correlates of recent successful cessation¹⁵ among US adult cigarette smokers (26,759 participants) using data from the July 2018 fielding of the 2018–2019 Tobacco Use Supplement to the Current Population Survey. Cessation was defined as quitting smoking for 6 months or longer within the past year. Results varied according to what “non-cigarette tobacco products” respondents were using (if any), and current exclusive e-cigarette users had a higher prevalence of recent successful cigarette smoking cessation than adults using other products. ***“Our findings indicate that 15% of smokers who were current exclusive users of e-cigarettes reported recent successful smoking cessation.”***¹⁶

- A widely publicised study published in the New England Journal of Medicine found that **e-cigarette users were twice as likely to quit smoking** compared with traditional NRT use.¹⁷
- Farsalinos and Barbouni, (2021), Farsalinos and Niaura (2020). Farsalinos et al., examined the relationship between e-cigarette use and cessation of smoking in the EU (n=13,057 in 28 countries) and US (n=9,935 current smokers and n=14,754 former smokers). **These studies found that current daily e-cigarette use was positively associated with recent (≤5-6 years) smoking cessation**¹⁸, and former daily e-cigarette use was also positively associated with recent (≤2 years) smoking cessation.¹⁹

*III. The Role of Flavours in Fully Transitioning Adult Smokers Away From Cigarettes, and Unintended Consequences of Flavour Bans*²⁰

Flavours can play an important role in helping adult smokers transition away from combustible cigarettes, but a balanced approach is needed to mitigate the potential for underage use. Flavoured e-cigarettes should be

¹⁴ KM Smith et al. “E-cigarettes versus nicotine replacement treatment as harm reduction interventions for smokers who find quitting difficult: Randomised controlled trial.” *Addiction*, June 29 2021. [Link](#)

¹⁵ Note: Unless approved by a medicinal licensing authority, e-cigarettes are not smoking cessation products and cannot be marketed or presented as such. E-cigarettes are consumer products intended to be alternatives to cigarettes for smokers who will not quit. NRTs, on the other hand, are medicinally licensed products marketed with the express intention of supporting smoking cessation.

¹⁶ Walton, K., Wang, T. W., Prutzman, Y., Jamal, A., & Babb, S. D. (2020). Peer Reviewed: Characteristics and Correlates of Recent Successful Cessation Among Adult Cigarette Smokers, United States, 2018. *Preventing Chronic Disease*, 17. [Link](#)

¹⁷ Hajek, P., Phillips-Waller, A., Przulj, D., Pesola, F., Myers Smith, K., Bisal, N., ... & McRobbie, H. J. (2019). A randomized trial of e-cigarettes versus nicotine-replacement therapy. *New England Journal of Medicine*, 380(7), 629-637. [Link](#)

¹⁸ Farsalinos KE, Niaura R. E-cigarettes and Smoking Cessation in the United States According to Frequency of E-cigarette Use and Quitting Duration: Analysis of the 2016 and 2017 National Health Interview Surveys. *Nicotine Tob Res*. 2020. [Link](#)

¹⁹ Farsalinos KE, Barbouni A. Association between electronic cigarette use and smoking cessation in the European Union in 2017: analysis of a representative sample of 13 057 Europeans from 28 countries. *Tob Control*. 2021. [Link](#)

²⁰ Prepared by Floe Foxon. Through PinneyAssociates, Floe Foxon provides consulting services on tobacco harm reduction on an exclusive basis to Juul Labs Inc. The preparation of this writing was supported by JLI, and JLI reviewed and provided comments on draft writing.

marketed in a way that can effectively reach adult smokers while limiting appeal to those who are underage. Packaging and flavour-naming that appeals to those who are underage should be reviewed including specific packaging design and naming elements. For example, cartoon, fantasy and fictional characters; sports references; colourful exaggerated graphics; confectionery, alcoholic drinks, energy drinks, and soft drinks may overly appeal to those who are underage. Specific research must be conducted on flavours and the impact on different groups (adult smokers and youth) in order to regulate them under the Tobacco Products Directive.

Taste and satisfaction are important features in products intended to move smokers away from combustible cigarettes.²¹ Research suggests that non-tobacco flavoured e-cigarettes help encourage adult smokers to try using e-cigarettes: Russell et al. conducted an online survey among 20,836 adult frequent e-cigarette users in the United States that assessed flavour initiation by smoking status. Those e-cigarette users who switched completely away from smoking were more likely to have initiated their e-cigarette use with non-tobacco flavours. The authors concluded: *“access to a variety of non-tobacco flavoured e-liquid may be important for encouraging and assisting adults to use e-cigarettes in place of conventional cigarettes. Restricting the availability of non-tobacco flavours could reduce adult smokers’ interest in switching to e-cigarettes or rationalise a return to cigarette smoking.”*²²

In addition, adult consumers of flavoured e-cigarettes are more likely to fully switch from cigarettes to e-cigarettes. Using cross-sectional data, Harrell et al. found that use of tobacco flavour at initiation was common among dual users of e-cigarettes and combustible tobacco, whereas use of non-tobacco flavours was significantly more common among former smokers.²³ Using longitudinal data from the Population Assessment of Tobacco and Health Study (PATH), Friedman and Xu found that adults who preferred non-tobacco flavours at baseline had more than two times the odds of stopping smoking at follow-up, after adjusting for other variables.²⁴ In a similar longitudinal study using International Tobacco Control study data, Li et al. also found that baseline smokers who used sweet flavours were more likely to have stopped smoking at follow-up compared to users of tobacco flavours.²⁵

Finally, adults using flavours may be less likely to later relapse to smoking. Jones et al. analysed cross-sectional data from the Georgia State University Tobacco Products and Risk Perceptions Surveys.²⁶ Crucially, in this study use of multiple e-cigarette flavours was more likely among adults who partially or completely switched compared to adult smokers who tried but later rejected e-cigarettes (current smokers, former e-cigarette users). The authors conclude that use of flavours “may discourage rejecting ENDS.”

²¹ Abrams, D. B., Glasser, A. M., Pearson, J. L., Villanti, A. C., Collins, L. K., & Niaura, R. S. (2018). Harm minimization and tobacco control: reframing societal views of nicotine use to rapidly save lives. *Annual review of public health*. [Link](#)

²² Russell, C., McKegane, N., Dickson, T., & Nides, M. (2018). Changing patterns of first e-cigarette flavor used and current flavors used by 20,836 adult frequent e-cigarette users in the USA. *Harm reduction journal*, 15(1), 1-14. [Link](#)

²³ Harrell, M. B., Weaver, S. R., Loukas, A., Creamer, M., Marti, C. N., Jackson, C. D., ... & Eriksen, M. P. (2017). Flavored e-cigarette use: characterizing youth, young adult, and adult users. *Preventive medicine reports*, 5, 33-40. [Link](#)

²⁴ Friedman, A. S., & Xu, S. (2020). Associations of flavored e-cigarette uptake with subsequent smoking initiation and cessation. *JAMA network open*, 3(6), [Link](#)

²⁵ Li, L., Borland, R., Cummings, K. M., Fong, G. T., Gravely, S., Smith, D. M., ... & McNeill, A. (2021). How Does the Use of Flavored Nicotine Vaping Products Relate to Progression Toward Quitting Smoking? Findings From the 2016 and 2018 ITC 4CV Surveys. *Nicotine and Tobacco Research*, 23(9), 1490-1497. [Link](#)

²⁶ Jones, D. M., Ashley, D. L., Weaver, S. R., & Eriksen, M. P. (2019). Flavored ends use among adults who have used cigarettes and ends, 2016-2017. *Tobacco regulatory science*, 5(6), 518-531. [Link](#)

The testimonial experiences of many thousands of former smokers are accessible in online forums under the tag ‘#FlavorsSaveLives,’ where these former smokers have shared their personal experiences of using flavoured e-cigarettes to switch.²⁷ In the words of Professor Linda Bauld, professor of public health at the University of Edinburgh, “... *flavours are an important part of the appeal to adult smokers trying to quit smoking. In Europe, flavoured e-cigarettes have contributed to recent declines in adult smoking and well-conducted randomised controlled trials show that these products do help people quit.*”

Flavour bans may lead to relapse in dual users and smokers while preventing current smokers from moving away from cigarettes. Buckrell et al conducted an experiment where adult smokers and recent quitters were asked to choose their preferred option from a set of four products under a range of flavour ban policy scenarios. The results suggest that banning all flavours but tobacco would increase choice of cigarettes and decrease choice of e-cigarettes.²⁸

The European Parliament has called on the Commission “to evaluate, in the framework of the Tobacco Products Directive, which flavours in e-cigarettes are in particular attractive to minors and non-smokers.” Some studies have suggested that adolescents cite the availability of flavours as a reason for using e-cigarettes,²⁹ and that use of flavours among adolescents is associated with more risky behaviours such as increased frequency of e-cigarette use.³⁰ However, flavours are just one of more than a dozen reasons adolescent e-cigarette users give for using these products. In the latest international data from the United States’ National Youth Tobacco Survey, the availability of flavours in e-cigarettes was just the seventh most commonly reported reason for e-cigarette use among 14 reasons surveyed (13.5% of ever e-cigarette users), surpassed by peer use (a friend used/uses them, 57.8%; a family member used/uses them, 18.6%) and curiosity (47.6%). Reasons for underage use of e-cigarettes are complex and varied; specific research would be required to establish what net proportion of underage e-cigarette use (if any) would be mitigated by introducing a ban on all flavoured products.

IV. The Gateway Hypothesis and E-cigarettes³¹

There is debate within the scientific community regarding the extent and scale of any “gateway” effects of e-cigarette use. While there are some studies reporting that the use of e-cigarettes among those underage is associated with later use of combustibles, population-level trends suggest that gateway effects, if present, are small. The ‘gateway’ hypothesis is supported by longitudinal cohort studies which collectively find a significant

²⁷ Kirkpatrick, M. G., Dormanesh, A., Rivera, V., Majmundar, A., Soto, D. W., Chen-Sankey, J. C., ... & Allem, J. P. (2021). # FlavorsSaveLives: An Analysis of Twitter Posts Opposing Flavored E-cigarette Bans. *Nicotine and Tobacco Research*, 23(8), 1431-1435. [Link](#)

²⁸ Estimates regarding effects of banning flavors in e-cigarettes. In a best-best discrete choice experiment with a sample of more than 2,000 adult smokers and recent quitters, the results suggest banning flavors in e-cigarettes, while allowing menthol in cigarettes would result in the greatest increase in the selection of cigarettes (8.3%), and a decline in the use of e-cigarettes (-11.1%). A ban on all flavors, but tobacco in both products would increase choice of cigarettes (2.7%) and decrease choice of e-cigarettes (-7.9%). Buckell J, Marti J, Sindelar JL. Should flavours be banned in cigarettes and e-cigarettes? Evidence on adult smokers and recent quitters from a discrete choice experiment. *Tobacco Control* Published Online First: 28 May 2018. [Link](#)

²⁹ Wang, T. W., Gentzke, A. S., Creamer, M. R., Cullen, K. A., Holder-Hayes, E., Sawdey, M. D., ... & Neff, L. J. (2019). Tobacco product use and associated factors among middle and high school students—United States, 2019. *MMWR Surveillance Summaries*, 68(12), 1. [Link](#)

³⁰ Morean, M. E., Butler, E. R., Bold, K. W., Kong, G., Camenga, D. R., Cavallo, D. A., ... & Krishnan-Sarin, S. (2018). Preferring more e-cigarette flavors is associated with e-cigarette use frequency among adolescents but not adults. *PloS one*, 13(1), e0189015. [Link](#)

³¹ Prepared by Floe Foxon. Through PinneyAssociates, Floe Foxon provides consulting services on tobacco harm reduction on an exclusive basis to Juul Labs Inc. The preparation of this writing was supported by JLI, and JLI reviewed and provided comments on draft writing.

and positive (though not causal) association between prior e-cigarette use and subsequent smoking among adolescents.³²

Studies purporting to evidence the gateway effect typically employ logistic regression techniques which control for a limited number of potential confounding variables. Indeed, Lee et al.³³ and Chan et al.³⁴ have seriously criticised these studies for insufficient adjustment for confounding attributes. To separate e-cigarettes' actual potential for causing smoking uptake among adolescents from existing risk factors which predispose adolescents to cigarette smoking, longitudinal cohort studies must control for variables including but not limited to (1) association with smoking peer group, (2) family members' smoking, (3) academic achievement / school commitment, (4) alcohol and other substance use, (5) susceptibility to future smoking, and (6) delinquent behaviour, which predict tobacco use among adolescents.³⁵ Lee and coauthors identify 34 possible confounding variables which complicate attribution of e-cigarette use to subsequent smoking.³⁶ This is crucial because spurious gateway effects have been shown to appear in studies which do not appropriately adjust for these confounders, and when the same data are used in analyses which do adjust for these confounders, the apparent gateway effect is greatly diminished or disappears entirely.³⁷ In another systematic review, Public Health Physician and Clinical Epidemiologist Dr Cother Hajat and co-authors have described these studies as “not reliably [able to] establish causation.”³⁸

An alternative hypothesis which explains the apparent gateway associations observed in longitudinal studies is common liability. Sociodemographic and even genetic overlaps between smoking and vaping adolescents have been identified,³⁹ which leads to the possibility that adolescents who go on to smoke would do so regardless of whether or not they have previously used e-cigarettes, and that adolescents who experiment with one product are likely to also experiment with the other in a way that is not causal between products. Common liability is supported by studies which have identified that the association between e-cigarette use and smoking is bidirectional; prior e-cigarette use is associated with subsequent smoking, but prior smoking is also associated with subsequent e-cigarette use.⁴⁰ This bidirectionality is explained if adolescents who are likely to use nicotine products do so regardless of previous product use. Hanafin et al. described e-cigarette use as “part of a pattern of teenage polysubstance use including cigarette smoking, providing some support for the common liability

³² Soneji S, Barrington-Trimis JL, Wills TA, Leventhal AM, Unger JB, Gibson LA, Yang J, Primack BA, Andrews JA, Miech RA 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 Pediatrics* 2017, 171(8):788–797. [Link](#)

³³ Lee P, Coombs K, Afolalu E: Considerations related to vaping as a possible gateway into cigarette smoking: an analytical review [version 3; peer review: 2 approved]. *F1000Research* 2019, 7(1915). [Link](#)

³⁴ Chan GCK, Stjepanović D, Lim C, Sun T, Shanmuga Anandan A, Connor JP, Gartner C, Hall WD, Leung J: Gateway or common liability? A systematic review and meta-analysis of studies of adolescent e-cigarette use and future smoking initiation. *Addiction* 2021, 116(4):743–756. [Link](#)

³⁵ Derzon, J. H., & Lipsey, M. W. (1999). Predicting tobacco use to age 18: a synthesis of longitudinal research. *Addiction*, 94(7), 995-1006. [Link](#)

³⁶ Lee P, additional file of ‘Considerations related to vaping as a possible gateway into cigarette smoking: an analytical review’. [Link](#)

³⁷ Kim, S., & Selya, A. S. (2020). The relationship between electronic cigarette use and conventional cigarette smoking is largely attributable to shared risk factors. *Nicotine and Tobacco Research*, 22(7), 1123-1130. [Link](#)

³⁸ Hajat, C., Stein, E., Selya, A., & Polosa, R. (2022). Analysis of common methodological flaws in the highest cited e-cigarette epidemiology research. *Internal and Emergency Medicine*, 1-23. [Link](#)

³⁹ Khouja, J. N., Wootton, R. E., Taylor, A. E., Davey Smith, G., & Munafò, M. R. (2021). Association of genetic liability to smoking initiation with e-cigarette use in young adults: A cohort study. *PLoS medicine*, 18(3). [Link](#)

⁴⁰ Staff, J., Kelly, B. C., Maggs, J. L., & Vuolo, M. (2022). Adolescent electronic cigarette use and tobacco smoking in the Millennium Cohort Study. *Addiction*, 117(2), 484-494. [Link](#)

theory,”⁴¹ and Copp et al. similarly state that “E-cigarette use and smoking initiation may be interchangeable outcomes amongst those with smoking risk factors.”⁴²

If e-cigarette use among adolescents were causally associated with subsequent smoking uptake, then an increase in e-cigarette use at the population level would have to be followed by an increase in population-level cigarette smoking. However, no such increase in adolescent smoking behaviour has been observed. On the contrary, time-series analyses of population-level trends in adolescent e-cigarette use and smoking behaviour consistently find that cigarette smoking has continued to decline among adolescents.^{43,44,45,46}

V. The Impact of Harm Misperceptions on Adult Smokers

Nicotine is addictive and is the main reason people continue to smoke despite knowing the risks. But epidemiological studies, including studies of the long-term impacts of nicotine replacement therapies (NRTs), show that nicotine delivered without smoke is not a major source of harm. Most of the harm associated with smoking comes from other chemical constituents in tobacco, and in the smoke created through combustion, such as tobacco-specific nitrosamines (TSNAs), carbon monoxide, and volatile organic compounds.

“Nicotine, though not benign, is not directly responsible for the tobacco-caused cancer, lung disease, and heart disease... other chemical compounds in tobacco, and in the smoke created by combustion, are primarily to blame for such health harms.” -Former FDA Commissioner Scott Gottlieb and Center for Tobacco Products Director Mitch Zeller

Unfortunately, many smokers are confused about the role of nicotine and wrongly believe that non-combustible products, such as e-cigarettes, and cigarettes present the same level of risk. This confusion is driven in part by misperceptions about nicotine and its role in smoking-related disease, which are widespread and have worsened over time. Misconceptions about these products are at an all-time high, which may hinder adult smokers’ ability to switch away from cigarettes.⁴⁷

These misperceptions are not limited to the public writ large but also are found among healthcare professionals. In one study, over 80% of physicians in the United States “strongly agreed” that “nicotine directly contributes to” cancer, COPD, and cardiovascular disease.⁴⁸ Ferrera et al found that 82%

⁴¹ Hanafin, J., Sunday, S., & Clancy, L. (2022). Sociodemographic, personal, peer, and familial predictors of e-cigarette ever use in ESPAD Ireland: A forward stepwise logistic regression model. *Tobacco Induced Diseases*, 20. [Link](#)

⁴² Copp, S. R., Wilson, M. N., & Asbridge, M. (2022). Smoking Susceptibility in Canadian Adolescent Electronic-Cigarette Users. *Substance Use & Misuse*, 57(7), 1022-1034. [Link](#)

⁴³ Foxon, F., & Selya, A. S. (2020). Electronic cigarettes, nicotine use trends and use initiation ages among US adolescents from 1999 to 2018. *Addiction*, 115(12), 2369-2378. [Link](#)

⁴⁴ Levy, D. T., Warner, K. E., Cummings, K. M., Hammond, D., Kuo, C., Fong, G. T., ... & Borland, R. (2019). Examining the relationship of vaping to smoking initiation among US youth and young adults: a reality check. *Tobacco control*, 28(6), 629-635. [Link](#)

⁴⁵ Sokol, N. A., & Feldman, J. M. (2021). High school seniors who used e-cigarettes may have otherwise been cigarette smokers: evidence from monitoring the future (United States, 2009–2018). *Nicotine and Tobacco Research*, 23(11), 1958-1961. [Link](#)

⁴⁶ Walker, N., Parag, V., Wong, S. F., Youdan, B., Broughton, B., Bullen, C., & Beaglehole, R. (2020). Use of e-cigarettes and smoked tobacco in youth aged 14–15 years in New Zealand: findings from repeated cross-sectional studies (2014–19). *The Lancet Public Health*, 5(4), e204-e212. [Link](#)

⁴⁷ Persoskie A, O'Brien EK, Poonai K. Perceived relative harm of using e-cigarettes predicts future product switching among US adult cigarette and e-cigarette dual users. *Addiction*. 2019 Dec;114(12):2197-2205. doi: 10.1111/add.14730. Epub 2019 Jul 25. [Link](#)

⁴⁸ M. Steinberg, et al., Nicotine Risk Misperception Among US Physicians, *Journal of General Internal Medicine* (2020). [Link](#)

of surveyed European residents in public health associated nicotine with smoking related diseases and 59% stated that nicotine contributes to lung cancer.⁴⁹

Correcting these misperceptions is very important. Without clear, risk-based communication from trusted sources, there is less of an incentive to switch away from cigarettes. It is imperative that alternatives can compete with combustible cigarettes and that adult smokers have clear information on a product's relative risk compared to smoking.

The current state of public (mis)understanding about the harms of nicotine and relative risk of noncombustible compared to combustible products highlights the need for research and messaging development to support accurate, non-misleading information for adult current users, particularly those of combustible cigarettes. This information, in turn, can help move adult smokers down the continuum of risk and support broader regulatory and public-health objectives based on the data and science and evidence.

⁴⁹ Ferrara, P., Shantikumar, S., Cabral Verissimo, V., Ruiz-Montero, R., Masuet-Aumatell, C., Ramon-Torrell, J. M., & EuroNet MRPH Working Group on Electronic Cigarettes and Tobacco Harm Reduction. (2019). Knowledge about e-cigarettes and tobacco harm reduction among public health residents in Europe. *International Journal of Environmental Research and Public Health*, 16(12), 2071. [Link](#)