

Review of controversial Canadian ‘gateway effect’ study

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Introduction

This note examines the interpretation of a recent Canadian study², which concludes:

E-cigarette use was positively associated with susceptibility to cigarette smoking.

Despite this modestly expressed conclusion, much more aggressive statements were presented by the authors to the media in a press release³:

Vaping doubles risk of smoking cigarettes for teens

[...] Teenagers who try e-cigarettes double their risk for smoking tobacco cigarettes, according to a new study. The study found that students in grades seven to 12 who had tried an e-cigarette are 2.16 times more likely to be susceptible to cigarette smoking.

[...] "Since e-cigarettes came on the market there has been a debate about whether their use may lead to cigarette smoking," said Bruce Baskerville, co-author on the study and a researcher at the Propel Centre for Population Health Impact at the University of Waterloo. "The answer among adolescents is yes."

1. Implying a causal relationship when the study shows an association

The main problem with the media claims is that they imply that the study establishes a *causal* link between early vaping and uptake of smoking – implying taking up vaping increases the likelihood of smoking. In fact, the study shows an *association* – and not with smoking, but ‘susceptibility to smoking’. The more likely explanation for the observed data is that young people who take up vaping also have a predisposition to smoking, and this is something to do with their personal characteristics, background, and social and family life. In other words, the same things that incline them to smoke also incline them to try vaping – a ‘smoking-like’ behaviour, albeit with much lower health risks, and it is no surprise that these behaviours cluster together. Responding to a 2015 study⁴ for which similar claims were made, Marcus Munafò, Professor of Biological Psychology at University of Bristol (UK), editor of the *Nicotine and Tobacco Research* journal and specialist in genetic and cognitive influences on addictive behaviour, explained this as follows⁵

People who try stuff, try stuff...

¹ About the author: [\[link\]](#)

² Azagba S, Baskerville NB, Foley K. Susceptibility to cigarette smoking among middle and high school e-cigarette users in Canada. *Prev Med* (Baltim). 2017 Oct;103:14–9. [\[link\]](#)

³ University of Waterloo. Media release. "Vaping doubles risk of smoking cigarettes for teens." ScienceDaily. 18 September 2017. [\[link\]](#).

⁴ Leventhal AM, Strong DR, Kirkpatrick MG, Unger JB, Sussman S, Riggs NR, et al. Association of Electronic Cigarette Use With Initiation of Combustible Tobacco Product Smoking in Early Adolescence. *JAMA*. 2015 Aug 18;314(7):700–7. [\[link\]](#)

⁵ Munafò M. Tweet, 20 August 2015 [\[link\]](#) In response to Bates CD. JAMA paper finds some adolescents experiment with stuff – so what? Counterfactual. 18 August 2015 [\[link\]](#)

It is an unfortunate but common trait in academic publishing for press statements to go beyond the realistic interpretation of the data published in the study, and for caveats about causation (“correlation is not causation”) to be dropped in favour of more newsworthy statements.

2. Study did not measure smoking, only ‘susceptibility’ to smoking

Despite the bold media claims about increased risk of smoking, the study does not actually confirm a progression to regular smoking, which is the actual behaviour of concern. The authors measured a personal characteristic at a point in time, so-called ‘susceptibility to smoking’, and considered that to be an adequate proxy for future smoking. Susceptibility to smoking is “*defined as the lack of a firm decision not to engage in smoking in the future*”. This is measured by asking young people a series of three questions:

Questions asked to establish ‘susceptibility to smoking’.

- (1) Do you think in the future you might try smoking cigarettes?
- (2) If one of your best friends was to offer you cigarette would you smoke it?
- (3) At any time in the next year do you think you will smoke a cigarette?

Answers to each of these three questions have four options:

- (1) definitely yes
- (2) probably yes
- (3) probably not
- (4) definitely not

Only students who answered ‘definitely not’ to all three questions were considered non-susceptible to smoking; otherwise, students were considered susceptible.

Researchers do use these questions to gauge susceptibility, and it is true that those who answer ‘definitely not’ to all three are less likely to go on to smoke. But as a way of describing young people’s behaviour it is very unsatisfactory. It is a binary yes/no characterisation of highly graduated intentions that tend to change over time – for example a new boyfriend or girlfriend can easily change a teenager’s likelihood of smoking. The standard susceptibility measure has poor predictive power when tested against actual smoking outcomes. In a California study, only 19% of those identified as ‘susceptible’ became young adult smokers⁶.

The original index classified almost half (48%) of the 12–15 year old population of California in 1996 as susceptible to smoking and 19% of these became young adult smokers (positive predictive value [PPV]). The sensitivity of this measure (i.e., the identification of those who actually became young adult smokers) was 62% and the specificity (the percent of long term never-smokers identified as committed never-smokers at 12–15 years) was 50%.

We should note that a rational response to a question about future behaviour is always a ‘probably’ or ‘probably not’ – no-one can be truly definite about how they will be in the future. But answering the question: ‘*If one of your best friends was to offer you cigarette would you smoke it?*’ with ‘*probably not*’ would identify the subject as susceptible to smoking. An important problem with the

⁶ Strong DR, Hartman SJ, Nodora J, Messer K, James L, White M, et al. Predictive validity of the expanded susceptibility to smoke index. *Nicotine Tob Res.* Oxford University Press; 2015 Jul;17(7):862–9. [[link](#)]

study is that it is using a very weak proxy for the behaviour of real concern, regular smoking – but in its press release headline, it does not draw this distinction, it baldly states: ‘*Vaping doubles risk of smoking cigarettes for teens*’.

3. Study does not show that vaping *increases* susceptibility to smoking

The study does not (and cannot) show that the susceptibility *increased* when the subjects used an e-cigarette – that would be a little more compelling, but there is nothing to suggest this happens in this study. It takes a cross-sectional (i.e. snapshot) view of susceptibility at a point in time. If the susceptibility is unchanged by vaping, then it is likely that the susceptibility to smoking is simply an indicator of susceptibility to vaping. This would not be a surprise: vaping is a ‘smoking-like’ behaviour, albeit with much less harm to the user.

4. The challenges of confounding in this survey are significant

The authors do recognise that other independent factors could be causing both the susceptibility to smoking and the experimentation with vaping as discussed above in Section 1. So they try to adjust for this effect using a range of variables collected in the survey that would predict whether the young person would have become a smoker anyway in the absence of vaping. Peter Lee provides a guide to this problem and how researchers try to address it⁷:

Observing an association between the use of A and the use of B does not, of itself, confirm the gateway hypothesis. An association may arise, in theory, for one of three reasons:

- *A causes B, i.e. the gateway hypothesis is true*
- *B causes A, i.e. reverse causation*
- *a third factor (or set of factors) C causes both A and B, i.e. confounding*

The main challenge is to separate out how much of the increased susceptibility to smoking (i.e. the equivalent of B) is caused by uptake of vaping (A) itself and how much is caused by characteristics of the individuals and their lives (C) that incline them to both smoke and vape – and the related problem of how they tell these two effects apart. This is the problem *adjusting for confounding*.

5. The problem of adjusting for confounding

To do this, researchers can try to estimate what part of the observed association between A and B is due to these independent ‘confounding’ factors C and what part is due to A causing B. This is known as *adjusting for confounding*. In this study, the authors use a range of variables that they believe predict for susceptibility for smoking (in fact they are predictors for smoking) and these are described in the study:

The analyses adjusted for gender, grade levels, region of residence, smoking-related exposure, school-level area household income, substance use, social responsiveness and relatedness.

⁷ Lee PN. Appropriate and inappropriate methods for investigating the ‘gateway’ hypothesis, with a review of the evidence linking prior snus use to later cigarette smoking. *Harm Reduct J* 2015;12:8. [\[link\]](#)

In his methods paper on gateway effects⁸, Carl V. Phillips outlines the weaknesses in this approach:

In practice in public health research, “controlling for confounding” consists of throwing in whatever variables the researcher has that might be (though often probably are not) proxies for real confounders.

Phillips continues:

But even when researchers are skilled at identifying optimal deconfounders, it is often the case that either no available variables offer good proxies for the postulated confounders or that they are not measured accurately enough for statistical adjustment to occur. For example, a researcher trying to assess whether an exposure causes smoking may realize that he needs to control for propensity for depression and willingness to defy social pressure, but the available covariates (age, race, level of education, income, etc.) offer little deconfounding for these. Controlling for the heterogeneous preferences for nicotine seems nearly impossible.

The reason that this is important for this study is that the researchers draw conclusions as if they have fully adjusted for all confounding factors, and therefore the residual association must be attributable to the relationship between vaping and susceptibility to smoking. As Phillips points out:

Seldom do researchers even discuss what hypothesized confounder variables they are attempting to proxy for, let alone offer any argument that the control variables they threw into their model achieve the goal of deconfounding.

Some part, or possibly all, of the effect size after adjusting for confounding with the available variables will be due to other variables that the authors do not have access to because they are not part of the survey, or that they do not know to be a factor in determining smoking.

If we hypothesise a situation where vaping experimentation and susceptibility were entirely explained by independent variables (i.e. vaping did not cause smoking susceptibility, but other factors caused both), then the residual association after adjustment with the available variables, such as that found in this study, would simply represent incomplete deconfounding (i.e. the effect of variables and precision not included in the calculation) and this would disappear as more variables and more relevant variables were added to the regression.

6. Ignoring potential benefits of vaping as an *alternative* to teenage smoking

One plausible explanation for the observed results is that those who were already susceptible to smoking noticed the rise of vaping and began to take an interest in vaping as an alternative to smoking. Their interest in vaping was *caused by their susceptibility to smoking* – this is reverse causation (B causes A). This holds out the prospect that vaping could be *beneficial* to these youth. It may have the effect of displacing smoking and meeting the need of those who are susceptible to engage in a ‘smoking-like’ behaviour in a way that does much less harm. This interpretation would be consistent with the data from the United States, where a rise in teenage vaping in the past 30

⁸ 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;12:5439–64. [[link](#)]

days has been accompanied by a rapid decline in teenage smoking – see [Appendix 1](#). The authors describe their findings with reference to the United States:

Using a nationally representative sample of Canadian students in grades 7–12, this study of never smokers, found that e-cigarette use was significantly associated with susceptibility to future cigarette smoking after adjusting for gender, grade level, region of residence, smoking-related exposure, school-level area household income, substance use, social responsiveness and relatedness. This finding is consistent with previous US studies.

But they fail to note the *anomalously rapid decline* in teenage smoking in the United States, which has been 3-4 times the long run rate of decline since 2010 among 12th graders ([Appendix 1](#)). If vaping is increasing susceptibility to smoking, then where are all the new smokers? These observational data cannot establish that vaping caused the decline in teenage smoking. Further, it is possible that smoking declines would have been even more rapid in the absence of vaping, but no credible theories have been advanced for why that should be. The simplest explanation is the one the authors avoid referring to.

Because the study does not assess future smoking status, we do not know whether susceptibility to smoking is still a reliable proxy for future *smoking* – past studies are not reliable in this respect because they were largely conducted without the option to switch to vaping. The authors simply have not considered this possibility: that the propensity to smoke is really a propensity to engage in ‘smoking-like’ behaviour, including vaping. It could be this that generates interest in vaping and that this might be an alternative pathway followed by those trying vaping. That is more consistent with US data than the alarming and alarmist explanation that the authors presented to the media.

7. Difference between experimentation and regular smoking

It is important to be clear what behaviour is under consideration. Teenagers undergo a period of *experimentation* – in which they try different behaviours, and this may include both smoking and vaping. *Experimentation* is different to the behaviour of concern, which is *regular smoking with signs of dependence* emerging from the period of experimentation. In a recent commentary⁹, Coral Gartner, Associate Professor at University of Queensland states:

It is plausible that vaping may increase the likelihood of experimenting with smoking through increased familiarity with a behaviour that resembles smoking and/or curiosity about how the two experiences compare. But it is unknown how many of those who might try smoking who would not have done so without trying vaping first will then go on to become regular smokers.

Equally, we do not know how many of those who would have smoked might not go on to smoke and may vape instead. The introduction of vaping creates a several new pathways that may appeal to young smokers – and many of these may be beneficial alternatives to smoking. The study reviewed here uses ‘ever-use’ and ‘used-in-last-30-days’ as its indicator of exposure. But these are extremely crude indicators – there is a big difference between using once or twice a month and daily use.

⁹ Gartner CE. E-cigarettes and youth smoking: be alert but not alarmed. *Tob Control*; 2017 Sep 8;tobaccocontrol-2017-054002. [\[link\]](#)

Analysis of US frequency-of-use data suggests that regular vaping is overwhelmingly concentrated in teenagers who smoke or would otherwise smoke¹⁰:

Few never tobacco users had used e-cigarettes on 10 or more days in the past month (absolute percent < 0.1%). Among past 30-day cigarette and smokeless users, the two highest frequency categories were 1–2 days and daily use;

Put simply, most teenage vaping use is occasional and experimental – perhaps teenagers just playing around, rather than a precursor to a substance use syndrome. This appears position in the UK, and the available data is encouraging. Professor Linda Bauld and colleagues examined UK survey data to date¹¹ and concluded:

In summary, surveys across the UK show a consistent pattern: most e-cigarette experimentation does not turn into regular use, and levels of regular use in young people who have never smoked remain very low.

The study reviewed here does not and cannot address these possibilities.

8. Other critiques of gateway claims

Professor Lynn Kozlowski and Professor Ken Warner address methodological weakness in the available studies claiming to identify gateway effects¹².

Prospective studies – the only evidence that e-cigarette use might lead to smoking – do not yet persuade that e-cigarettes are a substantial causal gateway to cigarettes. At best, they support that a minority of the relatively small number of e-cigarette triers – who haven't also been experimenting with other tobacco products already – will go on to some experimentation with cigarettes. We need to better understand and assess confounding variables, such as other tobacco use, other substance use (marijuana and alcohol), and mental illness, as they influence the behavior of high-risk youth.

[...] the unprecedented decrease in smoking during and following a period in which e-cigarette use was rising rapidly raises a possibility that must be considered: E-cigarettes may conceivably be a useful product for a subset of youth at high risk of smoking. For this subset, vaping may constitute a less dangerous alternative to cigarette smoking.

Note that the study under review here is not even a prospective study, i.e. one that compares behaviour at two or more points in time.

¹⁰ Villanti AC, Pearson JL, Glasser AM, Johnson AL, Collins LK, Niaura RS, et al. Frequency of youth e-cigarette and tobacco use patterns in the U.S.: Measurement precision is critical to inform public health. *Nicotine Tob Res.* December 2016 [[link](#)]

¹¹ Bauld L, MacKintosh A, Eastwood B, Ford A, Moore G, Dockrell M, 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.* Multidisciplinary Digital Publishing Institute; 2017 Aug 29;14(9):973. [[link](#)]

¹² Kozlowski LT, Warner KE. Adolescents and e-cigarettes: Objects of concern may appear larger than they are. *Drug Alcohol Depend.* 2017 May;174(1 May 2017):209–14. [[link](#)][[PDF](#)]

Professor Jean François Etter of the University of Geneva, summarises the literature¹³

A spurious gateway effect can be produced artificially by mathematical models in which a propensity to use substances is correlated with opportunities to use substances. Finally, neither nicotine medications nor smokeless tobacco produce gateway effects. Available data are compatible with a common liability model in which people who are liable to use nicotine are more likely to use both e-cigarettes and cigarettes.

Experts summarising the data for Public Health England, concluded that e-cigarettes (EC) do not create an established gateway to smoking, and that the concept is so poorly defined that its use should be abandoned¹⁴:

The gateway theory is ill defined and we suggest its use be abandoned until it is clear how it can be tested in this field. Whilst never smokers are experimenting with EC, the vast majority of youth who regularly use EC are smokers. Regular EC use in youth is rare.

9. Conclusions

The main concern with the study is that the claims made in the media release go considerably beyond what the published paper can support and use language that suggest the authors have discovered a gateway effect. The study itself does as well as can be done within its many limitations, but the limitations are profoundly challenging and a reason for caution in drawing any conclusions – let alone baldly stating that “*vaping doubles the risk of teenage smoking*”.

Most likely explanation. The most likely explanation for the results is ‘common liability’ – the characteristics, family and social environment that make young people inclined to smoke also make them inclined to vape. This would not be a surprise given both are ‘smoking-like’ behaviours. This does not mean the vaping causes the smoking, but both are caused by characteristics of the individual, family and social context.

The possibility of health benefits was overlooked. The study does not examine smoking behaviours, but a very weak proxy measure for smoking – a measure of *susceptibility to smoking* which has low (but not zero) predictive power. However, susceptibility measures may also reflect *susceptibility to vaping* and it is possible vaping could displace future smoking. This effect would be more consistent with the dramatic declines there have been in teenage smoking, for example in the United States ([Appendix 1](#)).

Fundamental limitations should have been a reason for caution not aggressive policy-sensitive media claims. The study relies on correcting for ‘confounding factors’ but is necessarily an approximate process that relies on the data that was collected in the survey. The survey was not designed for this purpose and the available variables are unlikely to remove all confounding. It is quite possible that all the effect observed could be explained by unadjusted confounding.

¹³ Etter J-F. Gateway effects and electronic cigarettes. *Addiction*. 2017 Aug 7; [\[link\]](#)

¹⁴ McNeill A, Brose LS, Calder R, *et al.* E-cigarettes: An Evidence Update. A Report Commissioned by Public Health England. London: 2015. [\[link\]](#) Section 4 *Gateway* page 37

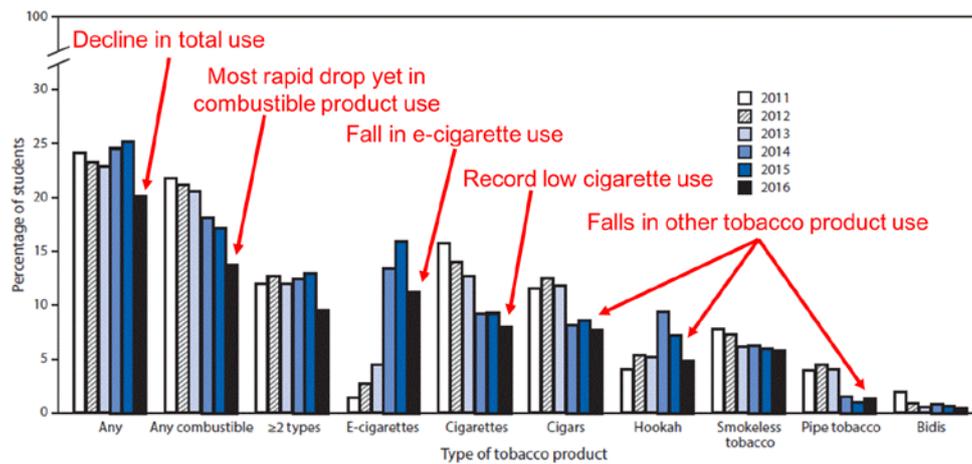
About the author

Clive Bates is director of Counterfactual, a consulting and advocacy practice focused on a pragmatic approach to sustainable development, energy policy and public health that he founded in 2013. He has had a diverse career in the public, private and nonprofit sectors. After securing a degree in engineering from Cambridge University, he worked in information technology for IBM before moving on to work as an energy specialist with several environmental nonprofits. From 1997 to 2003, he was the United Kingdom's director of Action on Smoking and Health, campaigning to reduce the harms caused by tobacco. In 2003, he joined Prime Minister Tony Blair's Strategy Unit as a civil servant and worked in several roles in the public sector in the United Kingdom and for the United Nations in Sudan. This report was written as part of Counterfactual's advocacy program without additional funding. Clive Bates and Counterfactual have no competing interests with respect to e-cigarette, tobacco or pharmaceutical industries.

Appendix 1: Trends in tobacco and nicotine use in the United States

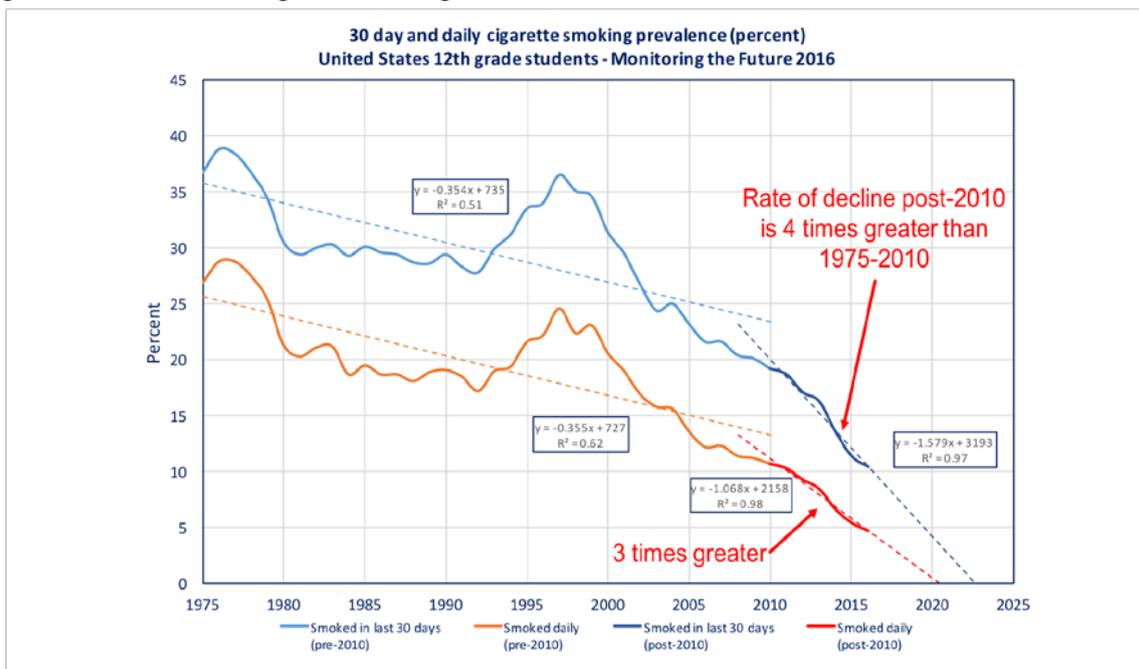
The two charts that follow are annotated to show salient features of the most recent data on youth smoking in the United States. The first is from the National Youth Tobacco Survey, published June 2017¹⁵.

FIGURE 1. Estimated percentage of high school students who currently use any tobacco products,* any combustible tobacco products,[†] ≥2 tobacco products,[‡] and selected tobacco products — National Youth Tobacco Survey, United States, 2011–2016^{†,*,**}



* Any tobacco product use is defined as past 30-day use of electronic cigarettes, cigarettes, cigars, hookahs, smokeless tobacco, pipe tobacco and/or bidis.

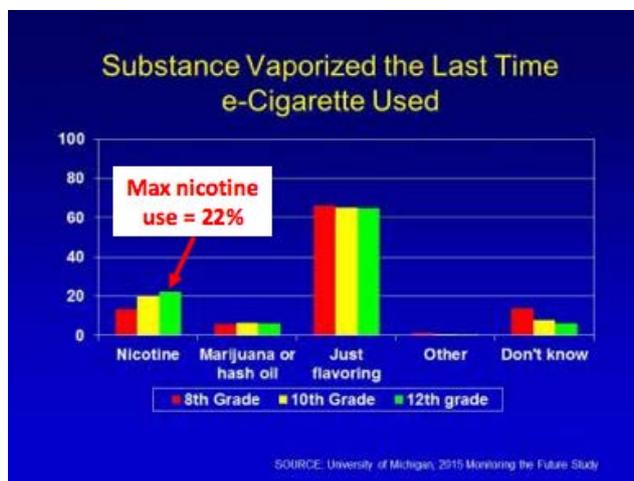
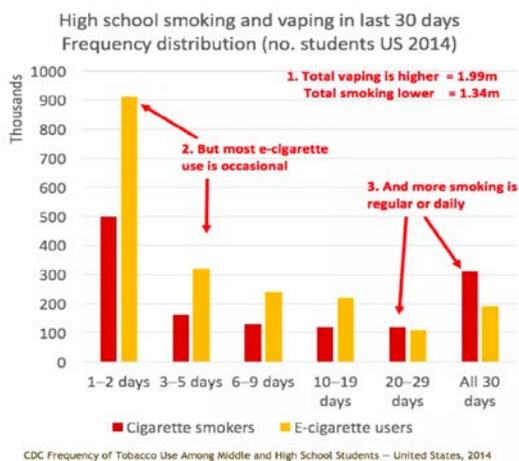
The second is from the 2016 University of Michigan Monitoring the Future survey, which has a time series dating back to 1975 for 12th grade smoking¹⁶.



¹⁵ Jamal A, Gentzke A, Hu SS, Cullen KA, Apelberg BJ, Homa DM, et al. Tobacco Use Among Middle and High School Students - United States, 2011-2016. *MMWR Morb Mortal Wkly Rep.* 2017 Jun 16;66(23):597-603. [\[link\]](#)

¹⁶ Miech RA, Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE. Monitoring the Future national survey results on drug use, 1975-2016: Data tables. Table 2 - Trends in Prevalence of Use of Cigarettes. University of Michigan; Ann Arbor: 2016. [\[Tables\]](#) [\[Dataset\]](#).

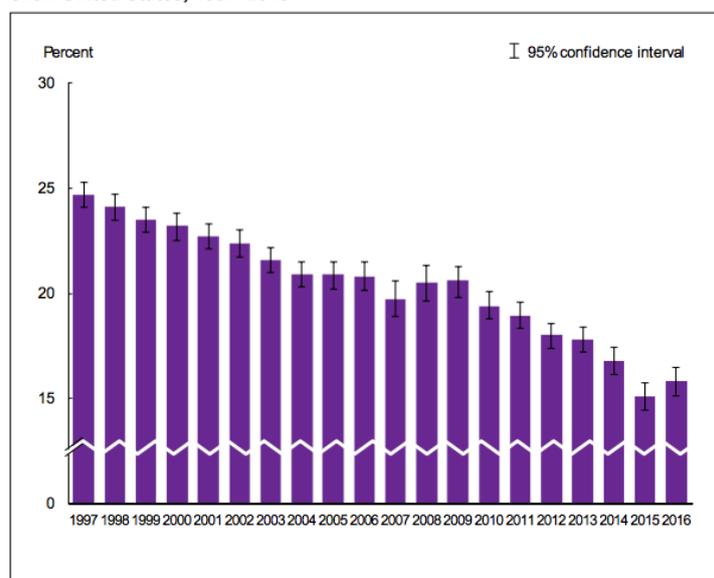
The third shows that the use of e-cigarettes is far less problematic than the headline numbers might suggest¹⁷. Though e-cigarette use rose sharply, from 2011-15 then fell back in 2016, much of this was occasional or experimental use. Also, students reported that most of their use did not involve nicotine liquids¹⁸.



Importantly, adult smoking has fallen at a rapid rate over the period vaping has risen¹⁹

Current smoking

Figure 8.1. Prevalence of current cigarette smoking among adults aged 18 and over: United States, 1997–2016



¹⁷ Neff LJ, Arrazola RA, Caraballo RS, *et al.* Frequency of Tobacco Use Among Middle and High School Students--United States, 2014. *MMWR Morb Mortal Wkly Rep* 2015;**64**:1061–5 Table 35. [\[link\]](#)

¹⁸ Miech R, Patrick ME, O'Malley PM, Johnston LD. What are kids vaping? Results from a national survey of US adolescents. *Tob Control*; 2016 [\[link\]](#).

¹⁹ National Center for Health Statistics, National Health Interview Survey [\[link\]](#), Sample Adult Core component. Figure 8.1. Prevalence of current cigarette smoking among adults aged 18 and over: United States, 1997–2016. [\[data\]](#) Accessed June 2017. Note the 2016 figure is not strictly comparable due to a new survey design.