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# Adolescents and e-cigarettes: Objects of concern may appear larger than they are<sup>☆</sup>

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## 1. Introduction

The debate about electronic cigarettes ranks as perhaps the most divisive in the history of tobacco control. Proponents believe that e-cigarettes could foster widespread abandonment of combusted tobacco products, by far the most dangerous form of tobacco use, and thereby dramatically reduce the disease and death caused by smoking (Abrams, 2014). Opponents fear these products may seduce new generations of youth into nicotine addiction, many of whom may even find a ‘gateway’ to cigarette smoking. They see in e-cigarettes the potential of ‘renormalizing’ smoking (U.S. Department of Health and Human Services, 2016). In striking contrast to supporters’ view, some oppo-

nents worry that dual use of cigarettes and e-cigarettes by adults will reduce smoking cessation. And in similarly striking contrast to opponents’ worries about kids, supporters believe that e-cigarettes may be providing young people an alternative to far more dangerous cigarette smoking (Kozlowski, in press; Kozlowski and Sweaner, in press; Warner, 2016).

Uncertainty about the health hazards associated with novel products, how they are used and how their use affects smoking, has created a burgeoning research field. A systematic review of empirical research through May 2016 included 687 articles (Glasser et al., 2016). The intensity of people’s ‘moral emotions’ (anger, disgust, or contempt) about the novel products can color their interpretation of the science, however (Kozlowski, 2013; Kozlowski, in press), consistent with the concept of signal detection (Anderson, 2015; Tanner and Swets, 1954). Detection of even simple signals, such as the presence or absence of a tone, is influenced by rewards for detecting or not detecting the stimulus. When the signals, including evidence, support favored narratives on complex issues, especially in a morally and politically-charged con-

text such as tobacco control (Kozlowski, 2015; Kozlowski, in press), there are biases for (a) seeking information that supports one’s position (confirmation bias), (b) more critically assessing opposing work (disconfirmation bias), and (c) inclining to support one’s prior beliefs (a prior belief effect) (Strickland et al., 2011). We believe that signal detection is playing a central role in the debate over e-cigarettes. People on both sides are finding evidence that supports what they want to believe.

In this essay we examine the relative merits of leading studies on whether e-cigarettes pose significant threats to youths’ health and well-being. While we focus on youth, the context occasionally requires that we address adult-relevant considerations as well. Overall we conclude that the risks for youth posed by e-cigarettes likely fall far short of those feared by the products’ opponents. Conceivably, e-cigarettes may create a net benefit for some high-risk young people. We are mindful of our own risk of falling victim to signal-detection biases. Readers will judge for themselves the probity of our effort to avoid such biases.

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## 2. Nicotine-containing vapor is not safe but is much less harmful than cigarette smoke

No one considers vaping risk-free. But neither is there any significant doubt that vaping is much less harmful than smoking cigarettes. The critical issue is how much. The UK Royal College of Physicians recently concluded that e-cigarettes are likely 95% less-harmful than cigarettes (Royal College of Physicians, 2016; see also McNeill et al., 2015; Nutt et al., 2014). Even those who dispute this degree of risk reduction still accept that risks are substantially reduced (Glantz, 2016). E-cigarettes emit a small fraction of the toxins found in cigarette smoke and, for the toxins vapor does include, the emission levels are much smaller than those in cigarette smoke (Glasser et al., 2016). Still, the nicotine in nicotine-containing vapor (not all e-cigarettes include nicotine) carries concerns similar to those associated with nicotine-containing cigarettes. This includes the ability to create or support nicotine addiction.

For adolescents' developing brains, use of any nicotine products may have negative effects (England et al., 2015). How these effects compare to those of other drugs (alcohol, caffeine, psychotropic medications) (Arain et al., 2013) is unclear. What we find fascinating, however, is that the issue of nicotine's effects on the developing brain has been brought forcefully to the public's attention only since sizable numbers of young people started using e-cigarettes. If anything, the concern should be greater regarding kids' cigarette smoking but it was rarely brought into discussions of youth smoking. Moreover, if vaping substitutes for smoking for some kids, e-cigarettes would pose no net additional nicotine-associated risk for those young people.

## 3. E-cigarettes as a gateway to smoking: a principal argument against e-cigarettes

The causal gateway theory is straightforward: E-cigarettes attract children who never would have become smokers, perhaps because they view e-cigarettes as potentially "fun" like smoking but without the risk. Their experience with e-cigarettes causes them to try conventional cigarettes, when they would not have done so otherwise, and a proportion become regular, addicted smokers. If they would have tried smoking anyway

but simply tried e-cigarettes first, there is no causal gateway.

### 3.1. Findings from prospective studies

Longitudinal studies have reported evidence consistent with a causal gateway. Researchers have identified children who use e-cigarettes in time 1 (T1) and compare their usage of cigarettes in time 2 (T2), generally 6–12 months later, to that of comparable children who did not use e-cigarettes in T1. In most of these studies, the researchers have found a statistically significant increase in cigarette use in T2 among the T1 e-cigarette users (Barrington-Trimis et al., 2016; Huh and Leventhal, 2016; Leventhal et al., 2015; Primack et al., 2015; Wills et al., 2016a; Wills et al., 2016b; Miech et al., in press).

To reduce the possibility that other factors account for any observed relationship between e-cigarette use and subsequent smoking, these studies attempt to control for some of the following: kids' risk-taking propensities (e.g., 'sensation-seeking'), other substance use, and other potential confounders such as peer and parental smoking.

### 3.2. Limitations of the prospective studies

When randomized controlled trials are impossible, as in this situation, prospective observational trials are preferred to cross-sectional studies. Nevertheless, one should recognize the challenge of making causal interpretations of the behavioral trajectories arising from longitudinal studies (Raudenbush 2001). It is not surprising that individuals who have not yet smoked one cigarette but who decide to try an e-cigarette would be likelier to later try cigarettes. The key questions are why and to what effect, and the minimal, two-time-period, prospective studies to date have not satisfactorily answered "why" and not addressed "to what effect" at all.

Never-smokers who try e-cigarettes likely differ in many ways from never-smokers who never try them. Some differences may be related to other individual preferences (e.g., liking other drugs or other tobacco products) and other differences may arise from differing contexts (e.g., their friends or parents are vaping). Having tried an e-cigarette, they might then try cigarettes because: (a) curiosity makes them interested in comparing effects; (b) they like the effects of e-cigarettes and hope cigarettes might be even better; (c) they dislike the effects of e-cigarettes and hope cigarettes might be better; (d) the friend who pushed them to try e-cigarettes uses both e-cigarettes

and cigarettes; or (e) they had been thinking of smoking anyway, but they thought, erroneously, that an e-cigarette might keep them from smoking (i.e., a 'reverse causation'; see Phillips (2015)). The public health concern is that possible increased smoking experimentation will lead to nicotine dependence and established daily cigarette smoking.

These prospective studies suffer from limited measures of smoking. Smoking has been defined (with the exceptions of Wills et al. (2016a,b) and Leventhal et al. (2016), as noted below) as having puffed on a cigarette at least once, with no indication of current use, frequency, or intensity. One puff on a cigarette, or even more experimentation, provides little evidence of progression to significant smoking. Using a longitudinal dataset that followed adolescents from 1994 to 1995 to 2008 (a time before e-cigarettes were important), Saddleson et al. (2016) found that, among non-daily smokers, just under 25% of those who had tried a cigarette but who had smoked 0–5 cigarettes in the past month were daily smokers and 38% who had smoked 6–60 cigarettes in the past month were daily smokers at follow-up. These numbers compare to 15% of youth never smokers and 61% of daily smokers at time 1 who were daily smokers at follow-up. In 2016, among 12th grade students who had ever smoked a cigarette in their lifetime, only 37% were past 30-day smokers and just 17% were daily smokers (Miech et al., 2016c). Note that smoking frequency and intensity among US students have declined dramatically over the two decades since the Saddleson et al. cohort was first investigated (Kozlowski and Giovino, 2014; Warner, 2015).

Leventhal et al. (2016) looked more closely at the intensity and frequency of T2 smoking. But even here, their definition of "highest intensity" ( $\geq 2$  cigarettes on smoking days) and "highest frequency" ( $\geq 3$  days in past 30 days) represents a low level of smoking that lacks sufficient distinction among usage levels. The sample likely did not include enough youth to support use of higher cut-points. The more refined measure of smoking used by Wills et al. (2016a) shows that at T2, among e-cigarette users at T1, 79% were still never smoking, and, among the new smokers, 52% had smoked 4 or fewer times, 14% were monthly smokers, and only 3% were daily smokers.

To understand any progression from e-cigarette use to regular cigarette smoking will require better longitudinal studies with large numbers of participants, a reasonably long time horizon with several repeated measures, and measures of smoking that capture estab-

lished, toxicologically-significant levels of tobacco use. The PATH study (Population Assessment of Tobacco and Health), covering 46,000 people  $\geq 12$  years old, may help (Hyland et al., 2016), by offering opportunities for more complex modeling of drug use and tobacco/nicotine use patterns.

Inferring that prior e-cigarette use causes subsequent smoking depends importantly on the quality of the measures used to assess confounding (Smith et al., 1992). More attention and more sophisticated thought need to be given to the growing problem of higher-risk youth. Smoking prevalence has declined least in high-risk, disadvantaged groups. Young individuals with mental illness, other alcohol and drug use issues, and school drop-outs are at a greatly elevated risk of cigarette smoking (Griesler, 2008; Mathur et al., 2013; Tauras et al., 2013).

Of course studies must limit the number of questions asked, but we are particularly concerned about the measures used (or lacking) concerning use of other psychoactive substances (e.g., alcohol, marijuana, psychoactive prescription drugs, and even harder drugs). The extent of their use by adolescents is arguably one of the most concrete and relevant measures of 'risk-taking' or 'sensation-seeking' that could confound gateway analyses. Leventhal et al. (2015, 2016) measured other substance use at baseline only as one binary (yes/no) response of any use ever of any of 14 products; youth who got drunk and used marijuana weekly would get the same score as youth who had only one drink years ago. Primack et al. (2015) did not include any assessment of other substance use at time 1, relied on a crude measure of 'sensation-seeking' with an internal consistency of only 0.72 (meaning that about half of the scores can be attributed to random error), and focused on only 16 e-cigarette users.

Wills et al.'s research is particularly illuminating. Their initial report of a prospective study on youth who were not cigarette smokers at T1 included age, gender, ethnicity, parental education, parental support and 'rebelliousness' as covariates and found that e-cigarette use predicted T2 cigarette smoking (Wills et al., 2016a). The authors later used the same dataset while controlling for other 'mediating' (or confounding) variables, adding measures of marijuana use, perceptions of smokers, peer smoking, and smoking expectancies measured at both T1 and T2 (Wills et al., 2016b). A prospective analysis using continuous measures (see their Fig. 2B) shows the importance of these T1 covariates in predicting T2 smoking levels, and their inclusion in the model

eliminates the direct effect of e-cigarette use at T1. Further, by adding measures of these covariates at T2, they show that changes in these covariates are even more influential in predictions of smoking at T2 and eliminate any direct effects of e-cigarette use on subsequent smoking (see Figs. 1B and 2B). A key message here is that more sophisticated measures of confounders (including at multiple times during follow-up) can dramatically alter causal interpretations.

Outside of tobacco research, appeal to causal drug gateway issues has diminished (Bell and Keane, 2014; Degenhardt et al., 2010; Kleinig, 2015), in part due to recognition that characteristics of the person and the context generally determine patterns of substance use more than which substance is used first. This has been called the 'common liability model' where inclination toward risk-taking, and psychosocial processes more generally, can be the factors that link patterns of multiple drug product use (Vanyukov et al., 2012). The gateway hypothesis has promoted a simplistic conception of linear progression from use of softer to harder drugs (e.g., marijuana to cocaine) (Anthony, 2012). Increasingly, however, progression from one drug to another is obscured by use of multiple products during a prolonged period of intermittent, often experimental use of different types of drugs, including a range of tobacco products along with alcohol, marijuana, and other substances. To sort out which came first, especially causally, is at best a serious logistical challenge. Experimentation with multiple tobacco and nicotine products has become common in youth who use at least one product (Creamer et al., 2015; Creamer et al., 2016; Singh et al., 2016). This pattern can render the gateway issue moot (Kozlowski and Sweanor, in press).

#### 4. Evidence that e-cigarette use by youth is not leading to more smoking

While cross-sectional data do not permit attribution of causality to correlated trends, data from two major surveys on use of both e-cigarettes and tobacco cigarettes by middle- and high-school students are inconsistent with the notion that e-cigarette use is increasing smoking.

Past-month use of e-cigarettes increased dramatically from 2011 to 2014. According to the National Youth Tobacco Survey (NYTS), students' use tripled in a single year, from 2013 to 2014, with 13.4% of high school students using e-cigarettes in 2014, compared to 4.5% in 2013, and middle school students'

30-day prevalence rising from 1.1% to 3.9%. These numbers brought e-cigarette use to the point that it exceeded use of any other tobacco product, including cigarettes (Centers for Disease Control and Prevention, 2015). Another national survey, Monitoring the Future (MTF), also reported high rates of students' e-cigarette use in 2014 (Miech et al., 2016b). However, in 2015 MTF recorded a small decrease, while NYTS reported only a small increase, and in 2016 MTF reported a decrease in e-cigarette use rates of more than 20% (Miech et al., 2016c).

Countering the rise in e-cigarette use through 2014 was a striking decrease in cigarette smoking. From 2013-15, NYTS reported a 27% decrease in 30-day smoking prevalence among high school students. MTF found a very similar decrease of 30% among high school seniors. Both are unprecedented declines. The decreases recorded by MTF for each of 2013-14 and 2014-15, each exceeding 16%, surpassed the largest annual percentage decline in the survey's 40-year history. (All of NYTS's two-year decrease reported occurred from 2013 to 14. A single-year 27% decrease seems implausibly large. It is conceivable that the 2014 figure was underestimated.) Further, MTF reports that from 2015 to 16 the decreases continued, with 12th graders' 30-day smoking prevalence falling by 7.9%, while the decreases for 10th and 8th graders both exceeded 20%, the largest percentage decreases ever. These decreases in cigarette smoking are not consistent with e-cigarette use spurring smoking. (It is instructive to note that in 1996, 34% of 12th graders, 30.4% of 10th graders, and 21% of 8th graders smoked within the past 30 days. The figures in 2016 were 10.5%, 4.9%, and 2.6%, respectively.)

The cigarette smoking decreases for 2013-15 were mirrored by comparable decreases in cigar smoking in NYTS, with even larger declines in pipe tobacco use. Hookah use increased dramatically 2013-14 but dropped significantly in 2014-15. Overall, the use of all combusted tobacco products declined significantly over the two-year period. MTF reported a decrease in smokeless tobacco, while NYTS found little change. For 2016 MTF reported decreases in all categories of tobacco products that they cover, including a one-third decline in the annual use of hookah by 12th graders.

This said, the Centers for Disease Control and Prevention (CDC) reported that from 2011 to 2015, owing primarily to the then-large increases in e-cigarette use, "there was no change in current use of any tobacco product among middle and high school students" (Singh et al., 2016). While

it is the case that electronic cigarettes have been classified by the Food and Drug Administration as tobacco products, such a classification for an e-cigarette that contains no nicotine is problematic. In 2015, MTF asked students “The last time you used an electronic vaporizer such as an e-cigarette, what was in the mist you inhaled?” Two-thirds responded “just flavoring.” Only about 20% of 12th and 10th graders and only 13% of 8th graders answered “nicotine” (Miech et al., 2016a). While it is certainly possible that some of the students answering “just flavoring” were using nicotine-containing e-cigarettes, these data challenge the notion that all or even most of the e-cigarettes used by students subject them to nicotine exposure. E-cigarettes lacking nicotine should not reasonably be called tobacco products or considered nicotine-delivery systems. Since the CDC estimates treated all vaping products as if they were ‘tobacco products,’ their judgment that overall tobacco use had not dropped from 2011 to 2015 is likely unwarranted. Overall tobacco product use (excluding non-nicotine vaping products) by students appears to have dropped in 2015 and has continued to do so since then as reported by Miech et al. (2016c).

The patterns of students’ e-cigarette use raise the possibility that e-cigarette use may be a passing fad, reinforced by the finding that e-cigarette use did not increase significantly in 2015 and decreased substantially in 2016, after multiple years of quite dramatic increases. Only time will tell at what level the e-cigarette market might settle, but fears that the e-cigarette market will keep increasing and attract more and more youth to nicotine use appear unsupported. Further, just a small percentage of never-smoking students use e-cigarettes. In 2014 only 6.5% of high school seniors who had never smoked had used an e-cigarette in the past 30 days, and of those the majority used them only 1 or 2 days. (The figures are similar for 8th and 10th graders.) (Warner, 2016) This mitigates concerns deriving from the prospective studies that support the gateway theory.

Finally, 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. No one has explored this possibility empirically. The subset of high-risk youth who will experiment (regardless of the law) may

benefit from the availability of less hazardous means of experiencing nicotine.

## 5. Policies for tobacco/nicotine harm reduction

In this section we propose policies that we support for all nicotine and tobacco products. In so doing, we are forced to diverge from our exclusive focus on youth. Policies appropriate for young people may be inappropriate for adults and vice-versa. For example, we support prohibiting youth from purchasing and using e-cigarettes, while we favor encouraging adult smokers to do so instead of continued smoking. The policies discussed below are intended to minimize the undesirable effects of novel nicotine-delivery products for kids, but to do so while recognizing that children and adults occupy the same broad environment, and that public health objectives for the two groups can and do differ. The overall goal is to employ evidence-based measures to prevent tobacco initiation by kids and encourage smoking cessation among adults. The policies we discuss do not comprise a comprehensive set of policies aimed at harm reduction. Rather they focus on a subset that clearly pertains to the issue of youth and e-cigarette use.

### 5.1. Prohibiting use by minors

A standard tool for protecting youth from dangerous drug products (e.g., tobacco or alcohol) is to prohibit their purchase by or sales to minors. We support prohibiting the use of all tobacco/nicotine products by minors, as do the vast majority of both e-cigarette opponents and supporters. We believe, in contrast, that adult smokers should have easy access to properly-regulated vaping products, smokeless tobacco, and medicinal nicotine-replacement products, all far less dangerous than cigarettes. (We recognize that the precise nature of ‘proper regulation’ of products like e-cigarettes is itself a highly contentious issue which we cannot tackle in this essay.)

Recently, California and Hawaii and a number of cities and counties have raised the legal age of purchase of tobacco products to 21. We support raising the minimum age to 21 in all states, as recommended by the National Academy of Medicine (Bonnie et al., 2015), although it might be worth evaluating the effects of a lower legal age ( $\geq 18$ ) for less harmful nicotine and tobacco products (Kozlowski, 2016). Two studies have found that state-based age restrictions on the purchase of e-cigarettes have been asso-

ciated with increased rates of cigarette smoking (Friedman, 2015; Pesko et al., 2016). This finding lends support to considering lower age restrictions for less harmful products like e-cigarettes.

### 5.2. Informing the public about meaningful differences in product risks

Accurate information on meaningful differences in product harms should be readily available, as is the case for other consumer products, such as safety ratings for automobiles (Kozlowski and Sweanor, 2016; Kozlowski and Sweanor, in press). Both U.S. government agencies and notable health-focused institutions have a long history of providing misleading information about tobacco product risks (Kozlowski and O’Connor, 2003; Kozlowski and Sweanor, 2016). For example, as recently as March 2016, the Mayo Clinic webpage promoted that smokeless tobacco was “not safer than cigarettes” and at one time the CDC’s “SGR 4 Kids” informed that there was “no way” that smokeless tobacco was safer than cigarettes, both inaccurate claims (see Kozlowski and Sweanor, 2016, for details). Recent messaging and publicity about e-cigarettes have contributed to confusion and poorer knowledge of the lower risks of e-cigarettes than existed just a couple of years ago (Majeed et al., 2016). The public has little appreciation of the large difference in harms from some nicotine-delivery products in comparison to cigarettes (Kiviniemi and Kozlowski, 2015; Kozlowski and Sweanor, 2016). Adults and youth deserve truthful information about the risks of products they might use, whether legally or illegally (Kozlowski and Sweanor, in press).

### 5.3. Differential marketing and pricing to discourage the use of more dangerous products

Regulations governing marketing and product pricing should be used to discourage use of the most dangerous products (e.g., cigarettes) (Kozlowski, 2007). Chaloupka et al. (2015) advocate taxing tobacco and nicotine products differentially, with a modest tax imposed on e-cigarettes, for example, while cigarettes would be taxed far more heavily than all non-combusted tobacco products. The authors support a tax on e-cigarettes to discourage use by kids, who are far more price sensitive than adults (U.S. National Cancer Institute and World Health Organization, 2016). A much greater tax on cigarettes would make less-harmful products relatively more

attractive to adult smokers and might thereby encourage smoking cessation.

Regarding promotion, advertising of cigarettes is prohibited in many media in which advertising of e-cigarettes can be permitted. Government policy might prohibit marketing of all nicotine and tobacco products in media frequented by kids. Marketing regulations could get quite specific, for example allowing e-cigarette companies to advertise their products to adult smokers as less dangerous than cigarette smoking while simultaneously prohibiting them from employing “life-style” ads (conveying sex appeal, sophistication, etc.) that might appeal to young people. Well-designed differential marketing regulations could encourage a subset of adult smokers to relinquish their cigarettes, while simultaneously reducing the appeal of lower-risk products to kids.

## 6. Conclusion

The role of e-cigarettes in the future of youth smoking has yet to be definitively assessed. 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 potential impact suggested by the prospective studies is critical to understand. The proportion of never-smoking youth who try e-cigarettes is small. With only a fraction of those being induced to try smoking (if the gateway theory does hold), the proportion of never-smokers so induced is much smaller still. Further, the percentage of youth who try smoking who go on to become dependent smokers is itself minor. So the aggregate risk implied by the prospective studies is very small. Further – and we consider this very important – the data from large national cross-sectional studies provide no evidence that kids’ use of e-cigarettes is increasing smoking. If anything, those data suggest the opposite.

Even if e-cigarettes serve as a gateway to smoking for a small subset of youth, a sensible approach to novel nicotine delivery products means that policy makers, and the public health community, must contemplate a potential trade-off,

in essence calculating the full costs and benefits of any policy, as should always be done (Kozlowski and Abrams, 2016). If, as seems likely, e-cigarettes contribute on balance to an increase in adult smoking cessation (Beard et al., 2016), the benefit in terms of premature deaths avoided could be substantial. If the causal gateway theory holds, however, it might come at the cost of some additional new smokers among the younger generation. While unpleasant to contemplate, this cost must be compared to the far more immediate benefit (in terms of health consequences) that would be realized by adults quitting smoking.

We also need to acknowledge more encouraging scenarios. Changing patterns of product use by youth may lead to reduced smoking in future generations. Young people’s use of e-cigarettes may not increase the number of future cigarette smokers, nor even the number of young people who become addicted to nicotine in any form. Since most adults will continue to begin using tobacco/nicotine products in their youth, their own use of e-cigarettes in youth instead of cigarettes may give them a better chance for a longer, healthier life. Finally, we need to appreciate that growing anti-smoking sentiment, accompanied and reinforced by more stringent tobacco control policies, is likely to increase the ranks of former smokers in the coming decades. With smoking cessation rates up in recent years (Mendez et al., 2016), the odds that a youth who begins smoking now remains a smoker 30 years from now are likely to decline substantially.

Assessing a large, fast-moving research literature is a kind of quest for ‘signals’ embedded in ‘noise.’ While research exists to support either side of the argument, we conclude, currently, that youth use of e-cigarettes is unlikely to increase the ranks of future cigarette smokers. Is it possible we could have our cake and eat it too? Perhaps, especially if sensible comprehensive harm reduction policies can earn a place in modern tobacco control efforts.

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## Conflicts of interest

None.

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