GARBAGE IN GARBAGE OUT: A CRITIQUE OF THE ANU GATEWAY THEORY ANALYSIS

Author: Sinclair Davidson
Abstract

A recent meta-analysis undertaken at the Australian National University indicates that e-cigarette usage serves as a gateway to the consumption of combustible cigarettes. In this short paper, I demonstrate that the meta-analysis itself is highly flawed, and that the statistical analysis contained in the underlying literature is contrived to produce that very result. Furthermore the hypotheses being tested are not clearly stated resulting in misleading interpretation of the empirical results. Unfortunately the underlying studies that purport to show that result are contaminated by bias, by a failure to clearly specify the underlying hypotheses being tested, and by statistical sleight of hand.
Introduction

Using e-cigarettes triples the chance of a non-smoker taking up cigarettes and there is “insufficient” evidence that they help smokers quit, according to a new report submitted to the Government. Research led by The Australian National University (ANU) reviewed the worldwide evidence on e-cigarettes and smoking behaviour, relevant to the Australian context.

“We found clear evidence that non-smokers who use e-cigarettes are around three times as likely to take up conventional smoking as their peers who don’t use e-cigarettes,” lead researcher Professor Emily Banks from ANU said.

That statement, taken from an Australian National University press release*, is highly misleading. It did, however, receive widespread coverage in the Australian media and will, no doubt, be used by anti-nicotine activists to bolster the arguments in favour of Australia’s e-cigarette prohibition.

In this short paper I will explain why that statement is entirely misleading. In fact, it goes beyond misleading, and should be characterised as being “alarmist”.

---

The Banks Study

The Australian National University press release links to a summary document\(^1\) which in turn links to a working paper\(^2\): “E-cigarette use and combustible tobacco cigarette smoking uptake among non-smokers, including relapse in former smokers: umbrella review, systematic review and meta-analysis”. By definition, this working paper – still very much in draft form – has not yet been peer reviewed. Nonetheless the results of the paper were used to inform a report made to the Australian government on the inherent risks of e-cigarette usage.

In summary the take-home message was that non-smokers that used e-cigarettes were about 3 times more likely than non-smokers who did not use e-cigarettes to subsequently become smokers (i.e. consume combustible cigarettes). That result was widely reported in the Australian media. The conclusion being that e-cigarettes are a gateway to combustible cigarettes.

The inference of the study – but not explicitly stated – is that individuals who otherwise would never have become smokers (i.e. consumers of combustible cigarettes) do become smokers as a result of having used e-cigarettes. That policy inference does not follow from the empirical analysis that has been performed.

The Banks study is a meta-analysis. This is a research methodology that attempts to provide an empirical summary of a large body of literature. It is a well-understood and well-known methodology that is employed in many disciplines.

The Banks study provides an update to three previous meta-analysis studies that have previously investigated the relationship between e-cigarette consumption and combustible cigarette consumption. In the Banks study these previous three studies are labelled as being “Umbrella” studies. From the studies used in these three meta-analyses, Banks and her co-authors select a total of 13 previous studies to use in their analysis. Banks and co-authors manage to identify another 12 studies. To be clear – the Banks study analyses 25 papers in total. Layperson readers can become confused by reports that 6,225 studies were identified in the analysis. This creates the false impression that there are many thousands of studies that report similar results. The evidence deployed in the Banks study is not nearly so conclusive.

An important statistic to consider when using (and interpreting) a meta-analysis is the so-called I\(^2\) measure. This refers to the amount of homogeneity or conversely heterogeneity in the results of the meta-analysis. If the results of the studies being used in the analysis are similar to each other, then the result is said to be homogenous. If the

\(^1\) Summary report on use of e-cigarettes and relation to tobacco smoking uptake and cessation, relevant to the Australian context. Available at https://openresearch-repository.anu.edu.au/handle/1885/211618

\(^2\) E-cigarette use and combustible tobacco cigarette smoking uptake among non-smokers, including relapse in former smokers: umbrella review, systematic review and meta-analysis. Available at https://www.medrxiv.org/content/10.1101/2020.09.16.20195438v1
results are dissimilar then results are heterogeneous. Ideally meta-analysis results should be homogenous – in practice, levels of heterogeneity should be low or moderate.

Heterogeneity arises from various sources. Studies included in the analysis might be addressing slightly different research question. The methodology in the underlying studies may be slightly different. There may be variation due to statistical measurement issues. Finally heterogeneity may arise purely due to chance or randomness. Well performed meta-analyses tend to report low levels of heterogeneity or plausibly explain “high” levels of heterogeneity.

In the meta-analysis literature, the $I^2$ measure is commonly used to indicate the level of heterogeneity in the analysis. $I^2$ is interpreted as follows:

- 0% - 40%: Heterogeneity might not be important.
- 30% - 60%: Moderate heterogeneity.
- 50% - 90%: Substantial heterogeneity.
- 75% - 100%: Considerable heterogeneity.

Looking then at the three umbrella studies that the Banks study relies upon:

- Khouja et. al (2020) employ 17 studies to examine whether e-cigarette use results in subsequent combustible cigarette use. They report an $I^2$ statistic of 88%. That falls within the range of substantial heterogeneity and considerable heterogeneity.
- Aladeokin and Haighton (2019) employ 3 studies to investigate whether e-cigarette use is associated with combustible cigarette usage. They report $I^2$ statistics of 52% and 58%. That falls within the range of moderate heterogeneity and substantial heterogeneity.
- Soneji et. al (2017) employ 7 studies to examine whether initial e-cigarette use results in subsequent combustible cigarette use. They report an $I^2$ statistic of 56%. They describe this as being “moderate” heterogeneity, but it also falls into the substantial heterogeneity range.

Of the 27 studies used in the umbrella studies, the Banks study selects just 13 for their purposes and combines those 13 with an additional 12 studies that had been published subsequent to the umbrella studies having been performed or published.

The Banks study then performs meta-analysis of those 25 studies over three sets of analyses. Importantly they break up their results to show the result for the original umbrella study papers, the newly identified papers, and a combined effect. The first

---

analysis examines whether never-smokers and e-cigarette users had subsequently taken up combustible cigarette use at a later date.

Original Umbrella studies: n = 12, I² = 87.07
Newly identified studies: n = 5, I² = 81.05
Combined studies: n = 17, I² = 85.67

The I² statistic falls within the range of substantial heterogeneity and considerable heterogeneity.

The second analysis examines whether current-smokers and e-cigarette users at a baseline (30 days prior) had subsequently taken up combustible cigarette use.

Original Umbrella studies: n = 1, I² = n/a
Newly identified studies: n = 7, I² = 91.86
Combined studies: n = 8, I² = 90.95

The I² statistic falls within the range of considerable heterogeneity.

The final analysis relates to quitters but e-cigarette users relapsing back into combustible cigarette usage.

Newly identified studies: n = 3, I² = 12.32

Heterogeneity is not important with an I² statistic that low. This confirms, of course, that giving up combustible cigarette usage is difficult for many individuals.

For two of the three analyses that the Banks Study performs the heterogeneity scores remain very high. They make no attempt to explain or explore that high level of heterogeneity despite the fact that they have had an opportunity to select the very studies that they included in the analysis. Nonetheless, their overall conclusion is that “non-smokers who use e-cigarettes are consistently more likely than non-e-cigarettes users to initiate combustible cigarette smoking and become current smokers”. They report an odds-ratio of about 3 as a result of their meta-analysis.

Examining the summary statistics of the underlying papers, however, suggests that figure is far too high. Furthermore that figure is contrived by the original researchers to inflate the impact of e-cigarette usage on subsequent combustible cigarette usage. What is the hypothesis being tested?

Many of the studies claim to be investigating the so-called Gateway Hypothesis. This is the notion that individuals who may consume e-cigarettes may then proceed to the consumption of combustible cigarettes. Combustible cigarette usage is associated with many adverse health conditions and impose a cost on the public health system. Many countries pursue public health policies to discourage the usage of combustible cigarettes amongst adults and ban the usage of combustible cigarettes amongst chil-
dren. Usage of e-cigarettes leading to the subsequent take up of combustible cigarettes would constitute a massive public health policy failure.

On those public policy grounds, the research summarised above is important. Yet it is also very flawed. In the very first instance the hypothesis itself being tested and alternative hypotheses are not clearly set out.

In the table 1 below I set out the Gateway Hypothesis (this has two sub-components) and in table 2 I set out the Exit Hypothesis (this has three sub-components).

In the Banks Study these two versions of the Gateway Hypothesis are partially tested. We are told that a Never Smoker is (about) three times more likely to become a smoker if they have consumed e-cigarettes. Similarly, we are told that Relapsed Smokers (i.e. quitters) are twice as likely to take up combustible cigarette consumption if they had also consumed e-cigarettes. What is not entirely clear is how many Never Smokers become Smokers without the intervention of e-cigarettes. We are told, however, that e-cigarettes make Never Smokers three times more likely to become Smokers. A casual reader might even surmise that but for e-cigarettes that a Never Smoker would not ever become a Smoker. We are also never explicitly told how many individuals attempt to quit the consumption of combustible cigarettes, but fail in their attempt to do so and resume the consumption of combustible cigarettes despite the existence of e-cigarettes.

In table 2, I set out some alternate hypotheses to the Gateway Hypothesis. I label this the Exit Hypothesis.

Readers will recognise that the Gateway Hypothesis and the Exit Hypothesis overlap. Combustible cigarette users have many avenues available to them to change their consumption behaviour. Here I only focus on the role that e-cigarettes may play in that consumer choice.
Combustible cigarette users may attempt to quit their consumption choices by taking up the use of e-cigarettes. In the Banks Study if they fail in their attempt this is classified as being a result that supports the Gateway Hypothesis. It is unclear from their analysis whether this is an appropriate interpretation. The Banks Study also neglects to analyse or reject two other versions of the Exit Hypothesis. The Harm Reduction Hypothesis is that existing combustible cigarette consumers substitute e-cigarettes for combustible cigarettes and continue to consume e-cigarettes. The public health consequences of this choice are disputed, but UK authorities for example have suggested that e-cigarette consumption is 95% safer than combustible cigarette consumption. Finally, there is a Displacement Hypothesis – a would-be smoker (i.e. someone who would otherwise have consumed combustible cigarettes) rather begins to consume e-cigarettes and never consumes combustible cigarettes.

The evidence from the studies, however, appears very strongly to support the Gateway Hypothesis, while the nuance and subtleties of the Exit Hypothesis appear to be ignored or understated. Perhaps given the magnitude of the results, this is entirely unnecessary. The table below is taken from Soneji et. al (2017) table 2:

It does appear from results such as that, that e-cigarette usage is a very large gateway into combustible cigarette usage. There is, however, some statistical sleight of hand going on. This sleight of hand is well illustrated by a paper published in Tobacco Control in 2018. The table below is reproduced from Best et.al (2018) in total.

Best et.al (2018) interpret the table as follows: Of 2125 students in the sample, 183 students consumed e-cigarettes (169+8+6 = 183). Of those 183, 74 students also consumed combustible cigarettes. Therefore 40.4% (74/183) of Never Smokers who had consumed e-cigarettes went on to consume combustible cigarettes. By contrast only

---

12.8% of Never Smokers went onto consuming combustible cigarettes (249/1942).

The hypothesis being tested, however, is not whether students had consumed an e-cigarette. The hypothesis being tested is whether those individuals who had consumed an e-cigarette then subsequently become consumers of combustible cigarettes. It may not be immediately obvious to many readers that Best et.al are not comparing like with like.

To illustrate the point I have summarised the table as below:

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Yes</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>I have never used an e-cigarette</td>
<td>1,693</td>
<td>249</td>
<td>1,942</td>
</tr>
<tr>
<td>I have used an e-cigarette</td>
<td>109</td>
<td>74</td>
<td>183</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1,802</td>
<td>323</td>
<td>2,125</td>
</tr>
</tbody>
</table>

Of the 2125 students in the sample, 1693 had never consumed either a combustible cigarette or an e-cigarette. That is 79.67% of all students. 249 students had consumed a combustible cigarette, but had not consumed an e-cigarette – that is 11.73% of all students. Then 109 students had consumed e-cigarettes but had not consumed combustible cigarettes – that is 5.13% of all students. Then 74 students had consumed both combustible cigarettes and e-cigarettes – that is 3.48% of all students.

To be clear: of the 323 students that became smokers (i.e. had consumed a combustible cigarette) 249 students (77.1%) did not do so after consuming e-cigarettes. Only 74 students (22.9%) became smokers after having consumed an e-cigarette. It may well be the case that of those 74 students some of them (all of them perhaps) may never have become smokers at all. Evidence to support that view, however, is simply absent from the study. It is the case, however, that of the 183 students that did consume e-cigarettes that 109 students (59.6%) did not go to consuming combustible cigarettes.
Conclusion

The notion that e-cigarette consumption results in combustible cigarette consumption (i.e. the Gateway Hypothesis) is of real public health concern. Unfortunately the underlying studies that purport to show that result are contaminated by bias, by a failure to clearly specify the underlying hypotheses being tested, and by statistical sleight of hand. It is no surprise then that meta-analyses relying on the flawed underlying studies are themselves flawed.

The public health lobby does itself no favours by producing results that are clearly inadequate and do not support the arguments they wish to convey.
About the Author

Sinclair Davidson

Sinclair Davidson is Professor of Institutional Economics at the RMIT Blockchain Innovation Hub at RMIT University, an Adjunct Fellow at the Institute of Public Affairs, an Academic Fellow at the Australian Taxpayers’ Alliance, an Adjunct Economics Fellow at the Consumer Choice Center, and a Research Associate at the University College London Centre for Blockchain Technologies. He is a member of the Centre for Independent Studies Council of Academic Advisers. Sinclair has published in academic journals such as the European Journal of Political Economy, Journal of Economic Behavior and Organization, Economic Affairs, and The Cato Journal. He is a regular contributor to public debate. His opinion pieces have been published in The Age, The Australian, Australian Financial Review, The Conversation, Daily Telegraph, Sydney Morning Herald, and Wall Street Journal Asia.

He blogs at Catallaxy Files and Tweets @SincDavidson and @Cryptoeconomico.