Vaping is still at least 95% lower risk than smoking – debunking a feeble and empty critique

written by Clive Bates | 17 January 2020

An empty and feeble critique misses its target and adds nothing

This paper turned up in my weekly search of PubMed.

> *Invalidity of an Oft-Cited Estimate of the Relative Harms of Electronic Cigarettes.*
> *Eissenberg T, Bhatnagar A, Chapman S, Jordt SE, Shihadeh A, Soule EK. Am J Public Health. 2020 Feb;110(2):161-162. doi: 10.2105/AJPH.2019.305424.*

The commentary claims to show the "invalidity" of the statements made by Public

Health England (PHE) and the Royal College of Physicians (RCP) regarding the relative risk of vaping and smoking – in short that vaping is likely to be at least 95% lower risk than smoking. As this is an important harm-reduction risk communication, it is worth asking: *how valid is this critique?*

I thought this might be a better critique than it actually is. *But somewhat to my surprise, it is very poor indeed*.

Short version

At best, the authors try to show the absolute risk of vaping is not zero and that some harm is plausible. In doing so, they are refuting a claim that neither PHE or RCP make and challenging an argument not used by anyone sensible in tobacco harm reduction. However, not a single word of their paper addresses the supposed foundation of their critique – that PHE/RCP are wrong and the risks of vaping are likely to exceed five per cent of those of smoking. As well as a number of baseless assertions that are not even relevant to the "at least 95 per cent lower" relative risk claim (gateway effects, smoking cessation efficacy and second-hand aerosol exposure), there is just *nothing* in the paper about the *relative magnitude* of smoking and vaping risks. No analysis, no data, no evidence – nothing that discusses relative risk and why PHE/RCP are supposedly wrong. Niente. Nada. Rien. Nichts. *Nothing*.

New (20 Jan 2020). See concise comment on PubPeer here: A critique that does not even address its target

Anyway, despite being an empty and feeble piece of work, it does provide an opportunity to discuss some of the issues raised, so I will proceed with a critique.

Longer version

The authors' supposed refutation of PHE/RCP rests on six propositions. You can read the article here and I will respond to the authors' main points in the order they make them.

1. That the 95% estimate comes from a single

expert panel held in 2013

This is a common error. The assessments of PHE and RCP do not rely exclusively on the 2013 expert panel reported in Nutt et al, 2014, though they do acknowledge it and see it as an early part of the evidence. However, PHE and RCP assessments were made by their own independent expert scientists in the course of formulating their extensive evidence reviews in 2015 and 2016 respectively (PHE 2015, RCP 2016). Neither has seen fit to revise their estimate in the light of new discoveries. This is because the new science since then has strengthened rather than refuted these estimates. The critique authors do not even bother to accurately cite the claims they are referring to, which are carefully constructed risk communications. In their most recent form, these are as below:

In 2016, the Royal College of Physicians said (Section 5.5 page 87):

> *Although it is not possible to precisely quantify the long-term health risks associated with e-cigarettes, the available data suggest that they are unlikely to exceed 5% of those associated with smoked tobacco products, and may well be substantially lower than this figure.*

In 2018, PHE said (Executive summary, section 9.2):

> *Vaping poses only a small fraction of the risks of smoking and switching completely from smoking to vaping conveys substantial health benefits over continued smoking. Based on current knowledge, stating that vaping is at least 95% less harmful than smoking remains a good way to communicate the large difference in relative risk unambiguously so that more smokers are encouraged to make the switch from smoking to vaping. It should be noted that this does not mean e-cigarettes are safe.*

Neither claim is a point estimate of harm relative to cigarettes. Both are designed as risk communications to help smokers, vapers and health professionals make informed choices based on the views of the experts involved. Both recognise uncertainty but both try to provide a risk-perception ‘anchor’ based on expert judgement following assessment of the evidence that exists. These statements contrast favourably with vague and ambiguous statements about relative risks that have a long and inglorious history in tobacco control – notably regarding

smokeless tobacco, but increasingly about vaping. See my post on sophistry in tobacco control – especially section 6: The "no long term evidence" gambit.

2. Today's electronic cigarettes are different

The authors claim that advances in e-cigarettes – notably the rise of nicotine salts – make them more dangerous. Yes, they are different: today's electronic cigarettes *are better than in 2013*. This is known as "progress" and this also includes progress on safety and risk reduction. There are three dimensions to the improved risk reduction over time.

1. The first and most important is the emergence of more effective devices for reducing the risk of smoking by making the much safer alternative, vaping, a better substitute. This is the bigger picture – but completely ignored (or misunderstood – see 5 below) by the authors. In fairness, this does not directly affect the relative risk of smoking and vaping, it just makes the risk reduction from switching more likely to succeed. The newer products deliver a more satisfying nicotine experience and are better competitors to cigarettes than the earlier models, and can do this with reduced toxic exposure (see 2). If these authors do not want e-cigarettes to be credible substitutes for cigarettes, they should declare their quit-or-die credentials and not complain about the innovations that allow for more effective harm reduction. The success of Juul in the US and the sharp acceleration of the decline in cigarette consumption caused by Juul and similar is a big public health win from these innovations. Though the authors make much of nicotine delivery, it is worth remembering that it isn't the nicotine that does the harm, it is the smoke. But it is effective nicotine delivery that will obsolete the cigarette.
2. Second, many new products can substitute for smoking with *lower* exposure to contaminants and better control of temperature (and hence exposure to thermal degradation products). Protonated nicotine (nicotine salts) and higher strength liquids allow for devices like Juul, which deliver a satisfying nicotine pharmacokinetic experience with lower liquid volume, less energy and lower temperature (i.e. lower risk). The authors see this as a problem – but actually it is the opposite. Regulation, product stewardship and experience mean the products and manufacturing standards are improving all the time. Meanwhile, pushing the other way,

activist-generated hysteria about nicotine is leading users in the wrong direction – to use weaker liquids and, therefore, to consume higher volumes of liquid.

3. Third, compared to engineering the highly complex and uncontrolled *de novo* chemical formation in cigarette smoke, it is much easier to modify vaping aerosol by changing the ingredients, heating regime, and device construction. The chemistry is much more straightforward and the physical processes much more controllable. This means adjustments can be made over time if there are emerging concerns. For example, after hyped and baseless scare stories about 'popcorn lung', many vendors responded by removing the additive diacetyl from their products, and regulators could have required it. If issues of material concern arise in future it will be much easier to fix them. Bear in mind that it takes many decades for the main health impacts of smoking to emerge and that smokers who quit before age 40 avoid almost all of the risk of premature death. So comparison over many decades should, in the case of vaping, take account of the evolution of the products over time and potential to respond to emerging hazards, if such ever emerge. I don't expect much progress on 'safer cigarettes' from a toxicology perspective.

3. Electronic cigarettes cause harm to cells

Yes, *in vitro* studies – cells outside the body exposed to vapour aerosol – do show some effects on cells. This is unsurprising. However, many of these studies use excessive (or opaque) exposures that are poor analogues for human exposure, and often without credible cigarette smoke comparators. If the authors want to criticise the PHE/RCP relative risk claims, they should be distilling *only* the results of cell studies that compare smoke and vapour aerosol. Such studies *always* show far higher cytotoxicity for cigarette smoke. But they have not assessed that literature. Not at all.

But the problem does not end there: cell studies expose cells without protective and regenerative mechanisms that are present in the actual human body. This can easily mislead the naive researcher into over-interpreting the results and a belief they have findings of clinical relevance, rather than a useful analytical tool. It's worse if they go further and broadcast such findings as if they have uncovered an actual health risk – almost invariably they have not. Cell and animal studies have

their uses, but they rarely provide a clear signal for material harm in humans. So what do these studies tell us about the PHE/RCP claim? Very little.

Even more perplexing: the PHE/RCP estimate is a *relative risk statement* – not a claim of zero absolute risk. The authors do not show that any of expected harm that they impute (aka "invent") from these cell studies is likely to result in more than five per cent of that arising from smoking. Yet that is the entire premise of their paper.

4. Electronic cigarettes harm users

The authors cite a study where the observed effects are obviously confounded by cigarette smoking ("*in a sample of healthy young occasional cigarette smokers who used an e-cigarette with or without nicotine*") and then point to relatively trivial (and often transitory) symptoms associated with e-cigarette use ("wheezing"). They misrepresent the acute cardiovascular risk data (acute stimulant effects are of little clinical relevance), misrepresent the evidence on carbonyls (many studies have operated in unrealistic 'dry puff' conditions). Once again, they fail to show that any harms they do identify come anywhere close to five per cent of the massive toll of harm done by smoking. Apart from that, their argument is compelling!

The basis for claiming greatly reduced harm that forms the basis of the PHE/RCP communication arises from four main sources:

1. The *obvious* difference in the physics, chemistry and biological impact of inhaling the products of combustion of organic material (smoking) and inhaling relatively simple liquid mixtures in heated aerosol form (vaping) – the processes are so different there is no reason to assume any kind of equivalence or to use smoking as a reference point for estimating vaping risks. In fact, there isn't any particular reason to assume these products cause any non-trivial risk at all and nothing much has been found so far.
2. The toxicology of vapour aerosol compared to smoking – including dramatically lower cancer potencies (99.6% lower than cigarette smoke in this study of a subset of carcinogens)
3. Biomarkers of exposure and risk comparisons comparing smokers, vapers, never-smokers and quitters – measurements in the blood, urine, saliva etc of users These exposures really are *much lowe*r. *Shahab et al., 2017,*

suggests vaping exposures as low as found with NRT users for selected biomarkers.
4. Improvements in health evident in smokers who switch. There is a good body of evidence showing improvements in health – respiratory and cardiovascular – among smokers who switch to vaping.

As you would expect from (1), the toxicology (2) and exposure data (3) show dramatic reductions compared to smoking – almost to the level of non-smokers or quitters – and this is why we see improvements in the health of smokers who switch (4). The authors do not engage *at all* with this evidence.

5. Electronic cigarettes increase smoking risk

The authors claim that vaping causes more smoking through gateway effects and reduced smoking cessation – an endlessly refuted claim. It isn't even relevant to the relative risk of vaping and smoking and the 95 per cent claim that is the subject of this paper (I noted this in 2.1 above while making the opposite argument) but they've just thrown it in all the same.

Even though this section is irrelevant to the supposed aim of the paper, a response is in order.

In a determined effort to confuse association and causation, the authors ignore the distinction between the gateway hypothesis and the far more likely "common liability" explanation for why adolescents who vape are also more likely to smoke. Common liability means that the same things that incline people to vape also incline them to smoke (parents, mental health, personal efficacy, social situation etc). It is a common trope in anti-vaping activism to claim "*e-cigarette users are X times as likely to take up smoking*" as if that means the vaping *causes* the smoking – it just doesn't. This is epidemiology 101 and I have discussed it in my critique of similar claims made by Professor Stanton Glantz here – see section 11.

In fact, four strands of evidence converge to strongly suggest that vaping substantially reduces smoking:

1. Randomised controlled trial evidence (showing about twice the efficacy of NRT in controlled conditions)
2. Observational studies (what happens when users switch)
3. Population data (the dramatic declines in smoking prevalence that

coincide with population uptake of vaping)
4. User experience – although pseudo-scientists dismiss user testimony, they are in fact part of the evidence base

None are decisive in their own right but the fact they all align should give confidence. Readers who want an update on 1-3 would do well to consult Professor Robert West's lecture on this subject. Before people gasp at the scandal of listening to user testimony, please read this or this series by Carl V Phillips. In addition, vaping duplicates other aspects of smoking – sensory, behavioural and social. Public health impact depends both on individual risk reduction *and* the number of people who adopt it. In this, vaping has a decisive advantage: people like it and are more likely to use it.

The slender thread the authors cling to is the NASEM finding that *ever-use* of e-cigarettes predicts for *ever-smoking* – yet this finding is extremely weak and vulnerable to unaccounted confounding (it is *impossible* to eliminate confounding by common liability factors – see Carl V Phillips' primer here). Also, trial or 'ever-use' represents a qualitatively different behaviour to regular substance use. It is more like a marker for 'curiosity' or 'propensity for risk-taking', which may need very different deconfounding variables to substance use.

NASEM's credibility was damaged by asserting the discovery of a causal gateway effect and the suspense of disbelief about confounding that it required. That said, it is notable that the authors do not draw on another NASEM finding, consistent with RCP/PHE:

> *While e-cigarettes are not without health risks, they are likely to be far less harmful than combustible tobacco cigarettes.*

6. Electronic cigarette aerosol is not harmless

Again, it is not enough to assert that there is a non-zero absolute risk to challenge a claim about relative risk, in this case on second-hand exposures. Once again, this section is not really relevant to the PHE/RCP relative risk claim, which is directed at active users. Even if indoor vaping is regarded as a nuisance and matter of poor etiquette by some, it is unlikely to present remotely the kind of risks caused by second-hand smoke.

Here's why. Three things are very different and toxic exposure to bystanders depends on all three:

1. The quantity emitted. Most of the inhaled vapour is absorbed by the user and only a small fraction is exhaled (15% or less, depending on the constituent). In contrast, about four times as much environmental tobacco smoke comes directly from the burning tip of the cigarette than is exhaled by the smoker. There is no equivalent of this "sidestream smoke" for vaping.
2. The toxicity of the emissions. Tobacco smoke contains hundreds of toxic products of combustion that are either not present or present at very low levels in vapour aerosol. Vapour emissions do not have toxins present at levels that pose a material risk to health – or are overall likely to be at least 95% lower.
3. The time that the emissions remain in the atmosphere. Environmental tobacco smoke persists for far longer in the environment (about 20-40 minutes per exhalation). The vapour aerosol droplets evaporate in less than a minute and the gas phase disperses in less than 2 minutes.

These three factors suggest that for bystanders the relative risk would be even less than the relative risk for active users.

Note: the evidence that secondhand smoke causes serious harm is still contested and somewhat marginal. Yet there is nothing to suggest that vaping comes close.

Conclusion

This is a truly *feeble and empty critique* of the PHE and RCP "95 per cent" relative risk communication. PHE and RCP are trying to help people gain a feel for the relative risk of vaping and smoking in a way that is accessible, clear and actionable and based in the science as we currently understand it. RCP and PHE do not make a zero-risk claim, yet all the authors manage to present is a few selected papers and arguments that show that risks *may* be non-zero in absolute terms.

Not a single word of this empty analysis addresses *relative risk* – the comparison between smoking and vaping that is the subject of the PHE/RCP estimates that the authors claim to invalidate.

The question I test myself with is: '*what would you tell your brother?*'… nothing in this critique dissuades me from using a merged version of the PHE and RCP formulation in discussing this with my actual brother (a former smoker and now a vaper – something he is happy about). This is what I would say:

> *Based what we do know, you should not assume these products are risk-free. But vaping is likely to be at least 95% less risky than smoking and may present substantially lower risks than that. If you switch from smoking to vaping you will be much better for it.*

I'd like to know what the authors would say to their family members… to a brother who smokes.

Taking the irresponsibility to a higher level – the press release

As has become common practice, the press release takes a poor quality journal paper and adds eye-catching made-for-media hype. And so it is here. I don't have time to criticise every piece of spin in the release. One example, the worst, will suffice. Unfortunately, lead author Tom Eissenberg made a statement of astonishingly irresponsible conjecture in the press release that accompanied this paper.

> *The fact is: we don't know whether e-cigarette use is as lethal as combustible cigarette use, less lethal than combustible cigarette use, or more lethal than combustible cigarette use.*

It's common for press releasees to contain a payload of propaganda that goes far beyond any analysis to which it relates. But this is so extreme, it is hard to fathom where such an assessment can come from – certainly, no evidence exists to support equivalence or excess risk, and truckloads of evidence are available to refute those claims.

So it must be down to what US Defense Secretary Donald Rumsfeld once called:

> *…unknown-unknowns … things we do not know we don't know.*

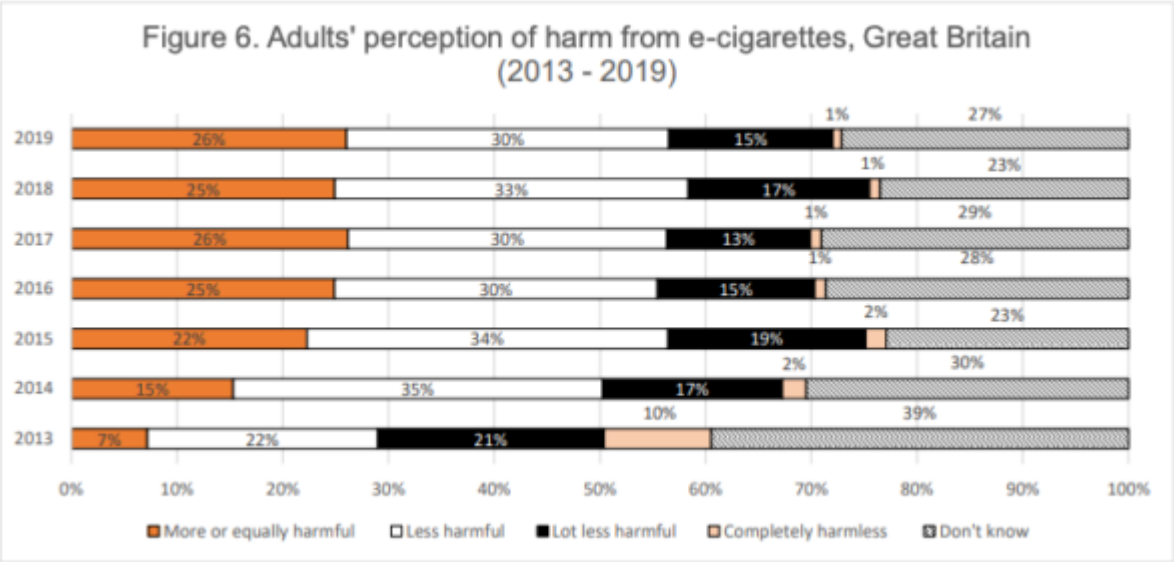
These unknown-unknowns must be doing a lot of heavy lifting in Dr Eissenberg's risk communication. Of course, this is an intellectual travesty. His formulation gives implicit equal weight to what we do know (which is a lot and convincingly shows greatly reduced risk) and to as yet unknown (and likely non-existent) mechanisms by which e-cigarette may eventually cause harm with the additional assumption that we would be unable to change the products to remove whatever was causing the harm.

Responsible risk communication goes beyond merely saying things that you think you can get away with as *not technically inaccurate* in some university debating chamber. If you are sincere about it, communication is less about *what is said* and more about *what is understood* by the audience. How would any vaper or smoker understand Eissenberg's statement other than as "in that case, I might as well smoke"? Words have consequences and, perhaps without realising, Eissenberg is promoting the very thing he has spent his career fighting.

For more on the absurdity of this posture, readers can review my analysis of Professor Stanton Glantz making an outrageous claim of equivalent risk: Vaping risk compared to smoking: challenging a false and dangerous claim by Professor Stanton Glantz.

Why do PHE and RCP make these statements?

They are addressing an important public health problem in the UK, and one that is visible almost everywhere. That is the public perceptions of the relative risk of smoking and vaping are miles away from what the science tells us – and this mismatch is worsening over time. This is the picture from the excellent annual ASH(UK) surveys (2019) – since 2014, less than one in five have reported realistic risk perception ("a lot less harmful"). Most exaggerate the risk or just don't know.



This problem is not confined to the UK. In the US it is worse. In 2018, a National Cancer Institute survey showed that only 2.6% of Americans thought, correctly, that e-cigarettes were much less harmful than cigarettes, while 43.2% thought they were as or more harmful – something for which no evidence exists and much evidence exists to refute. In a similar survey in 2017, 45.4% of Americans thought, incorrectly, that e-cigarettes are very harmful to health, There is no evidence for that belief.

Because risk perceptions inform behaviour, these misperceptions will be reducing the number of smokers who switch, increasing the proportion of dual users and reducing the numbers diverted from smoking at initiation. It will also encourage policies and professional practice that are not risk-proportionate and therefore amplify the effects of risk misperception.

The alternative to the PHE/RCP approach is to shift the problem of misperception onto the public by requiring them to figure it all out for themselves based on impressions from excitable news sources, friends and family, and unscrupulous media-friendly academics who specialise in alarmism and hype (and there are *a lot* of them). This type of communication from PHE and RCP is, in my view, highly responsible and ethical in this context. It also constitutes a measured response to irresponsible and unethical risk communications from activists, academics and clickbait media that have become the main output of mainstream tobacco control science and commentary, especially from the United States.

It would be so much easier to produce hedged and technically accurate

statements. By way of illustration, consider a statement of the form: "*some scientists and tobacco companies believe that e-cigarettes have potentially lower risks than smoking, though there are no long term data to confirm this*". This is pedantically correct for the speaker, but deeply misleading for the audience. PHE/RCP's formulation aims to avoid this problem.

What is going on here?

The "95 per cent" statements from PHE and RCP have generated frenzied and almost comical rage in the tobacco control community. If ever there was a "scream test", then they have passed it with this one.

I do not believe these authors are raising this issue out of some sort of concern for smokers, vapers or non-smokers being misled. Their 'call to action' is all about insiders being *against* this risk formulation:

> *Public health practitioners, scientists, and physicians should expose the fragile status of the factoid emphatically by highlighting its unreliable provenance and its lack of validity today, noting the many changes in e-cigarette devices and liquids, the accumulation of evidence of potential harm, the increased prevalence of use, and the growing evidence that e-cigarette use is associated with subsequent cigarette smoking.*

None of these arguments holds any water, as discussed above, but the notable feature of this call to action is that it completely disregards the at-risk populations and their information needs or rights. They don't say what they would tell the public – or their brother. Also, there are plenty of risk communication 'factoids' that are bandied around in tobacco control that rarely attract scrutiny: 480,000 Americans die each year from smoking? What does that even mean? One in two smokers die from smoking? Really? But these numbers support the dominant tobacco control campaigning narrative so they are rarely questioned.

So my hypothesis is that this reaction – and they are far from alone – is more about what these technologies mean for tobacco control and the career-long efforts of tobacco control academics and activists to do control tobacco in ways that they find gratifying (coercive, punitive, state-based, stigmatising etc). Vaping technologies are disruptive, but not just for the industry and the marketplace. They are disruptive to academics and activists too. Solutions to the

smoking and public health problem that are grounded in the interplay of willing and well-informed consumers with innovative technology businesses in a lightly-regulated market just aren't in their playbook *and they never will be*.

The PHE/RCP risk communication is designed to facilitate this consumer-driven approach and therefore I think the hostile response to it should be seen as reactionary indignation on the part of those threatened by progress or a different model to the one they have held dear for decades. In my view, the rage in tobacco control about the 95 per cent claim is about *them*, and how affronted they feel.