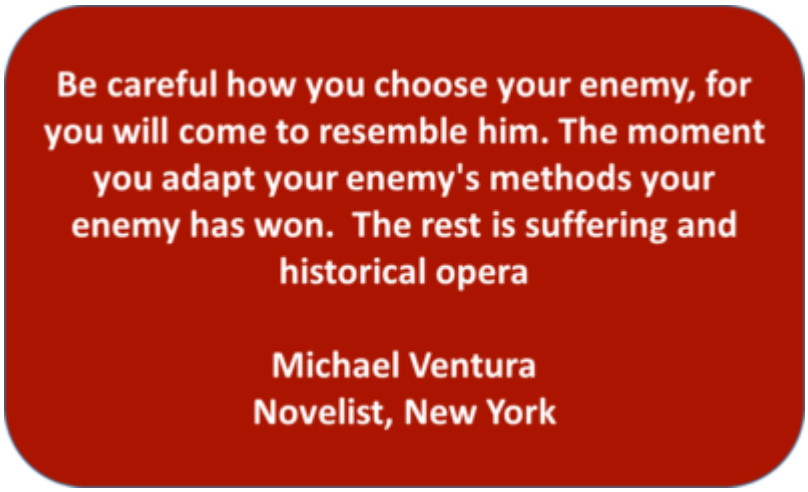
Professor Glantz makes an irresponsible and baseless claim about vaping risks

written by Clive Bates | 6 June 2016



I am particularly concerned about a sweeping statement made by one of the most vocal activists in tobacco control, Professor Stanton Glantz of the University of California at San Francisco. He asserts completely incorrectly and irresponsibly that a new study shows long-term vaping risk could equate to half the risk of smoking. *This is a grotesque exaggeration.*

Here I take a closer look at the claim and the study that supposedly lies behind it, looking at six failures in Professor Glantz's reasoning:

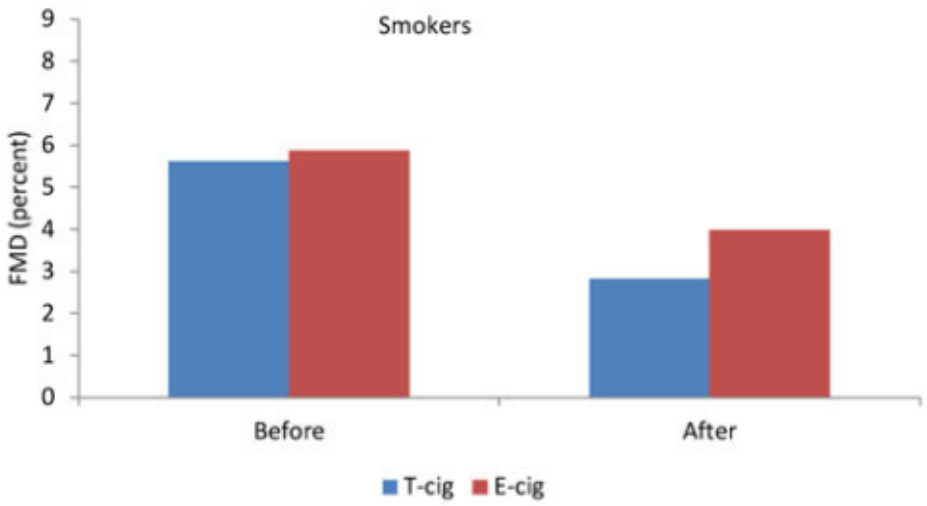
1. Coffee and exercise have similar acute effects
2. Smoking-related cardiovascular disease is caused by combustion compounds found in tobacco smoke but not found in vapour
3. Claiming to know the magnitude of cardiovascular risk when no risk is even established
4. Adding in respiratory risks for no apparent reason
5. Choosing a contrived and flawed explanation that suits anti-vaping activism
6. Ignoring what we already know about nicotine

Introduction

A moderately interesting paper came out in April 2016.

> *Carnevale R, Sciarretta S, Violi F, et al. Acute impact of tobacco versus electronic cigarette smoking on oxidative stress and vascular function. Chest : 21 April 2016. [PubMed]*
>
> *Conclusions: Our study demonstrates that both cigarettes have unfavorable effects on markers of oxidative stress and FMD after single use, although E-cigarette appeared to have a lesser impact. Future studies are warranted to clarify the chronic vascular effects of E-cigarette smoking.*

The paper takes some measurements of acute changes in vascular function and finds some measurable effects. Seeing this, Professor Glantz went into overdrive on his blog – see Important new study shows immediate effects of e-cigs on the cardiovascular system as big as smoking a cigarette, even drawing up his own graphs to drive the point home, just like this one:



It's a graph and it looks scientific, but does it mean what he says it means?

Unencumbered by caution and unfettered by professional responsibility, Professor Glantz draws the following astonishingly bold conclusion (emphasis added):

> *Professor Glantz*
> *These effects are, frankly, bigger than I expected. Given than heart and*

> *vascular disease and non-cancer lung disease cause over half the smoking-induced deaths, e-cigarettes could be half as dangerous as conventional cigarettes even if they cause no cancer.*

Look carefully. This is an extreme and unqualified claim about the *long-term impact on chronic vascular disease*. But the study itself is about *short-term acute changes in vascular function*. The distinction is extremely important, as we shall see, but ignored in Professor Glantz's claim.

Nevertheless, with this study he tries to dismiss the Royal College of Physicians' closely argued report: *Nicotine without smoke: tobacco harm reduction*. His claim contrasts with the RCP's carefully considered view of relative risk, set out in Section 5 of its report and summarised as follows (emphasis added):

> *Royal College of Physicians*
> *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.*

Why this matters. They can't both be right. If the Royal College of Physicians is right, then Professor Glantz is exaggerating vaping risk by at least 10 times and probably a lot more (or, to put it differently, downplaying the risk of smoking by at least 10 times and probably a lot more).

Claim and counter-claims like this have the effect and possibly the intent of creating confusion. This applies both to the UK where only 15% of the public accurately believe that electronic cigarettes are a lot less harmful than smoking (ASH) and in the United States where 47% said vaping was not healthier than smoking conventional cigarettes (Reuters/Ipsos). These radically false perceptions of relative risk amount to a protection of the cigarette trade and encouragement of smoking by removing or diminishing the of the most important advantages of vaping. If tobacco control activists are causing this deliberately or negligently then they have a lot to answer for.

So is Professor Glantz wrong? We will consider six challenges to his reasoning…

1. Coffee and exercise have similar acute effects

Lots of things can influence these acute measures of vascular function. Guidelines for measuring Flow Mediated Dilation (FMD)(see – Thijssen DHJ, et al, *Am J Physiol Heart Circ Physiol*, 2011) advise abstinence in the use of caffeine and other stimulants (which I guess includes nicotine) prior to taking these measurements. In other words, *effects are expected when stimulants are taken*:

> *FMD can be influenced by dietary intake (7), recent aerobic or resistance exercise (20, 41, 75, 120), caffeine and alcohol ingestion (44, 88), and supplement/medication use (39, 72, 111). We therefore recommend assessing FMD when subjects are fasted and have avoided exercise, caffeine, alcohol, drugs, stimulants, and medications for a consistent period of time (at least 6 h) to minimize the effect of these confounding factors (Table 2). [references via link above]*

So drinking coffee could have a similar effect? The first thing a credible neutral investigator would do is see if these effects occurred elsewhere. And it turns out they do:

> *Papamichael CM, Aznaouridis KA, Karatzis EN, et al. Effect of coffee on endothelial function in healthy subjects: the role of caffeine. Clin Sci (Lond) 2005;**109**:55–60[PubMed]*

> *In conclusion, coffee exerts an acute unfavourable effect on the endothelial function in healthy adults, lasting for at least 1 h after intake. This effect might be attributed to caffeine, given that decaffeinated coffee was not associated with any change in the endothelial performance.*

What a shame that the study didn't add a group of coffee drinkers to compare the magnitude of the observed effects. This may even have provided usefully reassuring contextual information, given we do not live in mortal dread of coffee or exercise.

Conclusion: similar effects are observable after exercise and coffee drinking – neither of which is a cause of vascular disease or a reason for concern. So it is simply not possible to draw conclusions about any disease risk from these

measurements.

2. Smoking-related cardiovascular disease is caused by combustion compounds found in tobacco smoke but not found in vapour

The reasoning in Professor Glantz's statement jumps from a handful of markers describing acute changes to the body (oxidative stress, FMD) to assertions about chronic vascular disease risk without showing that these markers are strong and exclusive predictors of chronic vascular diseases in any material way at all. In fact, evidence for the causes of cardiovascular disease from smoking point to other sources within the toxic mix in cigarette smoke. The US Surgeon General gives an extensive overview of smoking and CVD in the 2014 50the anniversary report (Chapter 8: Cardiovascular Diseases), and sums up (emphasis added):

> Although the hemodynamic effects of nicotine intake could potentially have implications for risk of CVD (USDHHS 2010), the results from the study by Murray and colleagues (1996) and from other studies (Joseph et al. 1996; Tzivoni et al. 1998) suggest that combustion compounds in tobacco smoke, such as carbon monoxide and nitrogen oxides, are the primary contributors to increased cardiovascular risk.

Perhaps because the authors know there *are* products of combustion in cigarette smoke but these are not present in e-cigarette vapour, they are reluctant to attribute a disease risk to their findings. Instead, they go no further than calling for more research.

> *Future studies are warranted to clarify the chronic vascular effects of E-cigarette smoking.*

To which they should really add "if any" for completeness.

Conclusion: Professor Glantz has ignored what we do know about the causes of cardiovascular disease in smoking and failed to acknowledge that these combustion products are not found in e-cigarette vapour.

3. Claiming to know the magnitude of cardiovascular risk when no risk is even established

Professor Glantz's claim goes further than mere attribution of cause and effect and asserts these bodily changes would result in the same magnitude of vascular disease impact for e-cigarettes as the entire vascular disease impact of smoking (and those include harms arising from CO exposure and several other cardiotoxic agents not found in e-cigarettes). The authors of the study, of course, do not make this leap – not least as they don't even claim there is necessarily a disease risk at all, let alone assume that they can predict its magnitude. This reasoning here is completely unfounded.

Conclusion: Professor Glantz has made a quantified claim based on nothing at all.

4. Adding in respiratory risks for no apparent reason

The hyperbole doesn't end with assuming cause and effect (2 above) and assuming the magnitude of the impact on cardiovascular disease is the same as for smoking (3 above)… Professor Glantz's statement implies that these markers and bodily changes will also cause *respiratory harms* equivalent to the burden of COPD arising from smoking (i.e. the "non-cancer lung disease" mentioned in his conclusion) without explaining how these measured markers are related to COPD and why the magnitude of the impact would be the same. Of course, the authors of the study don't say anything like that and he doesn't make a case either.

Supposing this unfounded assertion puts off smokers with pre-existing respiratory conditions from trying vaping? We have encouraging evidence that such a switch is beneficial:

- Polosa R. Electronic cigarette use and harm reversal: emerging evidence in the lung, *BMC Med*, 2015 [link]
- Campagna D, Amaradio MD, Sands MF, et al. Respiratory infections and pneumonia: potential benefits of switching from smoking to vaping. *Pneumonia* 2016;8:4. [link]

Conclusion: it is harmful and unethical to use a study like this to claim the entire

COPD risk from smoking may also arise from vaping (a completely baseless claim) – what if a COPD sufferer carried on smoking as a result?

5. Choosing a contrived and flawed explanation that suits anti-vaping activism

Professor Glantz claims to know what is causing these effects. He co-opts the study to back his own explanatory theory for e-cigarette risk, which centres on 'ultrafine particles'. He opens his blog with the assertion:

> *Ultrafine particles trigger inflammatory processes that lead to heart and lung disease and can trigger heart attacks.*

The expediency of blaming ultrafine particles. Particulate matter ('tar') in cigarette smoke is implicated in smoking-related disease. So naming 'ultrafine particles' as the problem with e-cigarettes allows for casual linking of e-cigarettes to the harms of smoking (though by word association, rather than by science). But here is the point: the 'tar' particles in cigarette smoke are very different chemically and physically to the liquid 'particles' that make up e-cigarette aerosol. Science-by-heroic-analogy simply cannot be applied in this case.

I'm not going to repeat the overwhelming arguments against assuming equivalence between ultrafine particles in cigarette smoke and the liquid droplets in e-liquid aerosol – other than to say a particle does not become a *harmful particle* simply because of its size. If that was the case, we'd be worried about getting in the shower or boiling the kettle – see Ogulei D, Hopke PK, Wallace LA. Analysis of indoor particle size distributions in an occupied townhouse using positive matrix factorization. *Indoor Air* 2006;16:204–15. [PubMed]

> *Boiling water for tea or coffee was found to be associated only with the smallest particles…*

The physics (eg. phase, viscosity, temperature) and chemistry (e.g. toxicity, reactivity) of the particles matter as much or more than particle size alone.

See Scientific sleight of hand: constructing concern about 'particulates' from e-cigarettes for my efforts to dispute Professor Glantz's theories on this seemingly

indestructible zombie argument.

Funnily enough, the words ‘particle’, ‘particulate’ and ‘ultrafine’ do not appear in the *Carnevale et al* manuscript. Professor Glantz has added this interpretation on his own initiative. Instead, the authors tentatively suggest several other explanations (emphasis added):

> *The effect of E-cigarette smoking on inflammatory markers may be explained by several potential mechanisms that warrant investigation in future studies. Nicotine is a pro-oxidant compound that may contribute to these alterations. Alternatively, additives and flavors may also elicit harmful effects on the inflammatory status. Finally, the inhalation of vapor may induce a cellular ROS [reactive oxygen species] increase that is sufficient to induce a lipid peroxidation reaction leading, in turn, to an increase in circulating inflammation markers.*

Conclusion: where did the argument about ultrafine particles come from? Not from the study. But nicotine is a more realistic explanation.

6. Ignoring what we already know about nicotine

The authors don’t say anything about ultrafine particles, but they do mention nicotine – see emphasis above. Nicotine delivery is the common characteristic of e-cigarette use and cigarettes – and both smokers and vapers are trying to obtain an equivalent hit, and therefore we might expect nicotine exposure to be roughly similar. It follows that any effects on the body arising from nicotine exposure are likely to be similar. So if we are looking for a common explanation for the similar findings for smoking and vaping being similar, nicotine exposure is the obvious place to start, given nothing else is remotely similar, and we know stimulants like caffeine have an effect (1 above).

But if you are a diehard anti-vaping activist rather than a scientist, that explanation doesn’t help you very much. The reason is that nicotine use in isolation from tobacco smoke doesn’t seem to be very harmful at all – this is known from many decades of study of snus use (see PN Lee on snus) and NRT (discussed on TreatTobacco.net). The US Surgeon General (Chapter 5: Nicotine) showed any harms arising from nicotine are limited primarily to certain vulnerable populations. We also know that nicotine can promote acute changes in

the cardiovascular system (for example, in blood pressure), but these do not result in a worsening chronic condition, like hypertension – see Pickering TG. The Effects of Smoking and Nicotine Replacement Therapy on Blood Pressure. *J Clin Hypertens* 2001;3:319–21. [link]

It is *the other things* in cigarette smoke that do the damage (possibly interacting with nicotine). Nicotine has acute effects, but it is not the major cause of the main diseases of smoking.

Conclusion: nicotine may be causing these observations, but evidence from other patterns of nicotine use do not suggest this in itself will be manifest as a serious disease risk from e-cigarettes. If we could conclude these short-term acute effects are a result of nicotine exposure, there would be little grounds for concern.

Overall conclusion

- The alarming assertion that "*e-cigarettes could be half as dangerous as conventional cigarettes*" is not even remotely supported by this study (or by anything else).
- The claim is not made by the authors of the study, who say that chronic effects are unknown and require further research.
- It is quite possible that the disease risks implied by these markers are approximately zero, as for coffee.
- If nicotine is the agent in e-cigarette vapour causing the measured changes, we have little reason for concern given what is known about nicotine delivered without tobacco smoke.
- Professor Glantz's claim is a wildly irresponsible statement with potentially harmful consequences if it influences the behaviour of smokers, vapers or regulators.

I'm seeing ever stronger parallels between the behaviour of the tobacco industry 30-40 years ago and the reckless propaganda that pours from tobacco control activists today. There is a strong logical and ethical equivalence between the tobacco industry of the past denying the risks of smoking and the tobacco control activists of today exaggerating the risks of vaping. Both approaches, if they work, mislead the public about risk and have the effect of protecting cigarette sales, increasing smoking, and treating smokers' health and welfare as mere collateral damage in the pursuit of some other goal.