Global Forum on Nicotine

Warsaw 2016

A report for the Tobacco Harm Reduction Association of Canada.

Part 2 / Day 1.

Safety and toxicology of e-cigarettes

Dr Konstantinos Farsalinos, Onassis Cardiac Surgery Center, Athens, Greece

The Global Forum on Nicotine (GFN) was held at the Marriott Hotel, in Warsaw, on Friday 17th and Saturday 18th June 2016. The Tobacco Harm Reduction Association of Canada (THRA) was represented at this conference.

The theme of this year's conference was, 'Evidence, Accountability and Transparency.'

The message was delivered by an impressive line-up of international speakers.

Safety and toxicology of e-cigarettes.

Dr Konstantinos Farsalinos, Onassis Cardiac Surgery Center, Athens, Greece

Dr Konstantinos Farsalinos is a cardiologist, working as researcher at Onassis Cardiac Surgery Center in Athens-Greece and at University of Patras in Greece. His main research interests are new modalities in cardiovascular imaging and he has received a scholarship from the Greek Society of Cardiology for research and education in this field. He has studied the effects of smoking on subclinical cardiac dysfunction using new imaging techniques since 2010.

He has been actively performing research on electronic cigarettes since 2011 as a principle investigator, in both clinical and laboratory level. Examples of his work include the first study on the cytotoxic effects of electronic cigarette vapour on cultured cells and the immediate effects of electronic cigarettes used on cardiac function and coronary circulation. He has presented his research in major international scientific congresses and has published more than 40 studies about e-cigarettes in peer-reviewed medical journals.

https://gfn.net.co/programme-2016/speakers-2016

Among the first words Dr Farsalinos spoke when taking to the podium were, 'media frenzy,' and, 'formaldehyde.'

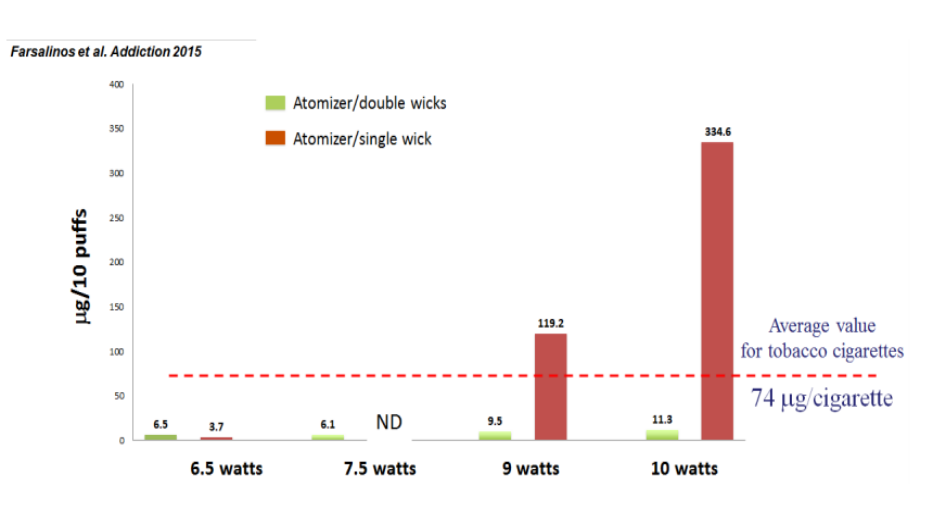
"Oh good!" I thought. "I'm going to enjoy this!"

And I did!

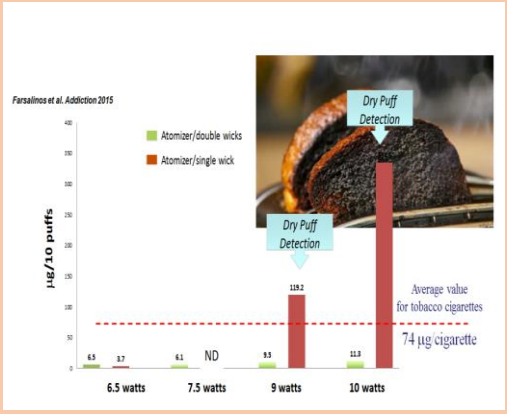
Dr Farsalinos, had chosen as part of his topic, to examine a study which had appeared in The New England Journal of Medicine, entitled, "Hidden Formaldehyde in E-cigarette Aerosols." This study managed to provoke media hysteria where the press, and others, screamed 'holy murder' about a perceived threat to health via the 'terrifying' spectre of the presence of huge amounts of deadly formaldehyde in e-cigarettes.

But there was something very badly wrong with the study… Dr Farsalinos explained…

In the wake of the New England Journal of Medicine report, Dr Farsalinos and his team decided to replicate the study. "The results were good." said Dr Farsalinos, "except in the cases where we were burning 'coal.'" Here he was referring to the power to the coil being ramped up to such high (ridiculous) levels that the liquid was not just being heated, but being burned.



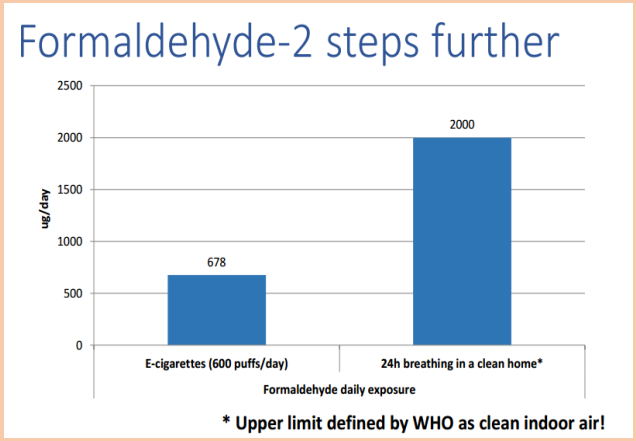
NOTE: I have deliberately used, "coil," in the singular.



Right away, Dr Farsalinos pointed out that no user would ever vape at levels where the liquid was being burned. "No user is ever exposed to such levels in the same way that no user is ever going to eat this piece of charcoal."

The replication went further than the original study. One step was to look more closely at the issue of formaldehyde, and at different levels of formaldehyde.

It is the case that 'normal' vaping can produce less formaldehyde exposure than breathing ordinary indoor air. Now, "Although formaldehyde is extremely toxic, the World Health Organisation(WHO) sets **acceptable levels** of formaldehyde for breathing in **clean** indoor air." Six hundred puffs per day produces three times less the amount considered acceptable (after 24 hours' occupation) for clean indoor air.



A second step further in the 'Farsalinos' study, was, 'a direct replication of the study done, as reported, in the New England Journal of Medicine.'

The replicate study used the same atomiser, a CE4. (This is a very old model of atomiser and Dr Farsalinos had to look far and wide to obtain one. Now, I am not a scientist, just an enthusiast, and, as such, I am perfectly free to voice my opinions and, in this case, my suspicions: You see, if Dr Farsalinos did not find it easy to obtain a CE4 atomiser, is it not just a little bit odd that the New England team just happened to pick one of these up, or, if it was not accidental, why would they choose this antiquated, inefficient device? I do not subscribe to the view that they did not know what they were doing).

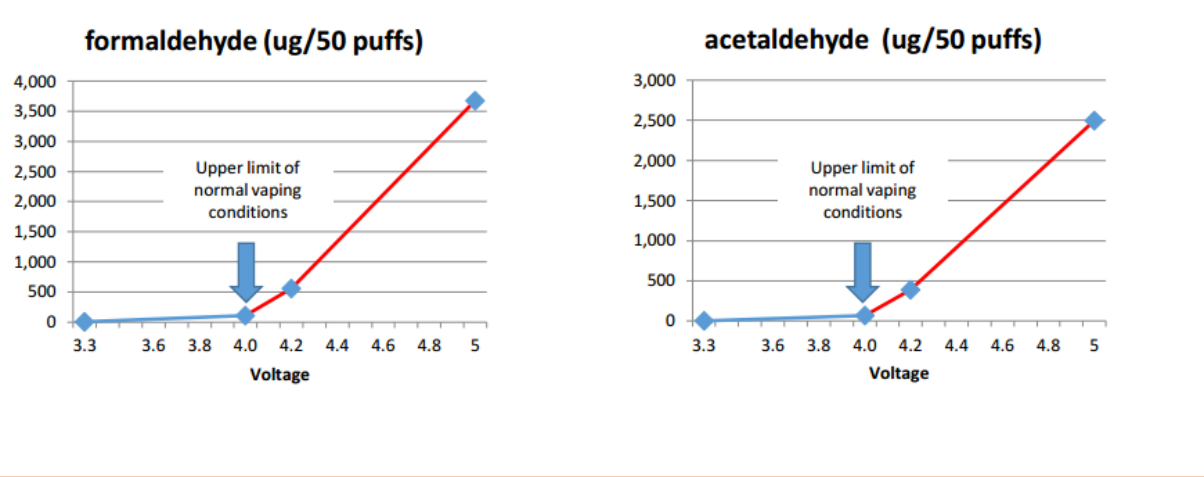
So the equipment being tested was identical in both studies.

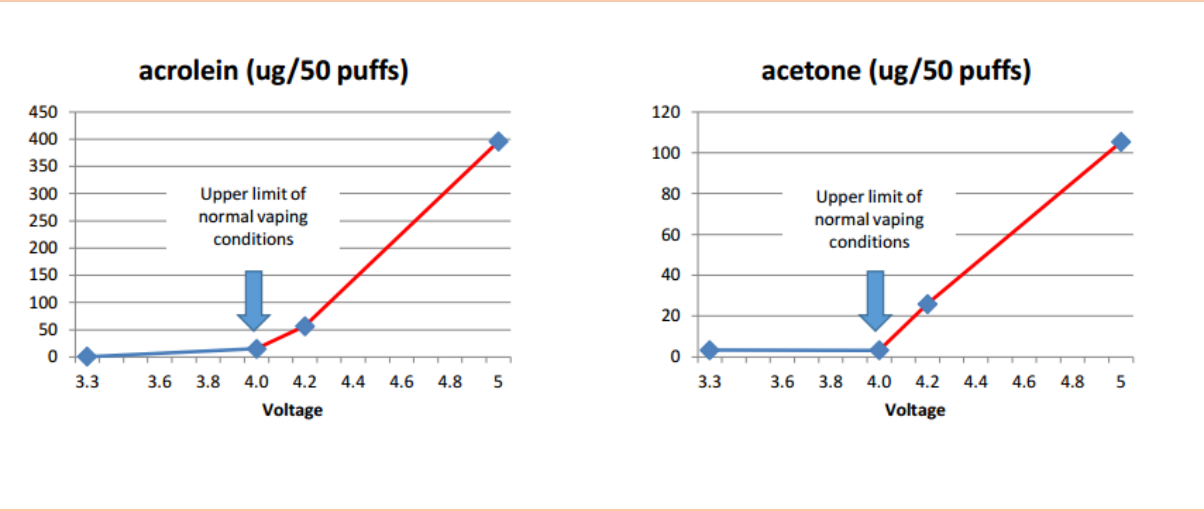
There was however a difference between the studies. Dr Farsalinos employed vapers. (Vapers also happen to be real people just like the ones you see out and about on the streets.) The vapers were asked to use the devices and report at which point the detected 'dry puff' at a level they would stop using the device. (Dry puff, the point at which taste is altered as a result of burning the liquid)

The victims (keeping in mind that the tabloids and the New Musical Express said they would die [they didn't say that but I just cannot resist having a dig]) The volunteers were blindfolded and were instructed to follow the puff regime of the original study. Through this upper vaping limits at which dry puff conditions could be identified and tolerated by actual use were established.

Dr Farsalinos pointed out that. as voltage is increased, so does the amount of liquid being used, and you cannot therefore compare puffs at different voltage settings.

The study looked at the production of: formaldehyde, acetaldehyde, acrolein, acetone, and the results were virtually the same for all, in that at the upper level of normal vaping conditions, [4.00] production of these substances remained extremely **low and only started to rise rapidly after normal vaping limits had been reached.**





And so what we have with the New England Journal of Medicine is a report of a study that has no relevance to actual use.

The presentation moved on to the topic of aortic stiffness and blood pressure. Recently a letter was published by the University of Athens on this topic and it created a deal of media interest.

From measurements made a 'remarkable' statement was made.

Dr Farsalinos described things thus:

"E-cigarette use increases blood pressure rapidly, of course nicotine increases blood pressure. We have known that for half a century. But, they also found that it increases aortic stiffness by comparing e-cigarette use for thirty minutes with smoking a tobacco cigarette… They measured the acute affects before and ***just after*** *use and they concluded that because aortic stiffness has a prognostic value in the future development of cardiovascular events, and because of the prolonged use of the e-cigarette among users, they basically say that this has a prognostic significance showing that there is an increased risk of cardiovascular events due to e-cigarette use.*

But, it is interesting, because if you look at the guidelines for measuring aortic stiffness, one of the ***main criteria*** *is that you should refrain from smoking for three hours, basically you have to refrain from any stimuli including caffeine, also alcohol, so basically, what they measured was the effects of nicotine intake, and, of course they found more with the use of an e-cigarette for thirty minutes, obviously users absorb more nicotine… What they did was violate the basic principle of measurements and the basic criteria for measuring aortic stiffness…*

Caffeine and aortic stiffness

Acute Effect of Caffeine on Arterial Stiffness and Aortic Pressure Waveform

Azra Mahmud, John Feely

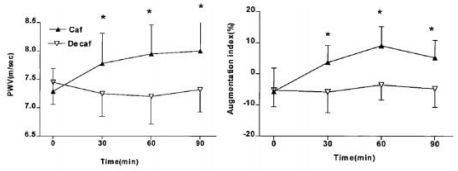


Figure 2. Acute changes in PWV and AI% at baseline and at 30, 60, and 90 minutes after ingestion of caffeinated (Caf) and decaffeinated (Decaf) coffee in 7 healthy subjects (mean±SEM, *P<0.05).

Nicotine and aortic stiffness

Clinical and Experimental Pharmacology and Physiology (2009) 36, 784–789 doi: 10.1111/j.1440-1681.2009.05141.x

ACUTE EFFECTS OF NICOTINE ON ARTERIAL STIFFNESS AND WAVE REFLECTION IN HEALTHY YOUNG NON-SMOKERS

Dionysios Adamopoulos,† Jean-François Argacha,* Marko Gujic, Nicolas Preumont, Jean-Paul Degaute and Philippe van de Borne

Department of Cardiology, Erasme Hospital, Brussels, Belgium

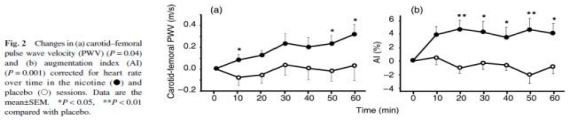


Fig. 2 Changes in (a) carotid–femoral pulse wave velocity (PWV) ($P = 0.04$) and (b) augmentation index (AI) ($P = 0.001$) corrected for heart rate over time in the nicotine (●) and placebo (○) sessions. Data are the mean±SEM. *$P < 0.05$, **$P < 0.01$ compared with placebo.

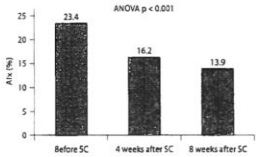
The second problem is that it is never the acute effect of intervention which is found to be a prognostic indicator of any kind… It is the measurement of aortic stiffness at base line at resting conditions without smoking, drinking coffee or eating for three hours etc. that has any prognostic significance, not the acute intervention of anything like smoking or e-cigarette use. And we know that because these are exactly the same effects that have been observed in the past for caffeine: exactly the same increase for aortic stiffness, just by drinking coffee, more delayed here because there is some time from the time you drink (the) coffee and the time you absorb the caffeine: ***Exactly the same effects as getting nicotine orally*** *when a tablet was given, and despite the low absorption rate in oral intake, still they have worse effects, but, what is very interesting* ***that although oral nicotine intake has the same effects acutely on aortic stiffness, on the long term quitting smoking with the use of NRT's is beneficial for aortic stiffness, so when you measure at base line resting conditions, people who have quit use with the use of nicotine, you see a significant improvement starting one month, and, becoming even better at two months, just two months after quitting smoking.***

NRT-smoking cessation and aortic stiffness

Early Improvement in Peripheral Vascular Tone following Smoking Cessation Using Nicotine Replacement Therapy: Aortic Wave Reflection Analysis

Antoine Roux[a, h] Pascal Motreff[a, f] Jean Perriot[c, e] Bruno Pereira[d] Jean-René Lusson[a, f, g] Christian Duale[b, h] Dominique Morand[d] Claude Dubray[b, g, h]

[a]Pôle Cardiologie, [b]CPC, [c]CMP B, Pôle Psychiatrie, and [d]DRCI, CHU Clermont-Ferrand, [e]Dispensaire Emile-Roux, [f]ERIM, EA 3295 and [g]Faculté Médecine, Université Clermont1, and [h]Inserm, CIC 501, Clermont-Ferrand, France



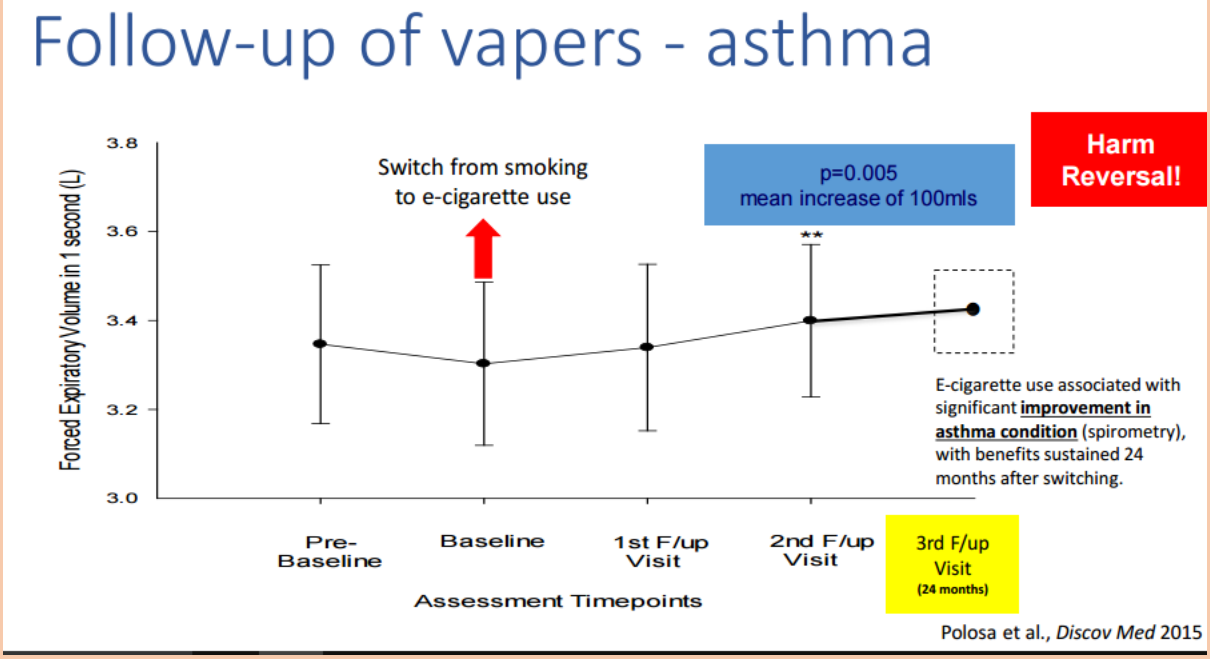
Conclusions: The improvement in AIx and the stability of PWV after SC with NRT indicate improved peripheral vascular tone. This impact may account for the early clinical benefit of SC observed even when associated with NRT.

<u>NOTE: The italicized section above was transcribed directly from Dr. Farsalinos' presentation at the GFN (2016) The video can be viewed Here.</u>

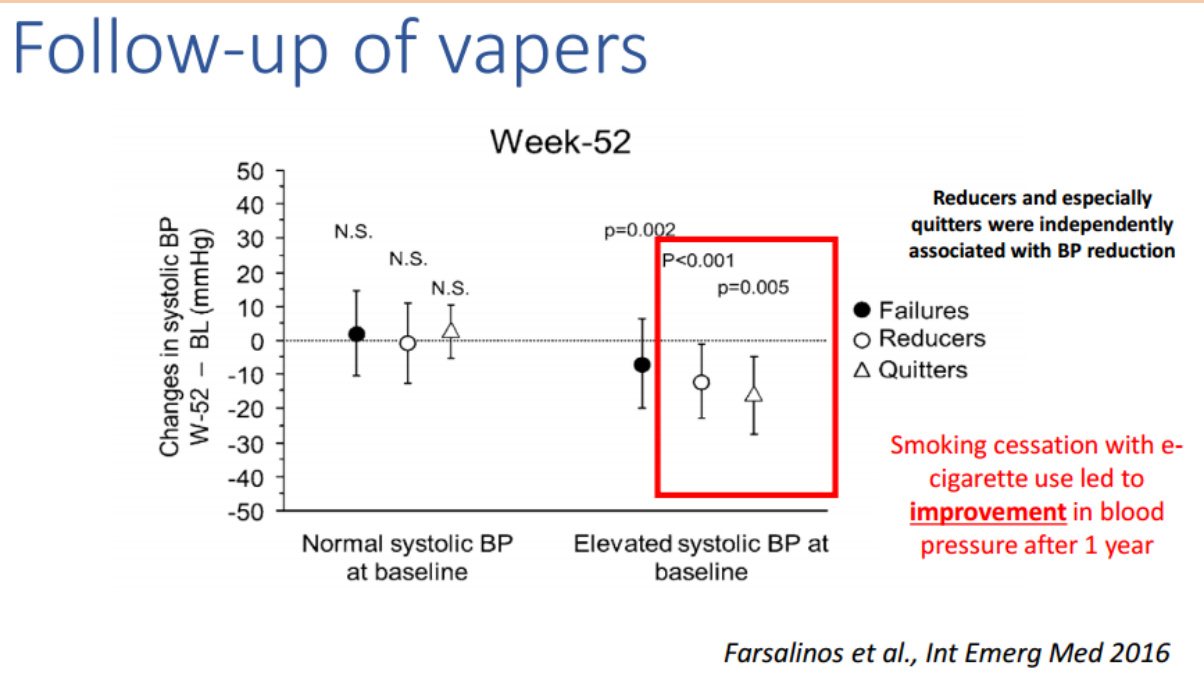
<u>Studies we should look for:</u>

The first example of the kind of study we should be looking at is one from Prof. Ricardo Polosa. This was a study of asthmatics where they were followed up, "**not acutely five minutes after intervention,"** but a study which monitored the condition of the participants for two years. Dr,

Farsalinos pointed out that these were spirometry measurements and were therefore an objective record of the improvement of people with asthma conditions, they were not subjective. They show a significant improvement of the condition – even after two years.



We were then directed to a study on smokers who had switched to vaping – including dual users. This was a fifty-two-week observation, again not just a short-term snapshot. The study looked at blood pressure and heart rate. This demonstrated an improvement after one year follow up



Dr. Farsalinos then moved on to discussing 'risks' of nicotine and mentioned that recently there had been mention of cancer and cardiovascular disease and the fact that there were major misconceptions among even health care professionals.

However, when we look at the example of Sweden where there is high tobacco use among men, this is mainly due to snus use. As a result of this, Sweden has, by far, the lowest mortality rates from cancer and cardiovascular disease of any other country in the EH.

This is proof of concept.

Dr, Farsalinos summed up the main points and I reproduce them here…

- *Current estimates (Public Health England report – August 2015 and Royal College of Physicians report - May 2016) consider that e-cigarettes are at least 95% less harmful compared to smoking*
- *Due to differences in e-liquid and aerosol chemistry: total absence of smoking-related toxins or presence in extremely low levels*
- *Expected due to the lack of combustion and the minimal impact of nicotine on smoking-related disease*
- *Strong opposition to tobacco harm reduction does exist*
- *Opposition to nicotine addiction acceptable, but should we care about addiction or about disease and death?*
- *Concerns about use by non-smoking adults and youth legitimate but unsupported by evidence so far abuse of precautionary principle*
- *Duty to help smokers unwilling or unable to quit with currently approved methods*
- *OR*
- *Punish smokers because smoking cessation medications are not very effective*

All images https://gfn.net.co/downloads/2016/Konstantinos%20Farsalinos.pdf

With special thanks to the GFN for the immaculate organisation of the conference, and for supplying much of the information from which this summary is gleaned.

Robert innes: Advisory Board Representative of the THRA at the GFN