

A Collection of Position Statements and Opinions on e-cigarette use and cardiovascular disease: On behalf of the Working Group on Epidemiology of the Hellenic Atherosclerosis Society

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ABSTRACT

There are accumulative evidences that the prevalence of cigarette smoking has gradually declined in most high-income countries since the 1990s, in part due to public health campaigns emphasizing on the relationship between tobacco use and detrimental health effects. In late 2000s electronic (e)-cigarettes were introduced in the world, as less harmful nicotine products that may also help people in quitting smoking. Since then, the use of e-cigarettes has increased rapidly from the time when their introduction in the global market. In this work we present a collection of position statements and opinions of scientific bodies and Organizations, regarding the safety of e-cigarettes, as well as their association with human health, and particularly, cardiovascular diseases.

KEY WORDS: Position statements, e-cigarettes, vaping, cardiovascular disease

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INTRODUCTION

It is well constituted that conventional cigarette smoking increases risk for cardiovascular disease, in current smokers and passive smokers¹, even among those smoking

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cigarettes of low tar², compared to non-smokers. Evidence took decades to accumulate since associated health risks to cigarette smoking are both dose and duration dependent³. Since this evidence came to light, tobacco related products emerged, one of which is the electronic cigarette/nicotine delivery systems, as safer tobacco products, driven from the tobacco companies themselves, although recent studies suggest increased health risks, at a level that may surpass the traditional cigarette smoking itself³.

In 2003, electronic (e)-cigarettes were patented by Hon Lik, in China. In the year that followed, they became available for purchase, firstly in China, and then, in the entire world⁶. In the United States of America, they have been available since 2007 and one year prior to that, in the European Union (E.U.)⁸. There are several synonyms of electronic (e)-cigarettes, i.e., Electronic Nicotine Delivery Systems (ENDS), "e-cigs", "vape-pens", "mods", "e-cigars", according to the Centers of Disease Control and Prevention (CDC)⁴. The American Heart Association (AHA) defines electronic cigarettes (e-cigarettes) and vaping, respectively, as *"battery-powered devices that can deliver nicotine and flavorings to the user in the form of an aerosol"*, and *"the act of inhaling and exhaling the aerosol, often referred as vapor, which is produced by an e-cigarette or similar device"*⁵.

From the time e-cigarettes became available in the market, and up to date, there are controversial findings regarding their effects on health. The principle, promoting idea was that e-cigarettes constituted a healthier option compared to traditional cigarettes, and assist in quitting cigarette smoking⁶. According to the European Heart Network (EHN), *"e-cigarettes are promoted as risk-reducing products compared to combustible tobacco cigarettes"*⁷, while the European Association of Preventive Cardiology (EAPC) states that they *"are promoted as safe alternatives for traditional tobacco smoking and are often suggested as a method to reduce or quit smoking"*⁸. In addition, it is stated by the World Health Organization (WHO), that with the pretense of helping public health, ENDS companies, advertise, and promote ENDS and make flavors to attract youths to increase the number of their customers⁹. This is an area of concern since ENDS-related harm perception did not increase among adolescents 12- to 17-year-old that did not have positive tobacco attitude and lived in smoke free home rules¹⁰. Furthermore, smoke free environments have been established in many countries for tobacco related products for public health prevention, but few for ENDS, which may also expose individuals to nicotine and particulate matters¹¹; substances that can trigger inflammation, oxidative stress, and other thrombotic effects³. A population survey of ENDS users reported that 58% of dual users (ENDS and cigarettes) used ENDS in public smoke free environments¹², intensifying the

need to review position statements and opinions by experts in the field.

POSITION STATEMENTS AND OPINIONS BY SCIENTIFIC ORGANIZATIONS AND REGULATORY BODIES

World Health Organization (WHO)

The past two decades data from the WHO indicated that global tobacco use has been significantly reduced, especially among women⁶; however, e-cigarettes is an emerging trend, especially among younger individuals. These are not harm free since it is stated that toxic materials and nicotine are present in ENDS at varying quantities⁶. Specifically, long-term effects to nicotine exposure have been associated with abnormal brain development, seen in fetuses, children, teenagers, and youths⁶. Chemical addiction can, therefore, occur through e-smoking as well, which in turn can result in the use of traditional tobacco products, instead of the preliminary reason they were marketed, which was tobacco smoke cessation. It has been estimated that the possibility of smoking increases two-fold for underage individuals who e-smoke, although they had never smoked⁶. Public health officials' positions report that e-cigarettes can constitute *"a gateway" to conventional smoking among young people*⁶.

The health of e-smokers is not the only one harmed by ENDS. As stated previously, ENDS emit nicotine and particulate matters, therefore expose individuals, that are near a person who is e-smoking, to second hand aerosols⁶, in an otherwise "smoke-free" environment. In addition, children may be exposed, or even drink e-liquid, and suffer from poisoning. Moreover, ENDS may be altered by their owners or may be faulted from the manufacturer leading to accidents, such as explosions or fires⁶.

Based on a recent scoping review, the toxicity of traditional cigarettes is probably higher compared to ENDS, since it was not revealed ENDS to be causative of CVD outcomes as well as that switching to e-cigarettes was associated with improved hypertension control¹³. However, the long-term effects of ENDS remain unknown, due to the inadequacy of evidence, and controversial findings remain due to the variety of ENDS products (device voltage, liquid composition, the amount of vapor inhaled, etc.). It is also important to note that most e-cigarette users are former smokers or dual users, increasing the difficulty to differentiate the effects. Various factors most likely will determine how risky tobacco products or ENDS are and can vary between person and by ENDS product. Specifically, for cardiovascular disease, it is supported that an increased risk can occur from e-smoking, due to various constituents, such as nicotine, carbonyls, and particulate matters, although a recent scoping review found

no such effect¹⁴. How health will be affected in the long term hasn't yet been determined for all people who breathe aerosols. Also, it hasn't been determined by evidence, so far, that ENDS can serve in smoking cessation, as aids, since most of the e-cigarette users are dual users¹⁵. Negative consequences have also been added to the previous fact, since it has been shown that never smokers are more likely to start ENDS products by younger individuals, viewed as safe products¹³.

Tobacco control measures can be weakened by ENDS, and there is a possibility that the certain devices might "escape" laws, because they change in a quick pace. Regulation of ENDS is suggested for countries where they are allowed⁶, and although 48 countries (58.3%) have legislation on e-cigarette use at the national level, only a third regulated e-cigarette indoors, failing to protect bystanders in indoor settings¹⁶.

World Heart Federation (WHF)

The WHF perceives un-regulated e-cigarette use a serious threat and recommends a set of precautionary measures to protect vulnerable population, prevent second-hand exposure and address misleading claims⁹. The following presents some statements from a Policy Brief by the WHF (2021), regarding cardiovascular health and e-cigarettes. It is noted by the WHF that an association exists between increased risk of cardiovascular mortality and morbidity, and vaping. Atherosclerosis, elevation of blood pressure, increased risk of myocardial infarction and oxidative stress are parts of several health problems that have been associated with vaping. Evidence supports that e-cigarettes may lead to similar cardiovascular problems as cigarettes, because they both share the same health-harming substances; yet, the risk is lower in e-cigarette smokers, at least in former smokers. According to the evidence, the short-term cardiovascular health benefits of e-cigarettes seem to be positive. In cases where vaping is used alongside with cigarette, then there is a possibility that the CVD risk rises. The WHF also noted that it is very difficult to determine the exact health effects of vaping, due to the various ways of use, devices, populations, flavors, and e-liquids. Moreover, regarding Public Health and e-cigarettes, it is stated that other diseases must be considered in the evaluation of the consequences.

Another crucial issue, according to the WHF, is the fact that popularity of e-cigarettes/vaping has risen tremendously in the past years, among younger ages. The design, the different flavors and because the new fashion trend are the main reason for increased use in youths. Misleading advertising on the safety of e-smoking and extended marketing remain serious incentives for smoking initiation on that vulnerable age group. It is therefore suggested

-among others- that an additional taxation on e-cigarettes, a ban on marketing, sale and distribution can effectively reduce e-cigarettes among those ages. In addition, vaping and smoking should share the same ban regarding the places where is it not allowed, and restrictions regarding commercialization of e-cigarettes shouldn't be lifted by countries who are applying them.

Irrespective of age, all individuals should be safeguarded and preventative strategies against e-smoking/vaping should be implemented. Tobacco control legislation must be reinforced by future laws regarding e-cigarettes, and more scientific evidence is needed regarding the long-term effects of e-smoking/vaping on cardiovascular health. Lastly, further studies must take place on the topic of long-term effects of e-cigarettes on cardiovascular health⁹.

European Commission: Scientific Committee on Health, Environmental and Emerging Risks (SCHEER)

The SCHEER was mandated (2019) by the European Commission for an opinion on the potential risks of e-cigarettes use on health. The Committee concluded that, in relation to vaping, risks of long-term systemic effects on cardiovascular system are supported moderately by evidence. Moreover, it is weakly supported that aerosol metals can cause adverse effects, particularly carcinogenicity. Evidence is characterized as weak to moderate, regarding "*risks of carcinogenicity of the respiratory tract due to long-term cumulative exposure to nitrosamines and due to exposure to formaldehyde and acetaldehyde*". In addition, it is not supported by specific data that certain flavors in the European Union are risky for health after repeated exposure. Risks of other adverse health effects, like reprotoxic effects and pulmonary disease, are weakly supported and there is a need for additional data that presents consistency. Also, it is moderately supported that cumulative exposure to aldehydes, polyols and nicotine causes risks of local irritative damage to the respiratory tract. Additionally, risks of poisoning and injuries due to burns and explosion are strongly supported by evidence. The incidence of the last two health problems is described as low.

Equivalently, for people who are exposed to vaping second-hand, evidence is described as weak to moderate regarding "*carcinogenic risk due to cumulative exposure to nitrosamines*". Additionally, it is moderately supported by evidence "*risks of local irritative damage to the respiratory tract mainly due to exposure to glycols*". Specifically, about cardiovascular health, evidence is characterized as weak to moderate, regarding risks of systemic cardiovascular effects due to nicotine exposure.

Possible health effects on people who vape occur

mostly due to the vapor's substances. The particular substances, including nicotine, differ in their quantities. Specifically, for nicotine, it is strongly supported that the pattern of which e-cigarettes are vaped by their owner and the specifications of the e-cigarettes, determine the quantity of the chemical that is being consumed. Moreover, the quantity can be put side by side with traditional cigarettes, regarding long term e-smoking adults.

It is strongly supported that one of the reasons of vaping is appealing to people due to e-liquid flavors. Moreover, evidence is characterized as strong, regarding the involvement of nicotine in people becoming addicted. It is moderately supported that vaping is a "*gateway to smoking*" for young individuals and weakly supported that e-cigarettes are effective for smoking cessation. Evidence is characterized as weak to moderate, regarding e-cigarettes assisting people to decrease smoking. People haven't been exposed to vaping for many years and health effects, especially those of the long term, need to be studied further¹⁷.

US Centers Disease Control (CDC)

The US CDC states that more harm is caused by traditional smoking compared to vaping, and however, vaping is quoted as not entirely safe for young ages⁴. E-cigarettes seem to be risky during pregnancy and for young adults and adults who do not use tobacco products. Children have been poisoned by swallowing, inhaling or ingesting e-cigarette liquid through the skin or eyes. Specifically, almost half of the calls to poison control centers for e-cigarettes, concern preschooler children. As referenced by the CDC, the Food and Drug Administration (FDA) does not recommend e-cigarettes for smoking cessation, and the U.S. Preventative Services Task Force reports evidence as inadequate to support the use of e-cigarettes as a stop smoking aid, regarding adults and pregnant women. However, it seems they may provide a kind of smoking cessation support only if they are not used dually with cigarette smoking. Yet, evidence reveals that most e-smokers are also cigarette smokers. It is obvious that more research is needed regarding the long-term health effects of e-smoking as well as the benefit in smoking cessation⁴.

European Heart Network (EHN), European Association of Preventive Cardiology (EAPC)

EHN

The recent report of the EHN addressed two main issues about the effects of e-cigarettes/vaping on cardiovascular health and their effectiveness on smoking cessation. Even though, the short-term effects on cardiovascular health are not quite clear and the evidence

seems to be inconclusive, however it is supported that the risk still exists. Compared to conventional smoking, e-smoking is less harmful due to the absence of several toxic and carcinogenic agents, but it does not mean that it is safe and without health complications. For the long-term effects, more robust evidence is needed. However, there is good evidence supporting that heart rate may increase shortly after nicotine intake from vaping and may affect platelet functionality, blood pressure, and oxidative stress⁷. Moreover, up to date there is no sufficient evidence that e-cigarettes constitute an effective mean regarding smoking cessation. Additionally, a large majority of those who use e-cigarettes, as a smoking cessation process, they end up as dual smokers with increased health risks. The increased rate of e-smoking/vaping among young ages, starting from adolescence is quite alarming. A factor that has led to this increase is the appealing flavors provided for e-cigarettes and since the perception of safe to consume in contrast to traditional smoking. There is a possibility that public health will be affected in a negative way by e-cigarettes. The industry-related conflict of interest influence on results of studies to support the safety of e-cigarettes, regarding their health effects, constitutes another problem. Regulations on e-cigarette taxation, on restricting e-smoking in public places and on banning marketing and flavors could eliminate the use of e-cigarettes mainly among young ages⁷.

EAPC

The EAPC of the European Society of Cardiology (ESC) published in 2021 a position statement on e-cigarettes and cardiovascular risk⁸. The EAPC concluded that, regarding the prevalence of vaping, it differs from country to country, within a country, and between people who currently vape or have vaped. However, the prevalence, among youth and teenage age groups, is rising. Additionally, it is supported that the possibility of smoking traditional cigarettes rises because of the prevalence of vaping in the certain age groups. Regarding CVD, the effects of vaping haven't been studied extensively. The belief that traditional cigarettes are more damaging than e-cigarettes is because the exposure to potentially toxic chemicals -with the exception of nicotine- is higher in cigarettes, under regular vaping circumstances. Regarding the cardiovascular system, the effects in the long term of vaping are mostly not comprehended. According to research, endothelial dysfunction and arterial stiffness constitute some health problems that can be caused by e-smoking. In addition, due to the rise of e-smoking in vulnerable populations, the "benefit" of lesser damage will not be completely balanced out. EAPC agrees that vaping is harming to the cardiovascular system,

according to evidence and additional research on its effects in the long term must take place, with young people being prone, due to their wrongful healthiness perception. Because of this, it is suggested that a ban should be placed on those flavors. Additionally, indoor smoking or vaping, the attainment of e-cigarettes by bypassing laws and the possible reasons why youths might be drawn to them constitute other existing issues. It can be concluded that young peoples' health can be put in danger, and for vaping to be as limited as possible, public health action must be taken. Regarding the previous, prevention via education and awareness can help. It is stated that regulations haven't been keeping up with the market of e-cigarettes and therefore laws must be adjusted accordingly and enforced. In addition, it is suggested that laws must be formed, regarding e-cigarettes, by countries that don't have them. It is also noted that evidence is described as inadequate, regarding e-cigarettes in smoking cessation and assisting in long-term maintenance of not smoking. It is also supported that abstinence percentages might grow if behavioral therapy and vaping are used together in smoking cessation. However, if e-smoking is utilized exclusively in a clinical environment, there is a possibility that cessation will be weakened for most adults that are trying to quit without attending such environments. Further studies must be conducted for longitudinal data to be attained regarding smoking cessation and the impact of e-cigarettes on it⁸.

Existing recommendations in relation to position statements

A recent Scoping Review, upon collecting 81 statements from international health organizations with regards to the use of ENDS, observed that they could be summarized in a total of 5 different types¹⁸. Overall, two encouraged their use by smokers and three were opposed to it. The most prevalent opposing statement was the restrictive non-use attitude.

a) Support Selective Use

Encouragement of current smokers to use ENDS as a smoking cessation assistance. The user should be informed of alternative licensed drugs and counseling alternatives. Regulating ENDS as pharmaceuticals would increase product safety and permit marketing limits. The availability and usage of ENDS cannot interfere with current tobacco control initiatives, such as smoke-free regulations.

b) Selective Use Encouragement

Encouragement of smokers to transition to only using e-cigarette or to use e-cigarette as a quitting aid. Product

innovation, user attractiveness, lower taxation, and health messages emphasizing e-cigarette's lower harm should be prioritized in vaping regulation.

c) Precautionary non-use

Although ENDS are probably less dangerous than cigarettes, it is still unclear whether they expose users to long-term hazards or serve as successful cessation assistance. Until more information is available, use is not advised. To be on the safe side, smokers should be urged to stop using medications that have already received approval. Until new safety precautions are put in place and/or new data is available, these recommendations shouldn't be changed. It is advised to carry on researching.

d) Restrictive non-use

ENDS should be avoided since they undermine tobacco control efforts. According to the evidence that is currently available, consumption is not advised, and restrictions should concentrate on limiting business operations and product accessibility. ENDS need to be governed like tobacco.

e) Prohibit use

To prevent health concerns, ENDS-containing items should be illegally unavailable.

Unresolved issues and evidence gaps

Even though e-smoking/vaping is not considered entirely safe and several efforts have been made to underline the risks posed by the exposure to first-hand and second-hand e-smoking, still several issues need to be clarified. In Table 1 unresolved issues and evidence gaps which need to be addressed by evidence-based research are presented.

Unresolved issues and evidence gaps

Even though e-smoking/vaping is not considered entirely safe and several efforts have been made to underline the risks posed by the exposure to first-hand and second-hand e-smoking, still several issues need to be clarified. In Table 1 unresolved issues and evidence gaps which need to be addressed by evidence-based research are presented.

Conclusive remarks

Although ENDS started as an initiative to help quit traditional smoking, there is weak to moderate evidence to support this strategy, as noted by the European Commission as well. On the contrary, there is research depicting

TABLE 1. Unresolved issues and evidence gaps.

Unresolved issues:	Evidence gaps:
<ul style="list-style-type: none"> • According to the FDA report, it is illegal to sell any type of cigarettes, including e-cigarettes in people under the age of 21 years. However, these products are still available to young adolescents due to limited policies (19). • E-smoking products are advertised as safer compared to other tobacco products and ideal for smoking cessation, but the main message tailored is “safe” not “safer”. • The chemical and nicotine content in e-cigarettes’ is rarely disclosed by tobacco companies. No policies are in place. • Regardless to the WHO recommendations on banning indoor e-cigarette smoking, it remains unregulated in many countries (20). • Taxation on e-cigarettes and vapor products varies according to the liquid volume and nicotine concentration, and by country as well. • Arguments still exist on the hazards of nicotine content of e-cigarettes. 	<ul style="list-style-type: none"> • Long-term effects of e-smoking on CVD remain unclear, due to the lack of longitudinal and clinical studies • Many e-cigarette smokers are either former smokers or dual smokers, eliminating the causality relationship between e-smoking and CVD • Limited evidence exists on the effectiveness of e-smoking as a smoking cessation tool

that ENDS cannot be regarded as a complete safe alternative to tobacco and further research needs to take place for the determination of its effects on health in the long term. In addition, many ENDS with vaping being higher in the list, has negative effects on the cardiovascular system and further research needs to be conducted for the determination of its effects in the long term on the said system. Moreover, youths may start smoking because of the appealing taste and wrongful perception of vaping and thus, more regulations to ban e-cigarette use for

minors are needed. Also, exposure to harmful particulate is rising again since indoor regulation of ENDS are lacking by two-out-of-three of the countries, worldwide²¹. Lastly, public health initiatives that discourage non-smokers from using e-cigarettes and/or conventional cigarettes, by intensifying health awareness programs are urgently required.

Conflict of interest

There are no conflicts of interest

ΠΕΡΙΛΗΨΗ

Τοποθετήσεις οργανισμών για τη χρήση ηλεκτρονικού τσιγάρου και την καρδιαγγειακή νόσο: εκ μέρους της Ομάδας Εργασίας Επιδημιολογίας της Ελληνικής Εταιρείας Αθηροσκλήρωσης

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Υπάρχουν επιστημονικά δεδομένα ότι, από τη δεκαετία του 1990, ο επιπολασμός του καπνίσματος έχει μειωθεί βαθμιαία στις περισσότερες χώρες υψηλού εισοδήματος, εν μέρει λόγω καμπανιών δημόσιας υγείας που έδιναν έμφαση στη σχέση μεταξύ της χρήσης καπνού και επιβλαβών επιδράσεων στην υγεία. Στα τέλη της δεκαετίας του 2000 τα ηλεκτρονικά τσιγάρα εισήχθησαν ως λιγότερο επιβλαβή προϊόντα νικοτίνης που μπορεί παράλληλα να βοηθήσουν και στη διακοπή καπνίσματος. Από τότε η χρήση των ηλεκτρονικών τσιγάρων έχει

αυξηθεί ραγδαία, σε παγκόσμιο επίπεδο. Σε αυτή τη μελέτη παρουσιάζονται τοποθετήσεις επιστημονικών φορέων και οργανισμών, σχετικά με την ασφάλεια των ηλεκτρονικών τσιγάρων, καθώς και τη συσχέτισή τους με την υγεία, και ιδιαίτερα, με την καρδιαγγειακή νόσο.

ΛΕΞΕΙΣ ΚΛΕΙΔΙΑ: Τοποθετήσεις οργανισμών, ηλεκτρονικό τσιγάρο, άτμισμα, καρδιαγγειακή νόσος

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