

Vaping and cardiac disease

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ABSTRACT

Tobacco cigarette smoking is the most prevalent reversible risk factor for cardiovascular disease in the USA. Electronic cigarettes, invented as an alternative nicotine source for smokers unable or unwilling to stop smoking, have gained skyrocketing popularity, but their cardiovascular risk remains uncertain. Although data recently analysed in a Cochran report do support their superior effectiveness to other forms of nicotine replacement therapies for smoking cessation, electronic cigarettes are also frequently used by non-smokers—especially high school students. There are no long-term outcome studies on the cardiovascular risk of vaping electronic cigarettes, but the effects of electronic cigarettes on known risk factors for cardiovascular disease, including neurohumoral activation, oxidative stress and inflammation, endothelial function and thrombosis, have been studied. In this review, we summarise evidence in humans that supports the notion that while electronic cigarettes may be less harmful than traditional cigarettes, they are not harmless. Additionally, the increasing popularity of vaping marijuana with its unknown cardiovascular risks as well as the outbreak in 2019 of EVALI (electronic cigarette, or vaping, product use-associated lung injury) related to bootlegged vaping products raise further concerns. Before physicians can confidently advise their smoking patients about the role of electronic cigarettes as a means of smoking cessation to lower cardiovascular risk, improved regulation and quality control is necessary.

INTRODUCTION

Electronic cigarette (ECIG) use has increased dramatically in the USA since the products first entered the market in the USA in 2007. The prevalence of current ECIG vaping among US adults was recently estimated at 2.3% (5.66 million adults).¹ ECIGs are handheld devices composed of a battery, a heating element and a cartridge filled with e-liquid. When the user activates the ECIG, typically by puffing on the mouthpiece, the e-liquid is heated without combustion and released as an aerosol into the user's mouth to inhale. The e-liquid contains a mixture of solvents, typically vegetable glycerol and propylene glycol, flavourings, and nicotine, although nicotine is not obligatory. Over time, the design of the ECIG device has evolved to promote more efficient nicotine delivery (figure 1).² The most recent, and popular, iteration, the fourth-generation pod-like device (eg, Juul), uses nicotine salts and is able to deliver nicotine into the alveoli with pharmacokinetics mimicking tobacco cigarette (TCIG) smoking.³ ECIG use has been promoted as an effective TCIG smoking cessation aid as part of a harm reduction strategy. However, since their introduction, ECIGs have found an expansive user base among teenagers and young adults, raising public health concerns about the long-term health risks

associated with ECIG vaping in never-smokers and their potential to act as a gateway to TCIG smoking.

More than 1 in every 10 deaths from cardiovascular disease are attributed to TCIG smoking each year.⁴ Given this strong association between TCIG smoking and cardiovascular disease, concerns about the cardiovascular effects of ECIGs are warranted. The purpose of this article is to review the acute and chronic effects of ECIG vaping on cardiovascular risk and in comparison with TCIG smoking.

WHO IS USING ECIGS?

Of the 5.66 million American adults who use ECIGs, the majority are current (39.1%, 95% CI 36.8% to 41.4%) or former (37.9%, 95% CI 35.6% to 40.1%) TCIG smokers.¹ Among dual users of TCIGs and ECIGs, the majority (69.3%, 95% CI 65.7% to 72.7%) reported using ECIGs to try to quit smoking. Importantly, of former smokers who currently use ECIGs, 80.7% (95% CI 77.4% to 83.5%) reported using ECIGs to quit smoking. Of concern, however, is that while most adults report using ECIGs for smoking cessation, almost a quarter of current ECIG vapers (23.1%, 95% CI 20.8% to 25.4%) were never-smokers.¹

In fact, use of ECIGs among youth in the USA has increased significantly over the last decade, and in 2019 ECIG use among teens was declared an epidemic. In 2019, almost 30% of high school seniors reported using an ECIG in the previous 30 days (figure 2).⁵ In the first 3 months of 2020, this percentage of recent ECIG use markedly diminished among teenagers.⁶ Although the proportion of teens who reported using ECIGs in the last 30 days had decreased, the proportion reporting daily ECIG use had increased, indicative of nicotine addiction.⁶ The concern that ECIG vaping may be a gateway to TCIG smoking among teens, however, is not supported by data. In fact, ECIG use seems to be a diversion from TCIG smoking, since smoking rates among teens have never been lower (figure 2).^{5,7} Nonetheless, the cardiovascular effects of lifelong ECIG use in a previous never-smoker are unknown and remain a major public health concern.

WHAT IS THE EVIDENCE THAT ECIGS HELP SMOKERS QUIT?

TCIGs are lethal, killing half the people who use them. It has been estimated that by switching from TCIGs to ECIGs, 1.6–6.6 million American lives could be saved over the next 10 years.⁸ Although majority of adult ECIG users report using ECIGs to quit smoking, until recently it has been uncertain that this strategy is effective. Several studies have examined the efficacy of ECIGs as a TCIG cessation aid, and these have recently been summarised in a Cochran report.⁹ After analysing 50 studies (26 randomised controlled trials), including 12 430



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Generation	Products	Features
First (early 2000's)	"Cig-a-like"	<ul style="list-style-type: none"> Disposable or rechargeable Low price Power setting not adjustable Early iterations had inefficient nicotine delivery
Second (mid 2000's)	"Vape Pen"	<ul style="list-style-type: none"> Rechargeable and refillable Low-moderate price Power setting with limited customizability (voltage)
Third (early 2010's)	"Mods"	<ul style="list-style-type: none"> Rechargeable and refillable Moderate-high price Highly customizable (voltage/wattage)
Fourth (mid 2010's)	"Pod-Based"	<ul style="list-style-type: none"> Rechargeable (USB charging deck) Prefilled or refillable cartridges Not customizable Most efficient nicotine delivery

Figure 1 The evolution of electronic cigarette (ECIG) devices. Since their invention in China in 2003, ECIGs have changed in both appearance and features. The first-generation ECIG, called the 'cigalike', physically resembled a tobacco cigarette. Initially equipped with a small, disposable battery, cigalikes were inefficient nicotine delivery devices. Over successive third-generation and fourth-generation devices, the 'vape-pens' and 'mods', the ECIG battery has become more powerful, is rechargeable, and is adjustable and modifiable. Additionally, the cartridge that holds the e-liquid has greater capacity. This combination of features has the capability of generating large plumes of aerosol, resulting in greater nicotine delivery, accompanied by a greater level of non-nicotine constituents and toxicants. The latest, fourth-generation device, the 'pod-like' device, takes advantage of novel nicotine chemistry to deliver addictive nicotine at lower temperatures, and perhaps with fewer non-nicotine toxicants, into the alveoli, replicating the pharmacokinetics of tobacco cigarettes.

participants, the authors concluded with moderate certainty that nicotine ECIGs were more effective (risk ratio (RR) 1.69, 95% CI 1.25 to 2.27) than certified nicotine replacement therapies (NRTs) for smoking cessation and more effective than behavioural support (RR 2.50, 95% CI 1.24 to 5.04). Adverse events associated with ECIG use were uncommon and mild (eg, throat/mouth irritation). Of note, a large number of former smokers who use ECIGs to stop TCIG smoking continue to use

Trends in U.S. youth e-cigarette use (2011-2019) national youth tobacco survey – high school students

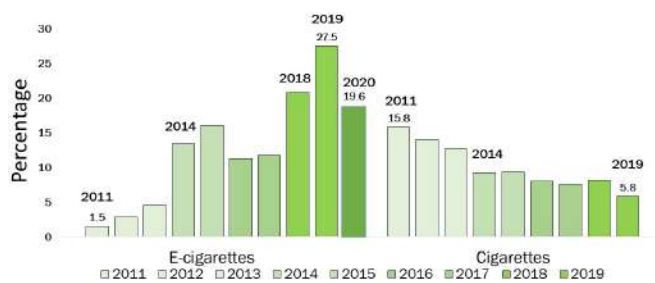


Figure 2 Trends in electronic cigarette (ECIG) use among US youth. Data from 2011 through 16 March 2020 from the National Youth Tobacco Survey, a cross-sectional school-based, self-administered survey of middle and high school students across the USA, have been analysed.⁵ These data demonstrate that a large proportion of high school students report using ECIGs, as defined by use in the last 30 days. Usage seems to have peaked in 2019, with the caveat that less than 3 months of data were available for 2020. However, despite this epidemic in ECIG use, tobacco cigarette use has declined during this period, supporting the notion that ECIGs are a diversion from, rather than a gateway to, tobacco cigarette smoking.

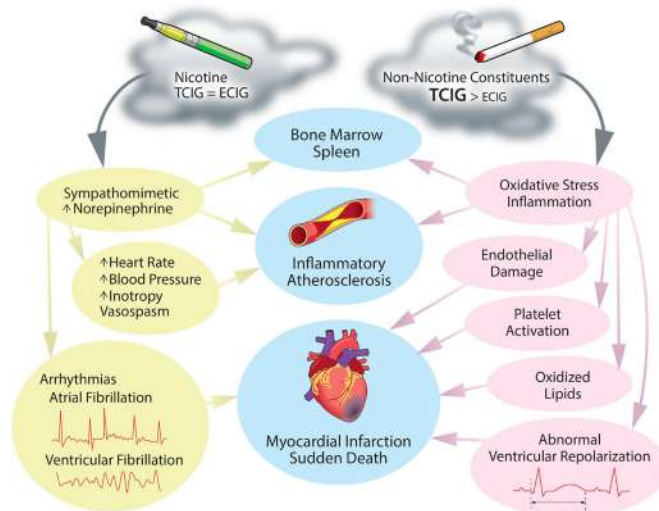


Figure 3 Cardiovascular effects of tobacco cigarettes (TCIGs) and electronic cigarettes (ECIGs). In considering the cardiovascular risks of tobacco cigarettes and electronic cigarettes, it is best to divide the risks into those largely attributable to nicotine and those largely attributable to non-nicotine constituents in their respective emissions. Cardiovascular effects associated with nicotine are attributable to nicotine's sympathomimetic effects, including increases in heart rate, blood pressure and inotropy, potentially accompanied by vasospasm, leading to ischaemia. Additionally, increased sympathetic tone is linked to heightened risk of arrhythmias, both atrial and ventricular. Increased sympathetic tone may be the instigator of activation of the splenic axis, increasing inflammation, and once again increasing the risk of inflammatory atherosclerosis and ischaemia.²⁵ Potential cardiovascular effects of non-nicotine constituents include increased oxidative stress and inflammation, leading to endothelial damage, platelet activation and lipid oxidation, increasing the risk of inflammatory atherosclerosis and ischaemia. Further, non-nicotine constituents may have adverse effects on ventricular repolarisation, once again increasing the risk of arrhythmias. See text for discussion.

ECIGs at 1 year.¹⁰ The cardiovascular effects of lifelong ECIG use in former smokers are unknown and remain a major public health concern.

CARDIOVASCULAR EFFECTS OF ECIG USE

Both nicotine and the non-nicotine constituents in TCIG smoke have been implicated in the mechanisms of the development of atherosclerosis and adverse cardiovascular effects from TCIG smoking.^{11–13} Levels of non-nicotine toxicants detectable in emissions from ECIGs, if present at all, are orders of magnitude lower than in smoke from TCIGs.¹⁴ Similarly, toxicant levels present in the urine or saliva from ECIG vapors are also orders of magnitude lower than in TCIG smokers.¹⁵ However, steady state plasma nicotine levels are similar in smokers and vapers, and the pharmacokinetics of nicotine delivery by the fourth-generation pod-like devices, which use highly concentrated nicotine salts, mimic the addictive alveolar delivery of TCIGs. Thus, it is best to consider the cardiovascular effects of ECIGs in terms of risks associated with nicotine and non-nicotine constituents (figure 3).

Nicotine is sympathomimetic, which may lead to vasospasm and acute, although modest, increases in heart rate (HR) and blood pressure (BP), potentially increasing the risk of ischaemia.¹³ Increases in sympathetic tone may also precipitate atrial and ventricular arrhythmias. Non-nicotine constituents

generated from combustion of organic materials in TCIG smoke and heating of e-liquid likely lead to increased oxidative stress and inflammation, which are important mediators of smoking-related cardiovascular disease.¹⁶ Endothelial damage, platelet activation, oxidised lipids and abnormal ventricular repolarisation may follow, leading to increased risk of myocardial ischaemia and sudden cardiac death. ECIG emissions, which contain nicotine, but lower toxicant levels and no combustion products, may increase sympathetic nerve activity similarly to TCIGs but may only modestly activate other mechanisms which underlie cardiovascular risk (figure 3). The relative effects of TCIG smoking and ECIG vaping on these risk factors will be discussed in the following sections.

Increased sympathetic nerve activity

Cardiac sympathetic nerve activity, as estimated by changes in heart rate variability (HRV), is increased in otherwise healthy chronic ECIG vapers compared with non-smokers.¹⁷ This abnormal pattern of HRV is the same pattern that is associated with increased cardiac risk in populations with and without known cardiac disease.¹⁷ Further, measures of HRV are not different in otherwise healthy ECIG vapers and TCIG smokers.¹⁸ Acutely, increases in sympathetic nerve activity as estimated by abnormal HRV, and haemodynamics, including HR and BP, are mediated by nicotine, not non-nicotine constituents, in ECIG emissions.¹⁹ Acute TCIG smoking leads to significantly greater increases in haemodynamics, specifically HR and BP, compared with ECIG vaping.²⁰ However, it is important to acknowledge two important limitations in the studies that support this observation.²⁰ First, changes in plasma nicotine levels were not reported in most studies comparing the acute effects of ECIGs and TCIGs, so it is unknown whether the exposures were equivalent. Second, most studies to date have not included the fourth-generation pod-like devices, which deliver nicotine efficiently, replicating the pharmacokinetics of TCIG smoking. Thus, further studies are needed.

In summary, acute and chronic ECIG vaping is associated with increased sympathetic activity and modest increases in HR and BP.^{17 19 20} These changes are attributable to nicotine, not non-nicotine constituents, in ECIG emissions.¹⁹ Although acute haemodynamic changes with ECIG vaping are modest, nonetheless they could contribute to the supply–demand mismatch, especially in the setting of vasospasm. Clinical sequelae of increased sympathetic nerve activity could include increased risk of arrhythmias, myocardial ischaemia and sudden arrhythmic death.¹³ Increased sympathetic nerve activity also results in increased epinephrine secretion, which may further contribute to an increased risk of arrhythmias and sudden cardiac death. Long-term outcome studies are necessary to determine if these changes in ECIG vapers are clinically relevant.

Oxidative stress and inflammation

Increased oxidative stress and inflammation are fundamental mechanisms that underlie the development of atherosclerosis and cardiovascular risk associated with smoking, but reports of oxidative stress and inflammation in ECIG vapers are limited.¹⁶ Carnevale *et al*²¹ were the first to report an acute increase in plasma markers of oxidative stress (increased soluble NADPH oxidase 2 (NOX2)-derived peptide and 8-iso-prostaglandin F_{2α} levels) in TCIG smokers after acutely using an ECIG, but these levels were significantly less compared with the acute effects of smoking a TCIG. Biondi-Zoccai *et al*²² reported similar findings; specifically, they also found an increase in soluble

NOX2-derived peptide levels as well as a significant increase in H₂O₂, a non-radical oxygen species, after use of both ECIGs and TCIGs, with TCIGs resulting in the largest increase. It should be noted that neither study reported changes in nicotine levels following each exposure, so it is unknown if the ECIG and TCIG exposures were comparable. We reported increased susceptibility to oxidative stress, as measured by low-density lipoprotein oxidisability, in young, otherwise healthy, chronic ECIG vapers, who had not vaped for 12 hours, compared with non-user controls.¹⁷ In a follow-up study, we compared cellular, rather than plasma, markers of oxidative stress in immune cells from otherwise healthy volunteers who were either chronic TCIG smokers or ECIG vapers compared with non-smokers.²³ Total cellular and cytoplasmic reactive oxygen species in immune cells were elevated to the greatest level in TCIG smokers and intermediate levels in ECIG vapers compared with non-smokers.²³ Importantly, smoking burdens were similar between vapers and smokers as estimated by plasma cotinine levels, a metabolite of nicotine. Notably, increases in cellular oxidative stress were most striking in proinflammatory monocytes, which are known to be the culprits in inflammatory atherosclerosis.²³

There are few other reports of inflammation in chronic ECIG vapers. Using ¹⁸F-fluorodeoxyglucose positron emission tomography/computer tomography imaging to detect increased metabolic activity and inflammation, Boas *et al*²⁴ found increased inflammation of the aorta in a small group of otherwise healthy TCIG smokers compared with non-smokers. Chronic ECIG vapers had intermediate levels of aortic inflammation. This vascular inflammation was accompanied by a similar increase in metabolic activity in the spleen, a source of circulating monocytes that invade the vascular wall and lead to inflammatory atherosclerosis.^{24 25} Nicotine is known to have anti-inflammatory effects via the cholinergic anti-inflammatory pathway,²⁶ but these anti-inflammatory effects are likely offset by proinflammatory, non-nicotine constituents present in ECIG emissions.

In summary, these findings are consistent with a continuum of oxidative stress and inflammation associated with tobacco product usage—greatest in TCIG smokers and intermediate in ECIG vapers, compared with non-smokers.

Endothelial dysfunction

Endothelial dysfunction, as measured by brachial artery flow mediated dilation (FMD), and arterial stiffness, as measured by pulse wave velocity (PWV) and augmentation index (AI), have all been recognised as predictors of atherosclerosis and markers of increased risk of cardiovascular disease.²⁷ Impaired FMD has been demonstrated in chronic TCIG smokers and in non-smokers exposed to secondhand smoke.²⁸ Until recently, the acute effects of ECIG vaping on vascular health had only been studied in chronic TCIG smokers, not in chronic ECIG vapers.¹¹ Further, the effects of chronic ECIG vaping on vascular health, especially compared with chronic TCIG smoking, had not been studied. Overall, these prior studies reported acute decreases in FMD, PWV and AI in TCIG smokers after using an ECIG, but these abnormalities were significantly greater following smoking a TCIG.¹¹

Recent studies have shown that switching from TCIG smoking to ECIG vaping is associated with improved endothelial function.²⁹ George *et al*²⁹ conducted a randomised controlled trial that showed a significant improvement in FMD within 1 month of switching from TCIG smoking to ECIG vaping, consistent with the notion that vaping is less harmful to the vascular endothelium. Interestingly, similar improvements were seen

when smokers switched to either nicotine-containing ECIGs or nicotine-free ECIGs, implicating non-nicotine constituents in TCIG smoke rather than nicotine. Similarly, Haptonstall *et al*³⁰ reported that baseline FMD was not different among otherwise healthy, young chronic TCIG smokers (n=40), chronic ECIG vapers (n=49) and non-smokers (n=47). However, acutely smoking one TCIG significantly decreased FMD compared with sham control. Surprisingly, however, a comparable ‘dose’ of acute ECIG vaping did not significantly affect FMD. Changes in nicotine levels were compared with each exposure and were similar, consistent with an equivalent exposure of each tobacco product type.³⁰ A subset of chronic ECIG vapers acutely used a fourth-generation pod-like ECIG device and findings were similar to exposures using earlier-generation devices.³⁰ Fetterman *et al*³¹ measured FMD, PWV and AI in ~400 volunteers in the Cardiovascular Injury to Tobacco Use study and found only AI, but not FMD or PWV, was abnormal in ECIG smokers compared with non-smokers.

Collectively, these findings suggest that the effects of ECIG vaping, although not harmless, may result in less harm to endothelial function compared with TCIG smoking.

Platelet aggregation

TCIG smoking results in increased platelet activation, which in turn predisposes to platelet aggregation and thrombus formation, which may result in myocardial ischaemia and infarction.³² Few studies have investigated the effect of ECIG vaping on platelet activation. Nocella *et al*³³ found that chronic TCIG smokers exhibit similar degrees of platelet aggregation, as evidenced by increases in soluble CD40 ligand and soluble P-selectin levels, with acute TCIG and ECIG smoking; however, non-smokers exhibit increased platelet aggregation when smoking TCIGs as compared with ECIGs. Ikonmidis *et al*³⁴ compared platelet function between chronic TCIG smokers and those who switched to ECIG vaping after 4 months, measuring *in vivo* platelet activation using the platelet function analyser PFA-100 and light transmission aggregometry. They found that switching to ECIG vaping had a neutral effect on platelet function. In summary, although the chronic effects of TCIG and ECIG use on platelet function remain unknown, there is limited evidence that ECIG use can adversely affect platelets and increase platelet aggregation.

Sudden arrhythmic death

Although TCIG smoking is associated with an increased risk of sudden death, the risk associated with ECIGs is unknown. As noted above, increased cardiac sympathetic nerve activity, as detected in chronic ECIG vapers, is associated with increased risk of adverse cardiac events, including ventricular arrhythmias and sudden death.¹³ Additionally, abnormal ventricular repolarisation in TCIG smokers has been reported, a finding that also increases the risk of ventricular arrhythmias.³⁵ Ventricular repolarisation is typically represented by the QT interval on the surface ECG, but this interval includes both ventricular depolarisation and repolarisation. The Tpeak-end (Tp-e) interval, measured from the peak of the T wave until the end of the T wave, has emerged as a more specific representation of abnormal ventricular repolarisation and has been associated with increased risk of sudden death in many populations.³⁶ The Tp-e interval is prolonged in TCIG smokers, but it remains unknown if ECIG vaping is also associated with prolonged Tp-e interval. In a study of 145 healthy young people, including 37 chronic TCIG smokers, 43 chronic ECIG vapers and 65 non-smokers, Ip *et al*³⁷

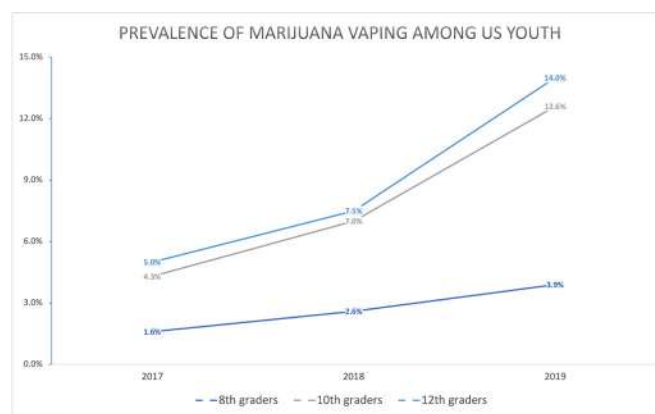


Figure 4 Marijuana vaping trends among US teens. Data from the Monitoring the Future study, a cross-sectional, school-based, self-administered survey of middle and high school students across the USA that has been collecting data for 49 years, have been analysed.³⁹ The increase in vaping in 2018–2019 among high school students was the second biggest increase in recreational drug use ever recorded by the study (the first greatest was the year before, the 2017–2018 increase in vaping nicotine products). The prevalence of vaping marijuana has surpassed tobacco cigarette smoking among high school students.

reported that Tp-e alone or corrected for QT interval was not different among the three groups. However, smoking just one TCIG significantly prolonged all three (Tp-e, Tp-e/QT and Tp-e/QTc) ECG indices of abnormal ventricular repolarisation. After a similar exposure (as estimated by changes in plasma nicotine) to an ECIG with nicotine, only one of the ECG indices was significantly prolonged. Importantly, the abnormal ventricular repolarisation was significantly greater after TCIG smoking compared with ECIG vaping, despite similar increases in plasma nicotine levels with each tobacco product exposure.³⁷ These findings are consistent with the notion that non-nicotine constituents in TCIG smoke are major contributors to acute changes in ventricular repolarisation with smoking.

In summary, changes in ventricular repolarisation associated with increased risk of sudden death are significantly greater following TCIG smoking compared with ECIG vaping. Although the repolarisation changes were less following ECIG vaping, they were still present and significant, and suggest that although ECIG vaping may be less harmful than TCIG smoking it is not harmless.³⁷

CANNABIS AND VAPING

Any discussion of the adverse cardiovascular effects of vaping would be remiss in omitting the cardiovascular effects of vaping cannabinoids, since cannabis is the most commonly used illicit substance in the USA and is frequently vaped in ECIG devices.³⁸ The number of youth vaping cannabis increased to record levels in 2018–2019 as the second greatest single-year increase in any recreational drug in the 49-year history this has been tracked by the National Institute on Drug Abuse Monitoring the Future Survey (figure 4).³⁹ A large-scale study showed that almost one-third of high school students who use cannabis have tried it in its vapourised form.⁴⁰ Although limited data exist regarding the cardiovascular effects of vaping compared with smoking cannabis, Spindle *et al*⁴¹ reported that inhaling an equivalent dose of vapourised cannabis led to greater plasma levels of THC, cognitive and psychomotor effects, and significantly greater increases in HR, compared with smoked cannabis. Whether

these greater physiological effects of vapourised cannabis lead to greater risk of clinical cardiovascular events remains unknown.

Most of what is known about cardiovascular risks associated with cannabis use stem from events in patients who have smoked it. An increasing number of cardiovascular emergencies temporally related to smoking cannabis have been reported, but the mechanisms by which cannabis adversely affects the cardiovascular system remain uncertain.⁴² The risk of myocardial infarction within 60 min of smoking marijuana is reportedly 4.8 times that at baseline, and cannabis use compared with non-use has been associated with a threefold increase in mortality following survival of an initial myocardial infarction.^{43–44} Potential mechanisms include acute increases in sympathetic nerve activity, HR and BP, thereby contributing to the supply–demand mismatch.⁴⁵ Further, cannabis has been associated with endothelial dysfunction and vasoconstriction of coronary and cerebral arteries, increasing the risk of vasospasm and atherosclerosis.⁴⁵ Additionally, cannabis has prothrombotic effects which have been noted in multiple cases of young adults suffering acute myocardial infarctions due to coronary thrombosis without underlying atherosclerosis.^{45–46} Research elucidating the effects of vapourised cannabis on cardiovascular health is imperative, since vapourised cannabis use is increasing, and a trend to legalise marijuana for medical and recreational use is spreading across the USA.

ELECTRONIC CIGARETTE, OR VAPING, PRODUCT USE-ASSOCIATED LUNG INJURY

In 2019, thousands of cases of acute lung injury primarily affecting adolescents and young adults who endorsed recent ECIG use were reported across the USA.⁴⁷ The disease became known as EVALI (electronic cigarette, or vaping, product use-associated lung injury) and was eventually linked to the presence of vitamin E acetate, used as thickener in bootlegged or black market *Tetrahydrocannabinol* (THC)-containing ECIG products.⁴⁸ Further investigation revealed that majority of patients reported acquiring the associated THC-containing products from illicit or informal sources.^{47–48} Fortunately, the prevalence of cases has decreased since the recognition of these risk factors. However, the epidemic of EVALI demonstrates the potential for harm from ECIG use and highlights the need for appropriate regulation of the products. Regulation of ECIG products will become increasingly relevant to healthcare providers who are asked by their patients whether the devices are a safe alternative to currently approved smoking cessation aids. Given the cumulative evidence showing that ECIGs have a lower cardiovascular risk profile than TCIGs, regulation and quality control are crucial for minimising harm to patients.

PYRAMID OF CARDIOVASCULAR RISK

In considering the effects of vaping on cardiovascular risk, one can place them within the context of other nicotine delivery systems, including NRTs (eg, gum or patches), smokeless tobacco (eg, snus or chewing tobacco) and combusted tobacco products. NRTs have been extensively studied and research has been summarised in meta-analyses. NRTs are associated with a slightly but significantly increased risk of minor cardiovascular effects, including palpitations and tachycardia.⁴⁹ Serious adverse cardiac events are not significantly increased.⁴⁹ Thus, NRTs may be placed at the tip of the pyramid, as conferring the lowest risk of cardiovascular events (figure 5). Adverse cardiovascular events, including serious cardiac events, associated with smokeless tobacco use are slightly but significantly increased.⁵⁰ Thus, smokeless tobacco may be best positioned in the middle of the



Figure 5 The pyramid of cardiovascular risk. Nicotine delivery products, including nicotine replacement therapies (NRTs), smokeless tobacco, electronic cigarettes and combustible tobacco cigarette products, can be arranged relative to one another in a pyramid, according to current knowledge of their relative cardiovascular risks. At the tip of the pyramid, with the least risk, reside NRTs.⁴⁹ At the broad base lie combustible tobacco products, which without a doubt carry the greatest cardiovascular risk. Based on available outcome data, smokeless tobacco carries intermediate risk⁵⁰; based on emerging data from their effects on biological risk factors, but no outcome studies, electronic cigarettes reside next to smokeless tobacco, also carrying an intermediate risk.

pyramid of cardiovascular risk. Without controversy, TCIGs and other combusted tobacco products are associated with the greatest cardiovascular risk and are placed at the large base of the pyramid of cardiovascular risk. Since outcome data are not available to help position ECIGs in this pyramid of risk, we must rely on the effects of ECIGs on known biomarkers and risk factors for cardiovascular disease. The effects of ECIG on markers of oxidative stress, inflammation, endothelial health, thrombogenesis and arrhythmia risk support the placement of ECIGs in the middle of the pyramid, likely less harmful than TCIGs, but with greater risk than NRTs. The uncertainty of this placement, however, is heightened by concern over a lack of regulation and product quality oversight, with the spectre of another EVALI-like outbreak lurking.

SUMMARY

ECIG use has grown significantly in the USA over the last decade, primarily among TCIG smokers who report using ECIGs as a smoking cessation aid, but also alarmingly among adolescents and young adults. Although long-term studies are needed, the evidence available to date suggests that ECIG vaping confers lower cardiovascular risk than TCIG smoking. Furthermore, there is mounting evidence that nicotine-containing ECIGs are effective as a TCIG smoking cessation therapy. Despite the promising results presented, ECIGs continue to pose potential health risks due to the lack of regulation and quality control. Additionally, the increasing prevalence of ECIG vaping among youth is alarming and raises appropriate public health concerns about the consequences of their long-term usage and their potential to contribute to cardiovascular disease later in life.

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Patient consent for publication Not required.

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