An evidence summary for health regulators and practitioners

The health effects of vaping

INTRODUCTION

In recent years health practitioners, public health officials and the public have been provided with inconsistent and contradictory information about the health consequences of using e-cigarettes. This fact sheet is intended to present information on some of the key health concerns.

Many people have heard that vaping is “95% less harmful” than smoking. This is an estimate that has been promoted by Public Health England since 2015 and which is based on a report it commissioned from a panel of scientists. (1,2,3) The relative risk of “95% less harmful” emerged from the pooled opinions of the scientists involved in the review, and not by using convention scientific methods of comparing risk. As a result, many other researchers have expressed concerns about the appropriateness of the methods and the validity of the statement. (4,5) Even the panel which developed it acknowledged that “the lack of hard evidence for the harms of most products on most of the criteria” limited their conclusions. (3) Public Health England continues to encourage smokers to consider using e-cigarettes as a quitting aid. (6)



Public Health England *(6)*

Other scientific panels have declined to suggest that e-cigarettes are considerably safer, let alone 95% safer. One of these was a review commissioned by the U.S. Food and Drug Administration and conducted by the United States National Academies of Science, Engineering and Medicine (NASEM). Like the Public Health England report, this was authored by a panel of independent scientists who reviewed the available scientific literature, including the evidence considered by the English panel. These American researchers, however, came to a very different series of conclusions in their 2018 report. (7) Considered together, their 47 conclusions (including 26 on health effects) would lead one to take a precautionary approach towards e-cigarette regulation. The U.S. Centers for Disease Control and Prevention and other federal agencies do not encourage the use of e-cigarettes.



U.S. Centers for Disease Control and Prevention. (67)

The evidence reviewed by both these panels is now at least 2 years old, and many subsequent studies have now been reported. With increasing evidence about their long- and short-term health effects, e-cigarettes remain a concern for public health.

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E-CIGARETTES AND HEART DISEASE AND STROKE

Although the 2018 review by the National Academies of Science, Engineering and Medicine found there was "no evidence" available to assess the impact of electronic cigarette smoking on increased cardiac risks, (7) subsequent studies have provided evidence to support conclusions that these products increase the risks of heart disease and stroke.

Researchers in Ohio recently reviewed preclinical and clinical studies on e-cigarettes and considered what theses results could mean for long-term risks to cardiovascular health. In their Figure 1, they identified three separate routes by which e-cigarettes could increase the risk of cardiovascular disease: the impact of nicotine, the effect of particulate matter and metals, and the impact of flavours and solvents used in vaping liquids. (8) They concluded:

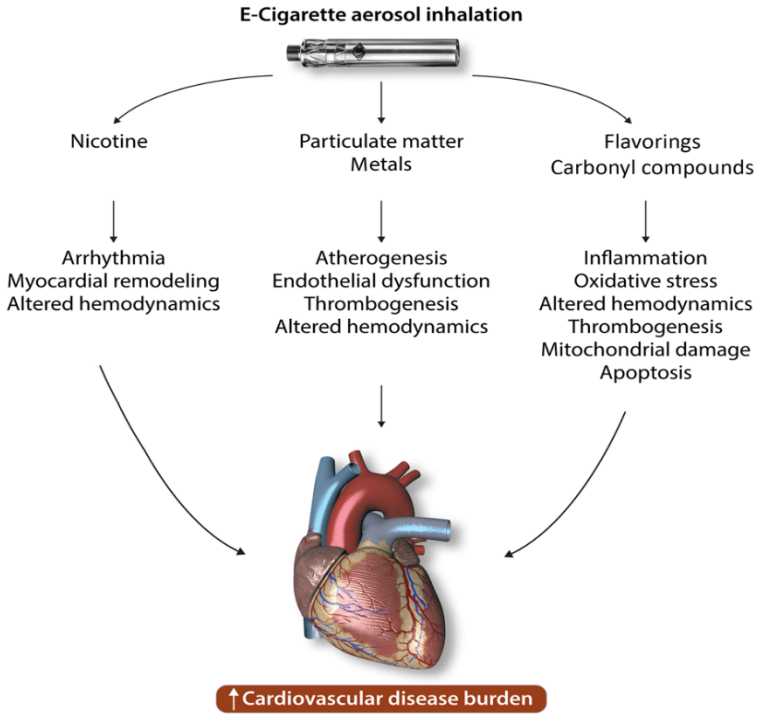


Figure 1 from Buchanan et al (8)

"The studies presented in this review have shown that e-cigarettes can induce negative cardiovascular effects through various mechanisms such as oxidative stress, inflammation, DNA damage, arterial stiffness, and altered haemodynamics and platelet activity. Individually and in combination with one another, these effects suggest pathways that chronic e-cigarette use could increase the development of CVD." (8)

The risks from ultrafine particles in e-cigarettes

E-cigarette vapour produces ultrafine particles, as small or smaller than those produced by conventional cigarettes as shown in Figure 2. (9) These ultrafine particles carry nicotine deep into the lungs, triggering inflammatory processes that lead to cardiovascular disease. E-cigarettes damage the vascular endothelium, thereby inhibiting the ability of arteries to dilate in response to increased blood flow. (10,11) E-cigarette aerosol harms important blood processes (including activation, aggregation and adhesion of platelets). (12,13) These and other adverse biological changes to the cardiovascular system are not diseases in and of themselves. They are biological changes that are mostly reversible – provided one quits vaping. However, many vapers are addicted to nicotine. Consequently, repeated vaping over years and decades increases the risk of heart disease and stroke from e-cigarettes. (14,15,16,17,18,19)

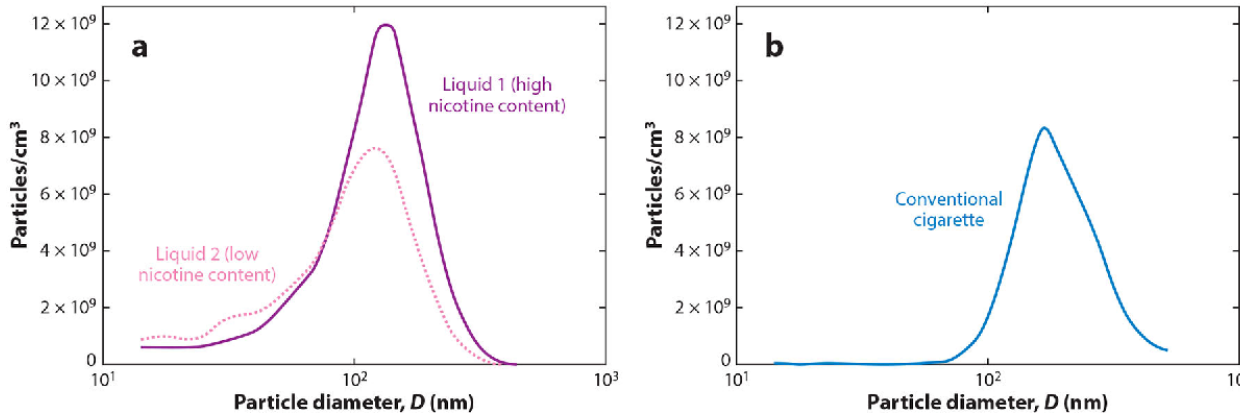


Figure 2: E-cigarettes produce smaller ultrafine particles than cigarettes do.

Particle number distribution from (a) mainstream aerosol IN e-liquid and from (b) conventional cigarette as a function of particle size (diameter, D) (9)

The higher risks of dual use of electronic and combustible cigarettes

Dual use of both e-cigarettes and conventional cigarettes is the most common form of e-cigarette consumption. Dual use increases the risk of heart disease compared to exclusive use of one product or the other. (14,16,20) One recent cross-sectional analysis examined the relationship between e-cigarette use, cigarette use and the risk of heart attack in the United States. (16) Risk, as measured by the adjusted odd ratio, was similar, whether one used e-cigarettes or e-cigarettes. Risk was considerably elevated for dual users, as shown in Table 1.

Table 1: Adjusted odds ratio for myocardial infarction (16)

E-cigarette use		Cigarette use		Dual use, e-cigarettes & cigarettes	
Never	Reference	Never	Reference	Never	Reference
Former	1.25	Former	1.48	All dual use	6.64
Some day	1.99	Some day	2.38		
Every day	2.25	Every day	2.95		

E-CIGARETTES AND LUNG DISEASES

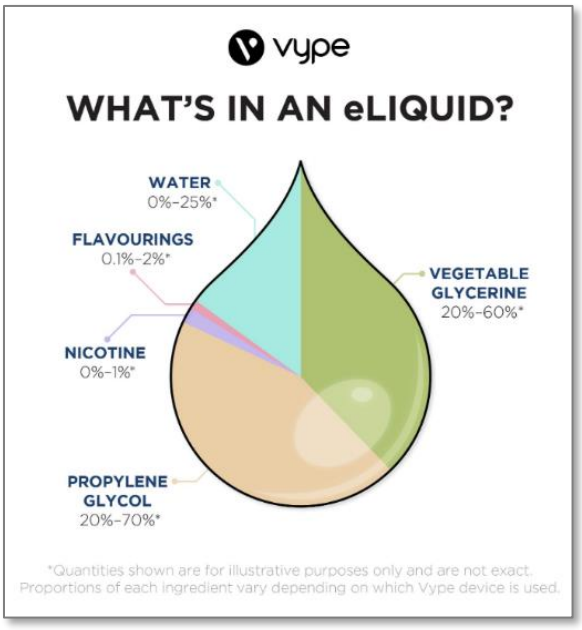
Acute lung disease

In August 2019, cases of acute lung disease linked to vaping began to be reported in the United States. The number of documented cases now number in the thousands and dozens of deaths have been reported, (21) as have a few cases in Canada. (22) The only common factor in all cases is vaping, whether nicotine, cannabis or both.

Some mechanisms have been suggested by which e-cigarettes could be implicated in acute and chronic respiratory disease.

- **Mouse studies link e-cigarettes with fat deposits in the lung.** A recent study of the effect of unflavoured e-cigarette vapour, with or without nicotine, on mouse lungs showed that fat globules built up in the mouse lungs. (23) Fat deposits in human lungs are also characteristic of the recent outbreak of acute lung disease in human e-cigarette users.

- **Inhaling propylene glycol and vegetable glycerin may harm the lungs.** 50% to 90% of e-liquid is made up of propylene glycol and vegetable glycerin. These substances have a long history of safe use in industrial applications, food and cosmetics. However, it has also been long known that they were never meant to be inhaled and cause respiratory irritation when inhaled accidentally. Propylene glycol is present in cigarette smoke and about 90% of it is transformed when burned into a variety of chemicals, including carcinogens. Less of it is transformed when it is heated, aerosolized and repeatedly inhaled in e-cigarettes. A recent report concluded that "heating propylene glycol and vegetable glycerin in e-cigarettes produces lung disease hazards not previously observed in cigarette smokers." (24)



- **E-cigarettes could trigger biological changes to the respiratory system that lead to chronic lung disease.** E-cigarette vapour damages the epithelial cells that line airways, thereby interfering with their normal healthy functioning. (25,26,27)

Other respiratory disorders

E-cigarette vapour also causes several other physiological changes that compromise the normal, healthy functioning of airways and lungs. (12,25,28) Consistent with these observations of biological changes as a result of exposure to e-cigarette aerosol, e-cigarette use also increases the risk of chronic obstructive pulmonary disease and other respiratory diseases. (29,30,31) Like the risk of heart disease, dual use of e-cigarettes and combustible cigarettes further increases the risk of lung disease compared to exclusive use of one product or the other. One longitudinal study found an odds ratio of 1.24, 2.68 and 3.3, for respiratory

diseases for current e-cigarette users, current cigarette smokers and dual users, respectively, compared to never users of e-cigarettes or tobacco. (31) Decades of observation of the dangers of cigarette use has shown that cardiovascular diseases, related metabolic diseases and lung diseases account for two-thirds of deaths caused by smoking. (32) The weight of available evidence indicates that, compared to combustible cigarette use, using e-cigarettes does not reduce the risk of cardiovascular diseases or lung diseases. Most e-cigarette users are dual users and for these people use of e-cigarettes increases the risk of cardiovascular and lung diseases.

A comprehensive review of the respiratory effects of e-cigarettes

A comprehensive review of the respiratory effects of e-cigarettes was recently published. (33) Among the over 100 studies reviewed were some which showed measurable adverse biologic effects on organ and cellular health in humans, in animals, and in vitro. The authors concluded that current knowledge of the population health effects of e-cigarettes is insufficient to determine whether the respiratory health effects of e-cigarette are less than those of combustible tobacco products.

CANCER

Many people believe that the fact that e-cigarettes have fewer carcinogens than cigarettes makes them safer. While fewer cancers may result from vaping than from smoking cigarettes, the risk of cancer is not necessarily reduced in lockstep with the reduction in numbers and amounts of carcinogens. There is no safe level of exposure to carcinogens. (34)

Nor does reducing carcinogens necessarily reduce risk from other diseases, like heart disease, stroke and lung diseases – the diseases that account for two-thirds of smoking-related deaths. (32)

There is evidence associating e-cigarettes with cancer risks. This includes research findings that:

- E-cigarette aerosol contains carcinogens that damage DNA. (35)
- E-cigarettes marketed in Canada produce carcinogenic emissions, including benzene. (36)
- E-cigarettes deregulate genes associated with cancer. (37)
- E-cigarettes deliver large amounts of nicotine. While not a carcinogen itself, nicotine speeds growth of cancerous tumours. (38)
- E-cigarette vapour induces cancer in mice. (39)

While there are as yet no studies demonstrating increased risk of cancer in e-cigarette users, the biological evidence suggests very strongly that such

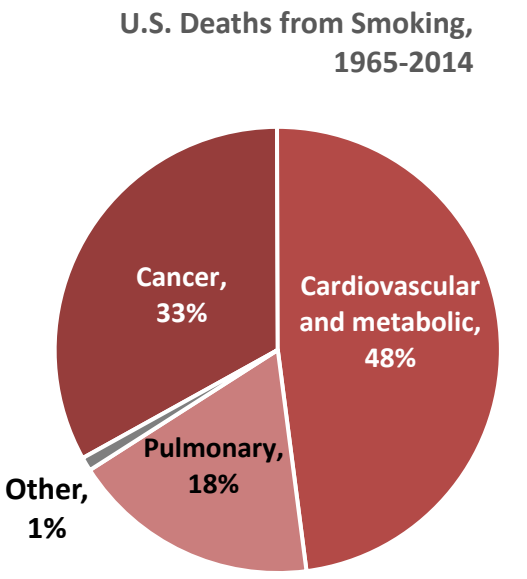


Figure 3: U.S. Surgeon General, 2014 (32)
Between 1965 and 2015, active and passive smoking killed 21 million people in the United States. Although most discussion of smoking and disease focuses on cancer, cardiovascular disease and metabolic and noncancer pulmonary disease kill most smokers.

evidence will appear when more people engage in prolonged use of e-cigarettes over many years. Dual users can also be expected to be at greater risk.

ADVERSE PREGNANCY OUTCOMES

Major health authorities and scientists recommend that pregnant women be advised to not use e-cigarettes. The US Office on Smoking and Health accepts that "prenatal nicotine exposure contributes substantially to adverse health outcomes in infants," and cautions that "tolerating acceptance of electronic cigarette use among pregnant smokers as part of a broader public health strategy to reduce smoking puts this population at great risk." (40) In 2016, the U.S. Surgeon General concluded that "nicotine can cross the placenta and has known effects on fetal and postnatal development. Therefore, nicotine delivered by e-cigarettes during pregnancy can result in multiple adverse consequences, including sudden infant death syndrome." (41) Subsequently, other researchers have concluded that pregnant women should be cautioned against using e-cigarettes. (42,43,44,45,46,47,48)

Vaping products are generally recommended against as cessation methods during pregnancy. Earlier this year, the American College of Protective Medicine issued a practice statement in which it advised that "Clinicians should screen pregnant women for the use of ENDS as part of tobacco screening. Those who smoke or vape should be advised to quit all nicotine products and provided with evidence-based tobacco cessation interventions including behavioral interventions and financial incentives," and "Clinicians should advise pregnant women who smoke cigarettes to use evidence-based treatments (e.g., behavioral counseling and financial incentives) rather than recommending ENDS." (49)

In its 2018 report, the National Academy of Science in Medicine concluded that there was insufficient evidence to conclude whether or not e-cigarette use affects fetal development, but did not conclude that there was sufficient evidence that nicotine or vaping did not adversely affect pregnancy outcomes. (7)

HEALTH RISKS FOR YOUNG PERSONS

In 2016, the U.S. Surgeon General produced a report on e-cigarette use among youth and young adults, (41) and concluded that "Nicotine exposure during adolescence can cause addiction and can harm the developing adolescent brain."

The U.S. Centers for Disease Control and Prevention is blunt in its assessment of the risks of e-cigarettes to young people. (50)

- "The use of e-cigarettes is unsafe for kids, teens, and young adults."
- "Using nicotine in adolescence can harm the parts of the brain that control attention, learning, mood, and impulse control. "
- "Each time a new memory is created, or a new skill is learned, stronger connections – or synapses – are built between brain cells. Young people's brains build synapses faster than adult brains. Nicotine changes the way these synapses are formed."
- "Using nicotine in adolescence may also increase risk for future addiction to other drugs."
- "Young people who use e-cigarettes may be more likely to smoke cigarettes in the future."

Youth vaping leads to heavier cigarette smoking

The impact of e-cigarette use by children on their later use of combustible cigarettes has been studied in multiple ways. Among significant findings are:

- Youth who started on e-cigarettes were four times more likely to go on to become cigarette smokers. (51)
- "Use of e-cigarettes by US young adults, most of which is not intended to help reduce smoking, is related to more rather than less frequent and intensive cigarette smoking." (52)
- Youth who vape misperceive the powerfully addictive nature of nicotine and are unaware of the increased risk they face for a lifetime of nicotine addiction and cigarette use. (53,54,55)

RISKS TO SUCCESSFUL SMOKING CESSATION

Smoking cigarettes is a very hard addiction to overcome, and most quit attempts result in failure. A great many studies over many years have assessed the effectiveness of different medicines, behavioural supports or other interventions at helping smokers successfully quit. In its most recent *Report on the Global Tobacco Epidemic*, the World Health Organization called for greater efforts to support smokers quitting and identified several pharmacological and behavioural interventions proven to be effective. The WHO reviewed recent evidence of the impact of e-cigarettes to smoking cessation and concluded "there is insufficient independent evidence to support the use of these products as a population-level tobacco cessation intervention to help people quit conventional tobacco use." (56)

One of the studies reviewed by the WHO was a much-publicized randomized control trial (RCT) of e-cigarettes as a quitting device, which found that 18% of e-cigarette users has successfully quit smoking after one year compared with 9.9% of those which used conventional stop-smoking medications. (57) The WHO found "several limitations" with this study, and other researchers have similarly urged caution in interpreting its results, (58,59,60), including Canadian experts. (61) A 2018 Ontario government review concluded that "recent evidence from RCTs and observational studies do not provide support for e-cigarettes as an effective cessation aid." (62) A 2019 review of the evidence on e-cigarettes as effective smoking cessation aids by Ontario tobacco experts found the evidence to be "inconclusive." (63)

Outside of the clinical trial environment, the impact of e-cigarettes can be assessed in the real-world settings in which smokers live and are trying to quit. Studies of the effects of e-cigarette use on the quit attempts of smokers in real life are not encouraging. One Canadian study found that e-cigarette use was negatively associated with smoking cessation. Furthermore, e-cigarette use lessened the effectiveness of smoking cessation treatment using NRT. (64) A meta-analysis of 37 mostly real-world studies showed that, overall, users of e-cigarettes were less likely to quit smoking. (65)

A major concern with the use of e-cigarettes as cessation devices is that even those who successfully stop smoking cigarettes continue to vape. In the recent RCT of e-cigarettes cited above, 80% of former smokers were still using e-cigarettes with addictive levels of nicotine after one year. (57) Data from this same study shows that NRT was much more effective at ending any form of nicotine use - 7% of those using NRT to quit smoking succeeded in quitting all nicotine use after one year, while only 3.2% of those using e-cigarettes to quit smoking successfully abandoned all nicotine use after one year. (66)

For most people, use of vaping products decreases the likelihood of successful smoking cessation and carries substantial risk for prolonged addiction to nicotine.

WHAT STANDARD OF PROOF IS REQUIRED FOR PUBLIC HEALTH ACTION?

Most of the epidemiological studies of heart disease and lung disease reviewed here (14,15,16,17,29,30) are cross-sectional in nature. As such, they offer contributory evidence, but not proof, of causal relationships. However, they are all consistent with the biological evidence that e-cigarettes are associated with adverse changes to the cardiovascular and respiratory systems. Based on biological evidence and epidemiological evidence from cross-sectional studies and one longitudinal study, (31) e-cigarettes are properly described as risk factors for cardiovascular disease and chronic lung disease. While research should continue to achieve better understanding of the relationship of e-cigarettes to heart disease and lung disease, enough is known to take public health action now to better limit the access of non-smokers to e-cigarettes. Waiting for more proof from longitudinal studies on humans before taking public health action would be irresponsible. Longitudinal studies of e-cigarette users, while scientifically elegant, do require a number of people to become sick and die in order to create data points.

SUMMARY OF HEALTH EFFECTS OF VAPING

- Vaping products are associated with acute lung disease. They have resulted in cases numbering in the thousands and dozens of deaths in the United States. There are also a few cases in Canada. The causal pathway or pathways from vaping to acute lung disease is not yet known.
- Vaping products are addictive. This is particularly problematic for non-smokers and never smokers who take up vaping.
- Vaping products increase the risk of cardiovascular diseases.
- Vaping products increase the risk of lung diseases.
- Vaping products adversely affect memory and concentration
- Vaping product adversely affect adolescent brain development, attention, mood, learning and impulse control.
- Vaping products adversely affect pregnancy outcomes.
- Adolescents who initiate nicotine addiction on vaping devices are more likely than others to become cigarette smokers.
- Dual use of vaping products and combustible cigarettes increases the risk of cardiovascular and lung disease compared to exclusive use of either product.
- Vaping products are not effective smoking cessation devices for most smokers. For most smokers, vaping lowers the likelihood of successful quitting.

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