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Health effects of electronic cigarettes: A review

E-cigarettes can be an effective smoking cessation tool for some smokers of combustible cigarettes but may be associated with potential cardiovascular and respiratory morbidity.

ABSTRACT: The use of electronic cigarettes (e-cigarettes) is rapidly growing. Recent surveys demonstrate particularly high uptake among young never-smokers and a possible association with increased uptake of combustible cigarette smoking. E-cigarettes may be associated with increased risk of cardiovascular disease, including myocardial infarction, stroke, coronary artery disease, hypertension, and elevated heart rate. However, there is a paucity of long-term clinical data to show the cardiovascular disease implications of these changes. With regard to pulmonary disease, e-cigarettes appear to be strongly implicated in the recent outbreak of acute e-cigarette, or vaping, product use–associated lung injury. The

relationship between e-cigarettes and chronic pulmonary disease is less clear, though possible associations with obstructive spirometric changes, chronic obstructive pulmonary disease, asthma, and chronic cough have been demonstrated. Nonetheless, the literature suggests that e-cigarettes are likely less harmful to the cardiovascular and respiratory systems than combustible cigarettes, and emerging evidence suggests that e-cigarettes can be an effective smoking cessation aid for smokers who are motivated to quit.

Electronic cigarettes (e-cigarettes), or vapes, are devices that use a battery-powered metal resistance coil to heat and aerosolize e-cigarette liquid (e-liquid), which is composed mainly of nicotine, propylene glycol, and vegetable glycerin, which is then inhaled by the user. E-cigarettes have been advertised as a safer way to consume nicotine compared with traditional combustible cigarettes.¹ However, emerging evidence is demonstrating detrimental health consequences related to e-cigarette use. This, coupled with the rapid uptake of e-cigarettes among youth,²⁻⁴ is cause for concern and warrants further research. Our aim is to review the epidemiology of e-cigarette use, discuss the evidence for e-cigarettes as a smoking cessation aid, and examine the known cardiovascular and respiratory effects of e-cigarette use.

There are four types of e-cigarettes: pods, tanks (also known as mods), vape pens, and cig-a-likes.⁵ The most recent trend in e-cigarette use involves the use of pods;⁶ they use disposable cartridges that contain e-liquids with

nicotine benzoate salt, which have a much higher nicotine concentration than e-liquids with freebase nicotine.³ Tanks, or mods, have an e-liquid storage tank attached to the main body, which contains a battery. Vape pens are similar but are slimmer and more easily portable. Cig-a-likes look similar to combustible cigarettes.⁷

In addition to nicotine, propylene glycol, and vegetable glycerin, e-liquids contain benzyl alcohol, terpenes, pyrazines, formaldehyde, acetaldehyde, acrolein, and toluene.⁸ The inhalational safety of these compounds is unknown.⁹ The presence of diacetyl in e-liquids is a concern because it is a known pulmonary toxin and has a propensity for causing bronchiolitis obliterans, also known as “popcorn lung.”⁹ Of particular concern is the addition of vitamin E acetate in tetrahydrocannabinol-containing e-liquids purchased on the black market because it appears to be associated with the recent outbreak of acute e-cigarette, or vaping, product use–associated lung injury (EVALI).¹⁰⁻¹² Further research is necessary to better characterize the inhalational health risks of these compounds.

Epidemiology

E-cigarette use is a common and rapidly spreading phenomenon, particularly among youth. The 2017 Canadian Tobacco, Alcohol and Drugs Survey (which included all ages) found that 15.4% of Canadians reported ever trying an e-cigarette, while 2.9% had used an e-cigarette in the past 30 days.² Ever use of e-cigarettes was significantly higher among adolescents (15 to 19 years old) and young adults (20 to 24

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years old) at 22.8% and 29.3%, respectively, compared with older individuals.² Furthermore, e-cigarette use is increasing at an alarming rate among young people. Hammond and colleagues found that in their longitudinal study sample, ever use of e-cigarettes among Canadian adolescents (16 to 19 years old) increased from 29.3% in 2017 to 37.0% in 2018.³ Similarly, the 2018–19 Canadian Student Tobacco, Alcohol and Drugs Survey (CSTADS), which included only students, found that past 30-day e-cigarette use among Canadian grade 7 to 12 students doubled (20% versus 10%) compared with the 2016–17 CSTADS results.⁴ Data from the US are similar: past 30-day e-cigarette use among US high school students increased from 11.7% in 2017 to 27.5% in 2019,^{13,14} which is the largest recorded increase in the use of any substance among US adolescents.

Multiple studies have demonstrated that e-cigarettes may be a risk factor leading people toward combustible cigarette use. A meta-analysis showed that among adolescent and young adult never-smokers, e-cigarette use was associated with increased odds of initiation of combustible cigarette smoking (odds ratio [OR] 3.50, 95% CI, 2.38–5.16, $P = 0.03$).¹⁵ Another study showed similar results (adjusted OR [aOR] 6.8, 95% CI, 1.65–28.25).¹⁶ This association was further supported by Azagba and colleagues,¹⁷ who used data from the 2016–17 CSTADS to demonstrate that Canadian students who used an e-cigarette for more than 21 of the past 30 days had increased odds of both trying combustible cigarettes (aOR 4.83, 95% CI, 3.33–7.01) and smoking regularly (aOR 3.39, 95% CI, 2.16–5.34). These data collectively suggest that e-cigarette use may be associated with higher rates of both occasional and regular use of combustible cigarettes. This is of special concern because 42% of Canadian student e-cigarette users have never smoked a combustible cigarette.⁴

However, there are two important counterarguments to the proposition that e-cigarette use is a gateway to combustible cigarette use. First, there is a common liability of use between combustible and e-cigarettes, meaning that there are common factors that drive people to use both combustible and e-cigarettes, but the two are not necessarily causally related. Second,

if increased e-cigarette use were causally related to increased smoking initiation, one would expect to see this reflected in population-level studies, but this is not the case. Hammond and colleagues found increased rates of e-cigarette use among adolescents in Canada, the US, and the UK (from 2017 to 2018) but increased rates of combustible cigarette smoking only among

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Canadian adolescents, which, as per the authors' conclusions, suggests that e-cigarette use may not be causally related to increased smoking uptake.³ E-cigarettes may indeed be a gateway to combustible cigarette smoking, and this is a valid concern, but there is not yet enough evidence to state a conclusive causal association.

Smoking cessation and harm reduction

E-cigarettes are widely used as a smoking cessation tool: 32.4% of Canadian smokers used e-cigarettes for this purpose in 2017,² and the UK National Health Service officially recommends e-cigarettes as a smoking cessation aid.¹⁸ Though older studies^{19–21} have shown that e-cigarettes are not superior to traditional nicotine replacement therapy (NRT) for smoking cessation, more recent randomized controlled trials have shown e-cigarettes to be superior to NRT [Table 1]. A UK randomized controlled trial published in 2019 showed a 1-year smoking abstinence rate of 18.0% in its e-cigarette group compared with 9.9% in the NRT group (relative risk [RR] 1.83, 95% CI, 1.30–2.58, $P < 0.001$), with a number needed to treat of 12 (95% CI, 8–27).²² Similarly, another randomized

controlled trial published in 2020 showed the superiority of e-cigarettes plus nicotine transdermal patches compared with patches alone for smoking cessation (RR 2.92, 95% CI, 0.91–9.33, $P = 0.05$).²³ Though these more recent results are encouraging for smoking cessation interventions, one caveat is that e-cigarette users may remain nicotine dependent even after quitting combustible cigarettes. The previously mentioned UK randomized controlled trial showed that 80% of participants in the e-cigarette group continued to use e-cigarettes after 1 year of abstinence from smoking, while only 9% of participants in the NRT group continued to use NRT after 1 year.²²

For smokers of combustible cigarettes, another possible beneficial aspect is harm reduction via partial substitution of combustible cigarettes with e-cigarettes. This is conceptually plausible because e-cigarettes deliver nicotine via a similar smoking-like behavior but with fewer apparent health risks compared with combustible cigarettes. Moreover, e-cigarettes offer the psychological and sociocultural aspects of cigarette smoking that traditional NRT does not, which places e-cigarettes in a unique position as a more desirable combustible cigarette substitute.²⁴ However, the limited data available thus far suggest that e-cigarettes have either no effect or a net detrimental effect on harm reduction at the population level. In smokers who are not intending to quit, ad libitum e-cigarette use while continuing ad libitum combustible cigarette use is not associated with reduced combustible cigarette use.^{25,26} Another study found that e-cigarette use was associated with a net effect of increased combustible cigarette use; only 13.2% of ever e-cigarette users were able to successfully quit combustible cigarette smoking, while 22.2% of e-cigarette users started or restarted smoking combustible cigarettes.²⁷ Nonetheless, e-cigarettes may provide a viable harm reduction strategy at the individual level for smokers who are able to successfully transition partially or exclusively to e-cigarettes.²⁴ However, this is likely most effective if reviewed on a case-by-case basis rather than as a general recommendation for smokers not intending to quit because the data do not currently support the use of e-cigarettes as a population-level harm reduction intervention.

Cardiovascular effects

Combustible cigarette smoking is one of the strongest preventable risk factors for cardiovascular disease.²⁸ Though the association between e-cigarette use and cardiovascular outcomes is largely unclear at this point, new data suggest that e-cigarettes are associated with cardiovascular morbidity [Table 2], though it is likely less than that of combustible cigarette smoking.²⁹ This section highlights the potential associations between e-cigarette use and cardiovascular disease, hypertension, endothelial health, and myocardial function.

Of greatest concern is the emerging potential relationship between e-cigarette use and cardiovascular disease. Observational studies have noted associations between e-cigarette use and higher incidence of coronary artery disease (OR 1.4, 95% CI, 1.35-1.46),³⁰ stroke (OR 1.71, 95% CI, 1.64-1.80),³⁰ and myocardial infarction

(OR 1.59–2.25, $P < 0.001$).^{30,31} One of these studies compared the myocardial infarction risk of combustible versus e-cigarette use and found that, as expected, combustible cigarette smoking was more strongly associated with myocardial infarction (OR 2.72 versus 1.79).³¹ Collectively, these observational associations warrant further study because a causal relationship between e-cigarettes and cardiovascular disease has not yet been established.

Early evidence suggests an association between e-cigarette use and the development of hypertension and elevated resting heart rate. This is important because these hemodynamic changes are thought to precede the development of cardiovascular disease. A recent meta-analysis found that chronic e-cigarette use (compared with no use) was associated with increased heart rate (mean difference [MD] 2.27, 95% CI, 1.64-2.89, $P < 0.0001$), increased systolic

blood pressure (MD 2.02, 95% CI, 0.07-3.97, $P = 0.042$), and increased diastolic blood pressure (MD 2.01, 95% CI, 0.62-3.39, $P = 0.004$).³² The cardiovascular disease implications of these small but statistically significant hemodynamic changes remain unclear. These shifts appear to be at least partially associated with nicotine, as one randomized controlled study found that systolic blood pressure, diastolic blood pressure, and heart rate were significantly higher when participants used nicotine-containing e-cigarettes (compared with nicotine-free e-cigarettes).³³ An encouraging finding from this meta-analysis is that positive hemodynamic changes were seen in association with switching from combustible to e-cigarette use, including a significant reduction in systolic blood pressure (MD -7.00, 95% CI, -9.63 to -4.37, $P < 0.0001$) and diastolic blood pressure (MD -3.65, 95% CI, -5.71 to -1.59, $P = 0.001$), but

TABLE 1. Evidence for e-cigarettes as a smoking cessation aid.

Article	Study type	Population	Research question	Statistical result	Conclusion
Hartmann-Boyce et al. ¹⁹	Cochrane systematic review and meta-analysis	Various	Effectiveness of e-cigarettes (vs NRT) as a smoking cessation aid	RR 1.26 (95% CI, 0.68-2.34)	E-cigarettes are no more effective than NRT for smoking cessation.
Kalkhoran et al. ²¹	Systematic review and meta-analysis	Various	Effectiveness of e-cigarette use (vs no use) as a smoking cessation aid	OR 0.72 (95% CI, 0.57-0.91)	E-cigarette users are less likely than nonusers to successfully quit smoking combustible cigarettes.
Hajek et al. ²²	Randomized controlled trial	UK adults attending the UK National Health Service smoking cessation services	Effectiveness of e-cigarettes (vs NRT) for smoking cessation	RR 1.83 (95% CI, 1.30-2.58, $P < 0.001$) NNT 12 (95% CI, 8-27)	E-cigarettes are more effective than NRT for smoking cessation among smokers intending to quit.
Walker et al. ²³	Randomized controlled trial	New Zealand adult smokers who were e-cigarette naive and motivated to quit smoking	Effectiveness of combining nicotine patches with e-cigarettes (vs nicotine patches alone) for smoking cessation	RR 2.92 (95% CI, 0.91-9.33, $P = 0.05$)	E-cigarettes used in combination with nicotine patches are more effective than nicotine patches alone for smoking cessation among smokers intending to quit.
Bullen et al. ²⁰	Randomized controlled trial	New Zealand adult smokers motivated to quit smoking	Effectiveness of e-cigarettes (vs nicotine patches) for smoking cessation	RR 1.26 (95% CI, 0.68-2.34, $P = 0.46$)	E-cigarettes are no more effective than nicotine patches for smoking cessation among smokers intending to quit.
Caponnetto et al. ²⁵	Randomized controlled trial	Italian adult smokers not intending to quit smoking	Effectiveness of nicotine-containing e-cigarettes (vs nicotine-free e-cigarettes) for smoking reduction and cessation	Reduction: 10% vs 12% ($P = 0.24$) Cessation: 13% vs 4% ($P = 0.24$)	Nicotine-containing e-cigarettes are no more effective than nicotine-free e-cigarettes for smoking reduction or cessation among smokers not intending to quit.
Liu et al. ²⁷	Observational study	Italian e-cigarette users	Association between combustible cigarette and e-cigarette use	Ever e-cigarette users: 13% quit smoking 22.2% started or restarted smoking	E-cigarette use may be associated with increased combustible cigarette use.

NRT: nicotine replacement therapy; RR: relative risk; OR: odds ratio; NNT: number needed to treat.

no difference in heart rate (MD 0.03, 95% CI, -2.57 to +2.52, $P = 0.983$).³² This suggests an improved cardiovascular risk profile for smokers of combustible cigarettes who switch completely to e-cigarettes.

Another key aspect of cardiovascular health is myocardial function. This is estimated by the myocardial performance index, which uses echocardiographic parameters to calculate an expression of global systolic and diastolic ventricular function. Smokers of combustible cigarettes have worse myocardial function parameters and worse scores on the myocardial performance index after smoking a combustible cigarette.³⁴⁻³⁶ However, e-cigarette users appear to have no change in myocardial function parameters or myocardial performance index scores immediately after e-cigarette use.³⁷ This suggests improved myocardial health for smokers of combustible cigarettes who switch completely to e-cigarettes, thereby providing another possible benefit of cardiovascular harm reduction.

Respiratory effects

Combustible cigarette smoking is strongly associated with poor respiratory health. E-cigarettes are likely less harmful to the respiratory system

than combustible cigarettes,⁹ but new data suggest that e-cigarettes are associated with independent respiratory health risks, most notably acute EVALI.¹⁰ Weaker associations have been shown between e-cigarettes and chronic respiratory diseases, including higher incidence of chronic obstructive pul-

monary disease,³⁸ asthma,³⁹⁻⁴³ and obstructive lung disease not otherwise specified.⁴⁴⁻⁴⁶ Because the data on the respiratory effects of e-cigarettes are expansive, we provide an overview of the key points. For a more detailed review of the respiratory effects of e-cigarettes, see Gotts and colleagues.⁹

New data suggest that e-cigarettes are associated with independent respiratory health risks, most notably acute e-cigarette, or vaping, product use-associated lung injury.

In the US, there was a national outbreak of EVALI, with 2807 hospitalizations and 68 deaths as of 18 February 2020.⁴⁷ This illness peaked in September 2019 and is now steadily declining.^{48,49} In comparison, EVALI cases in Canada have been relatively sparse, with a total of 19 cases, 15 hospital admissions, and no deaths reported as of 11 March 2020.⁵⁰ EVALI was first reported in the US in August 2019 in a case series that included 53 patients.⁵¹ Most of those patients presented with respiratory symptoms (dyspnea, cough, chest pain), gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal pain), and constitutional symptoms (fever, chills, malaise). Many of those patients had severe acute illness: 58% required admission to the ICU, 32% required intubation and mechanical ventilation, and 17% had acute respiratory distress syndrome. Two patients required extracorporeal membrane oxygenation, and one of them died. On CT scanning of the chest, key findings included bilateral ground-glass lung opacities, sometimes with subpleural sparing. Most patients received glucocorticoids, which resulted in respiratory improvement. Although the specific etiological agent within the e-cigarette vapor is unconfirmed at this time, vitamin E acetate has been strongly implicated.¹¹

TABLE 2. Cardiovascular effects of e-cigarettes.

Article(s)	Study type	Association	Statistical result	Conclusion
Ndunda and Muutu ³⁰	Observational study	Coronary artery disease	OR 1.4 (95% CI, 1.35-1.46)	E-cigarette use is associated with higher incidence of coronary artery disease.
Ndunda and Muutu ³⁰ Alzahrani et al. ³¹	Observational studies	Myocardial infarction	OR 1.59 (95% CI, 1.53-1.66) ³⁰ OR 1.79 (95% CI, 1.20-2.66, $P = 0.004$) ³¹	E-cigarette use is associated with higher incidence of myocardial infarction.
Ndunda and Muutu ³⁰	Observational study	Stroke	OR 1.71 (95% CI, 1.64-1.80)	E-cigarette use is associated with a higher incidence of stroke.
Skotsimara et al. ³²	Systematic review and meta-analysis	Hemodynamic parameters	sBP: MD 2.02 (95% CI, 0.07-3.97, $P = 0.042$) dBP: MD 2.01 (95% CI, 0.62-3.39, $P = 0.004$) HR: MD 2.27 (95% CI, 1.64-2.89, $P < 0.0001$)	E-cigarette use is associated with higher sBP, dBP, and HR.
		Improved hemodynamic parameters after switching from combustible cigarettes to e-cigarettes	sBP: MD -7.00 (95% CI, -9.63 to -4.37, $P < 0.0001$) dBP: MD -3.65 (95% CI, -5.71 to -1.59, $P = 0.001$) HR: MD -0.03 (95% CI, -2.57 to +2.52, $P = 0.983$)	Switching from combustible cigarettes to e-cigarettes is associated with lower sBP and dBP but no difference in HR.
Farsalinos et al. ³⁷	Observational study	No acute change in myocardial function	Mitral flow early diastolic velocity: $P = 0.13$ Mitral flow late diastolic velocity: $P = 0.083$ Deceleration time of early mitral flow: $P = 0.581$ Isovolumetric relaxation time: $P = 0.286$ Myocardial performance index: $P = 0.330$	E-cigarette use is not associated with acutely worsened myocardial function.

OR: odds ratio; sBP: systolic blood pressure; dBP: diastolic blood pressure; HR: heart rate; MD: mean difference

Vitamin E acetate is added to black market e-liquids as a condensing product, and it is problematic because it is sticky, which results in vitamin E acetate remaining in the lungs longer than other ingredients. The exact mechanism of vitamin E acetate-mediated pulmonary toxicity is unknown, but it is thought to interfere with pulmonary surfactant function.¹¹ One study found vitamin E acetate and tetrahydrocannabinol in the bronchoalveolar lavage fluid in 94% of EVALI patients;¹⁰ other studies found 77% to 84% of EVALI patients reported using tetrahydrocannabinol-based products.^{10,49,51} It is

important to note that vitamin E acetate is present mainly in tetrahydrocannabinol-containing e-liquids purchased on the black market, not in nicotine-containing e-liquids purchased through licensed businesses.¹² Therefore, the risk of EVALI is likely low among users of commercially available nicotine-only e-liquids.

There is also evidence of long-term respiratory risk from e-cigarette use [Table 3], though the evidence is less conclusive than that of acute EVALI. Several retrospective observational studies have noted that e-cigarette users report symptoms of airway obstruction and

alveolar injury. This includes increased chronic productive cough (OR 2.1, 95% CI, 1.8-2.5, $P < 0.001$),⁵² higher incidence of asthma (highest OR 2.36, 95% CI, 1.89-2.94, $P < 0.001$)³⁹⁻⁴³ and asthma exacerbations,⁵³ chronic obstructive pulmonary disease,³⁸ and dyspnea.³⁸ Other studies have found e-cigarette use is associated with reduced cough sensitivity⁵⁴ and ciliary dysfunction in cell culture models,⁵⁵ which suggests that e-cigarette users may be at higher risk for pulmonary infection.⁹ Case reports have also described diffuse alveolar hemorrhage, exogenous lipoid pneumonia, organizing pneumonia,

TABLE 3. Respiratory effects of e-cigarettes.

Article(s)	Study type	Association	Statistical result	Conclusion
Meo et al. ⁴⁴ Vardavas et al. ⁴⁵ Staudt et al. ⁴⁶	Randomized controlled trial	Obstructive spirometry results	FEV1: 4.6 vs 5.2 ($P = 0.007$) ⁴⁴ No difference before and after use ^{45,46} FEV1/FVC: 77.4 vs 83.4 ($P = 0.001$) ⁴⁴ No difference before and after use ^{45,46}	Conflicting evidence.
Vardavas et al. ⁴⁵	Randomized controlled trial	Increased airway resistance (as measured by IOS)	Increased IOS at 5, 10, and 20 Hz: $\beta > 0.034$ ($P < 0.02$)	E-cigarette use is associated with increased airway resistance.
Polosa et al. ⁵⁹ Cibella et al. ⁶⁰ Veldheer et al. ⁶¹	Observational study	Improvement in spirometry after switching from combustible to e-cigarettes	FEV1: 3.33 vs 3.43 ($P = 0.013$) ⁵⁹ 3.46 vs 3.62 ($P = 0.69$) ⁶⁰ $\beta = 0.0009$ ($P = 0.84$) ⁶¹ FEV1/FVC: 80.3 vs 80.7 ($P = 0.96$) ⁶⁰ $\beta = 0.0028$ ($P = 0.51$) ⁶¹	Conflicting evidence.
Layden et al. ⁵¹	Case series	E-cigarette, or vaping, and vaping product use-associated lung injury (EVALI)	Hospitalization: 94% ICU: 58% Intubation: 32% Death: 2%	E-cigarette use is associated with EVALI.
Wang et al. ⁵²	Observational study	Chronic productive cough	OR 2.1 (95% CI, 1.8-2.5, $P < 0.001$)	E-cigarette use is associated with chronic productive cough.
Cho and Paik ⁴⁰ Osei et al. ⁴¹ Schweitzer et al. ⁴²	Observational studies	Asthma	OR 2.36 (95% CI, 1.89-2.94, $P < 0.001$) ⁴⁰ OR 1.39 (95% CI, 1.15-1.68, $P < 0.01$) ⁴¹ aOR 1.48 (95% CI, 1.26-1.74, $P < 0.01$) ⁴²	E-cigarette use is associated with higher incidence of asthma.
Wang et al. ³⁸	Observational study	Chronic obstructive pulmonary disease (COPD)	6.7% vs 3.7% ($P < 0.0001$)	E-cigarette use is associated with higher incidence of COPD.
Carson et al. ⁵⁵	In vitro experimental study	Ciliary dysfunction	Decreased ciliary beat frequency and decreased secretory function ($P < 0.05$)	Exposure to e-cigarette vapor induces ciliary dysfunction in a human airway epithelium cell culture model.
Agustin et al. ⁵⁶ McCauley et al. ⁵⁷ Flower et al. ⁵⁸	Case reports	<ul style="list-style-type: none"> • Diffuse alveolar hemorrhage • Exogenous lipoid pneumonia • Organizing pneumonia • Eosinophilic pneumonia • Acute respiratory bronchiolitis interstitial lung disease 	N/A	N/A

FEV1: forced expiratory volume in 1 second; FEV1/FVC: ratio of FEV1 divided by forced vital capacity; IOS: impulse oscillometry system; OR: odds ratio; aOR: adjusted odds ratio

eosinophilic pneumonia, and acute respiratory bronchiolitis interstitial lung disease associated with e-cigarette use.⁵⁶⁻⁵⁸ Several of these associations were noted to be independent of combustible cigarette use; this suggests that e-cigarettes carry their own unique respiratory health risks, which are just starting to be understood.

E-cigarette use may be associated with the development of obstructive lung physiology. To date, studies have found mixed results with re-

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gard to e-cigarette use and spirometric changes. One study found e-cigarette use was associated with lower forced expiratory volume in 1 second ([FEV1] 4.6 versus 5.2, $P = 0.007$) and lower ratio of FEV1 to forced vital capacity ([FEV1/FVC] 77.4 versus 83.4, $P = 0.001$).⁴⁴ Since smokers of combustible cigarettes were excluded from this study, these results suggest that e-cigarette use may be independently associated with obstructive airway changes. However, spirometry was performed after only 1 hour of abstinence; thus, it potentially reflected acute bronchospasm rather than lasting changes in the airways. Furthermore, this association is still unclear, as two other studies have shown no difference in spirometric measurements before and after e-cigarette use.^{45,46} However, one of these studies did show an increase in pulmonary airflow resistance by impulse oscillometry,⁴⁵ which indicates evidence of obstructive airway changes before they can be seen on spirometry. In terms of improving obstructive lung physiology among smokers of combustible cigarettes who have switched completely to e-cigarettes, there are conflicting results: one study showed improved spirometry;⁵ two others showed no changes.^{60,61} Overall, the data suggest that e-cigarette use is potentially associated with early obstructive pulmonary changes, but this association remains inconclusive.

Summary

E-cigarette use is a rapidly growing phenomenon, especially among young people and never-smokers. There is emerging evidence that e-cigarettes can be an effective smoking cessation tool for smokers of combustible cigarettes. However, they are not benign: there is evidence of potential cardiovascular and respiratory morbidity. Nonetheless, e-cigarettes do appear to have an improved cardiopulmonary risk profile compared with combustible cigarettes and therefore may provide a viable harm reduction strategy for some smokers. ■

Competing interests

Dr Khara has received personal fees from the Pfizer Canada Inc. Champix advisory board. All other authors report no competing interests.

References

- Sears CG, Walker KL, Hart JL, et al. Clean, cheap, convenient: Promotion of electronic cigarettes on YouTube. *Tob Prev Cessat* 2017;3:10.
- Health Canada. Canadian tobacco, alcohol and drugs survey (CTADS): Summary of results for 2017. Accessed 6 March 2020. www.canada.ca/en/health-canada/services/canadian-tobacco-alcohol-drugs-survey/2017-summary.html.
- Hammond D, Reid JL, Rynard VL, et al. Prevalence of vaping and smoking among adolescents in Canada, England, and the United States: Repeat national cross sectional surveys. *BMJ* 2019;365:l2219.
- Health Canada. Summary of results for the Canadian student tobacco, alcohol and drugs survey 2018-19. Accessed 10 March 2020. www.canada.ca/en/health-canada/services/canadian-student-tobacco-alcohol-drugs-survey/2018-2019-summary.html.
- Centers for Disease Control and Prevention. E-cigarette, or vaping, products visual dictionary. 2019. Accessed 10 February 2020. www.cdc.gov/tobacco/basic_information/e-cigarettes/pdfs/ecigarette-or-vaping-products-visual-dictionary-508.pdf.
- Bach L. JUUL and youth: Rising e-cigarette popularity. 2019. Accessed 7 January 2020. www.tobaccofreekids.org/assets/factsheets/0394.pdf.
- Harvanko AM, St. Helen G, Nardone N, et al. Twenty-four-hour subjective and pharmacological effects of ad-libitum electronic and combustible cigarette use among dual users. *Addiction* 2020;115:1149-1159.
- Burstyn I. Peering through the mist: Systematic review of what the chemistry of contaminants in electronic cigarettes tells us about health risks. *BMC Public Health* 2014;14:18.
- Gotts JE, Jordt S-E, McConnell R, Tarran R. What are the respiratory effects of e-cigarettes? *BMJ* 2019;366:l5275.
- Blount BC, Karwowski MP, Shields PG, et al. Vitamin E acetate in bronchoalveolar-lavage fluid associated with EVALI. *N Engl J Med* 2020;382:697-705.

- Boudi FB, Patel S, Boudi A, Chan C. Vitamin E acetate as a plausible cause of acute vaping-related illness. *Cureus* 2019;11:e6350.
- Lewis N, McCaffrey K, Sage K, et al. E-cigarette use, or vaping, practices and characteristics among persons with associated lung injury—Utah, April–October 2019. *MMWR Morb Mortal Wkly Rep* 2019;68:953-956.
- Cullen KA, Ambrose BK, Gentzke AS, et al. Notes from the field: Use of electronic cigarettes and any tobacco product among middle and high school students—United States, 2011–2018. *MMWR Morb Mortal Wkly Rep* 2018;67:1276-1277.
- Centers for Disease Control and Prevention. National youth tobacco survey (NYTS). 2019. Accessed 7 January 2020. www.cdc.gov/tobacco/data_statistics/surveys/nyts/index.htm.
- Soneji S, Barrington-Trimis JL, Wills TA, et al. Association between initial use of e-cigarettes and subsequent cigarette smoking among adolescents and young adults: A systematic review and meta-analysis. *JAMA Pediatr* 2017;171:788-797.
- Primack BA, Shensa A, Sidani JE, et al. Initiation of traditional cigarette smoking after electronic cigarette use among tobacco-naïve US young adults. *Am J Med* 2018;131:443.e1-443.e9.
- Azagba S, Kah K, Latham K. Frequency of e-cigarette use and cigarette smoking among Canadian students. *Prev Med* 2019;126:105769.
- National Health Service U.K. Using e-cigarettes to stop smoking. 2019. Accessed 21 January 2020. www.nhs.uk/live-well/quit-smoking/using-e-cigarettes-to-stop-smoking.
- Hartmann-Boyce J, McRobbie H, Bullen C, et al. Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev* 2016;9(9):CD010216.
- Bullen C, Howe C, Laugesen M, et al. Electronic cigarettes for smoking cessation: A randomised controlled trial. *Lancet* 2013;382(9905):1629-1637.
- Kalkhoran S, Glantz SA. E-cigarettes and smoking cessation in real-world and clinical settings: A systematic review and meta-analysis. *Lancet Respir Med* 2016;4:116-128.
- Hajek P, Phillips-Waller A, Przulj D, et al. A randomized trial of e-cigarettes versus nicotine-replacement therapy. *N Engl J Med* 2019;380:629-637.
- Walker N, Parag V, Verbiest M, et al. Nicotine patches used in combination with e-cigarettes (with and without nicotine) for smoking cessation: A pragmatic, randomised trial. *Lancet Respir Med* 2020;8:54-64.
- Notley C, Ward E, Dawkins L, Holland R. The unique contribution of e-cigarettes for tobacco harm reduction in supporting smoking relapse prevention. *Harm Reduct J* 2018;15:31.
- Caponnetto P, Campagna D, Cibella F, et al. Efficiency and Safety of an eElectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: A prospective 12-month randomized control design study. *PLoS One* 2013;8:e66317.
- Halpern SD, Harhay MO, Saulsgiver K, et al. A pragmatic trial of e-cigarettes, incentives, and drugs for smoking cessation. *N Engl J Med* 2018;378:2302-2310.
- Liu X, Lugo A, Davoli E, et al. Electronic cigarettes in Italy: A tool for harm reduction or a gateway to smoking tobacco? *Tob Control* 2020;29:148-152.

28. Lee PN. Tar level of cigarettes smoked and risk of smoking-related diseases. *Inhal Toxicol* 2018;30:5-18.
29. Stratton K, Kwan LY, Eaton DL, eds. Public health consequences of e-cigarettes. National Academies of Sciences, Engineering, and Medicine; 2018.
30. Ndunda PM, Muutu TM. Electronic cigarette use is associated with a higher risk of stroke. *Stroke* 2019;50 (suppl).
31. Alzahrani T, Pena I, Temesgen N, Glantz SA. Association between electronic cigarette use and myocardial infarction. *Am J Prev Med* 2018;55:455-461.
32. Skotsimara G, Antonopoulos AS, Oikonomou E, et al. Cardiovascular effects of electronic cigarettes: A systematic review and meta-analysis. *Eur J Prev Cardiol* 2019;26:1219-1228.
33. Franzen KF, Willig J, Cayo Talavera S, et al. E-cigarettes and cigarettes worsen peripheral and central hemodynamics as well as arterial stiffness: A randomized, double-blinded pilot study. *Vasc Med* 2018;23:419-425.
34. Lichodziejewska B, Kurnicka K, Grudzka K, et al. Chronic and acute effects of smoking on left and right ventricular relaxation in young healthy smokers. *Chest* 2007;131:1142-1148.
35. Karakaya O, Barutcu I, Esen AM, et al. Acute smoking-induced alterations in Doppler echocardiographic measurements in chronic smokers. *Texas Heart Inst J* 2006;33:134-138.
36. Farsalinos K, Tsiapras D, Kyrzopoulos S, Voudris V. Acute and chronic effects of smoking on myocardial function in healthy heavy smokers: A study of Doppler flow, Doppler tissue velocity, and two-dimensional speckle tracking echocardiography. *Echocardiography* 2013;30:285-292.
37. Farsalinos KE, Tsiapras D, Kyrzopoulos S, et al. Acute effects of using an electronic nicotine-delivery device (electronic cigarette) on myocardial function: Comparison with the effects of regular cigarettes. *BMC Cardiovasc Disord* 2014;14:78.
38. Wang JB, Olgin JE, Nah G, et al. Cigarette and e-cigarette dual use and risk of cardiopulmonary symptoms in the Health eHeart Study. *PLoS One* 2018;13:e0198681.
39. Bhatta DN, Glantz SA. Association of e-cigarette use with respiratory disease among adults: A longitudinal analysis. *Am J Prev Med* 2020;58:182-190.
40. Cho JH, Paik SY. Association between electronic cigarette use and asthma among high school students in South Korea. *PLoS One* 2016;11:e0151022.
41. Osei AD, Mirbolouk M, Orimoloye OA, et al. The association between e-cigarette use and asthma among never combustible cigarette smokers: Behavioral risk factor surveillance system (BRFSS) 2016 & 2017. *BMC Pulm Med* 2019;19:180.
42. Schweitzer RJ, Wills TA, Tam E, et al. E-cigarette use and asthma in a multiethnic sample of adolescents. *Prev Med* 2017;105:226-231.
43. Reid KM, Forrest JR, Porter L. Tobacco product use among youths with and without lifetime asthma—Florida, 2016. *MMWR Morb Mortal Wkly Rep* 2018; 67:599-601.
44. Meo SA, Ansary MA, Barayan FR, et al. Electronic cigarettes: Impact on lung function and fractional exhaled nitric oxide among healthy adults. *Am J Mens Health* 2019;13:1557988318806073.
45. Vardavas CI, Anagnostopoulos N, Kougias M, et al. Short-term pulmonary effects of using an electronic cigarette: Impact on respiratory flow, resistance, impedance, and exhaled nitric oxide. *Chest* 2012;141:1400-1406.
46. Staudt MR, Salit J, Kaner RJ, et al. Altered lung biology of healthy never smokers following acute inhalation of e-cigarettes. *Respir Res* 2018;19:78.
47. Centers for Disease Control and Prevention. Outbreak of lung injury associated with the use of e-cigarette, or vaping, products. Last updated 25 February 2020. Accessed 28 February 2020. www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html.
48. Krishnasamy VP, Hollowell BD, Ko JY, et al. Update: Characteristics of a nationwide outbreak of e-cigarette, or vaping, product use-associated lung injury—United States, August 2019–January 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:90-94.
49. Hartnett KP, Kite-Powell A, Patel MT, et al. Syndromic surveillance for e-cigarette, or vaping, product use-associated lung injury. *N Engl J Med* 2020;382:766-772.
50. Government of Canada. Vaping-associated lung illness. 2020. Accessed 3 March 2020. www.canada.ca/en/public-health/services/diseases/vaping-pulmonary-illness.html.
51. Layden JE, Ghinai I, Pray I, et al. Pulmonary illness related to e-cigarette use in Illinois and Wisconsin—Preliminary report. *N Engl J Med* 2020;382:903-916.
52. Wang MP, Ho SY, Leung LT, Lam TH. Electronic cigarette use and respiratory symptoms in Chinese adolescents in Hong Kong. *JAMA Pediatr* 2016;170:89-91.
53. Choi K, Bernat D. E-cigarette use among Florida youth with and without asthma. *Am J Prev Med* 2016;51: 446-453.
54. Dicipinigaitis PV, Lee Chang A, Dicipinigaitis AJ, Negassa A. Effect of e-cigarette use on cough reflex sensitivity. *Chest* 2016;149:161-165.
55. Carson JL, Zhou L, Brighton L, et al. Temporal structure/function variation in cultured differentiated human nasal epithelium associated with acute single exposure to tobacco smoke or e-cigarette vapor. *Inhal Toxicol* 2017;29:137-144.
56. Agustin M, Yamamoto M, Cabrera F, Eusebio R. Diffuse alveolar hemorrhage induced by vaping. *Case Rep Pulmonol* 2018; 2018:9724530.
57. McCauley L, Markin C, Hosmer D. An unexpected consequence of electronic cigarette use. *Chest* 2012;141: 1110-1113.
58. Flower M, Nandakumar L, Singh M, et al. Respiratory bronchiolitis-associated interstitial lung disease secondary to electronic nicotine delivery system use confirmed with open lung biopsy. *Respirol Case Rep* 2017;5:e00230.
59. Polosa R, Morjaria JB, Caponnetto P, et al. Persisting long term benefits of smoking abstinence and reduction in asthmatic smokers who have switched to electronic cigarettes. *Discov Med* 2016;21:99-108.
60. Cibella F, Campagna D, Caponnetto P, et al. Lung function and respiratory symptoms in a randomized smoking cessation trial of electronic cigarettes. *Clin Sci* 2016;130:1929-1937.
61. Veldheer S, Yingst J, Midya V, et al. Pulmonary and other health effects of electronic cigarette use among adult smokers participating in a randomized controlled smoking reduction trial. *Addict Behav* 2019;91:95-101.

Multiple studies have demonstrated that e-cigarettes may be a risk factor leading people toward combustible cigarette use.