Qeios

Peer Review

Review of: "Are electronic cigarettes associated with the risk of myocardial infarction and stroke? A systematic review and meta-analysis"

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Summary

Several problems with the analysis mean no useful insights can be drawn about e-cigarettes and myocardial infarction (MI or heart attack) or stroke. This is because of the challenge of taking account of the smoking history of current vapers, the possibility of reverse causation (smokers switching to vaping because of their ill health), and the likelihood that heart attacks or strokes may have happened before the users started vaping. The observed correlations must not be treated as causal, and the most notable associations between vaping and MI or stroke are driven by former smoking.

I will expand on this summary in the points below.

Review

First, the critical challenge in all such studies is to account for the cigarette-smoking history of current e-cigarette users ("vapers"). Those suffering from MI or stroke are likely to be old enough to have smoked cigarettes for many years or decades before trying e-cigarettes. It is not even a matter of adjusting for smoking status (current, former, never smokers who now vape); it requires a measure of cumulative smoking exposure (for example, pack-years) and the date of quitting smoking. Equally, the e-cigarette exposure needs to be properly characterised: current or ever use is inadequate. It would need at least the length of time using e-cigarettes; the authors note they have not addressed this in the limitations ("*There is a lack of information on the frequency of e-cigarette use and the duration-dependent effect on cardiovascular health*"). Suppose someone has smoked cigarettes for three decades, switched to e-cigarettes for three

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years, and then had a myocardial infarction: is the condition attributable to the e-cigarette use, the smoking history, or some of each? Suppose it was four decades of smoking and three months of vaping? Could anything be attributed to vaping? There is no indication that the authors have addressed these challenges or that they were addressed in the underlying studies included in the review. I am not aware of any study that satisfactorily addresses this problem, and it may not be possible to characterise smoking history well enough to separate smoking from vaping effects.

Second, any causal analysis is further complicated by reverse causation in this case. It is quite possible that people with deteriorating health switch from smoking to vaping to reduce their risks without quitting nicotine use, which some people find difficult. This would be like attributing heart attacks to the consumption of statins or aspirin - people are using these products precisely because they are at elevated risk. The authors have not shown how they have addressed reverse causation.

Third, a further related challenge is temporality (timing). All but one of the studies are cross-sectional, but most cannot determine whether vaping preceded or followed the recorded MI or stroke. It is possible that some of the recorded events happened before vaping started, caused by smoking, and the user migrated to vaping instead of quitting altogether. In this situation, vaping could be a marker of higher dependence and a more intensive smoking history. It is plausible that a heavily dependent smoker would switch to vaping after experiencing an MI. In which case, it is obviously not possible to attribute the MI to vaping. The authors find a correlation between a history of MI and current vaping, but they do not show that the observed effect is driven by vaping that came before the MI.

Fourth, the study uses causal language to frame its conclusion: "*The use of e-cigarettes may be linked with a higher risk of myocardial infarction as well as stroke*". There is no basis for drawing a causal conclusion about vaping and either MI or stroke from this analysis. In the case of stroke, there is not even a statistical basis for claiming a meaningful correlation: "*Similarly, stroke was found to be 1.05 times more frequent among e-cigarette users than non-users (95% CI 0.91–1.19)*". Of the four relationships between e-cigarette use and stroke shown in Table 1 (reproduced below with annotations in red), the only one that shows a significant association is e-cigarette users who are former smokers, suggesting the observed effect is driven by smoking history. To detect any vaping effect would therefore require a sophisticated adjustment for smoking history. A similar pattern is seen for MI; the strongest effects arise from former-smoker status, with smaller effects when some attempt is made to adjust for smoking status. Yet there is considerable scope for residual confounding by smoking history, smoking intensity, nicotine dependence, and reverse causation that would eliminate these effects completely.

Table 1 Results of meta-analysis for the association of e-cigarettes and myocardial infarction or stroke

Outcome	Parameter	Comparator	No. of estimates	Meta-RR (95% CI)
Myocardial infarction	Overall	Non-e-cigarette users	11	1.53 (1.17-1.89)
	Smoking adjusted	Non-e-cigarette users	9	1.24 (1.11-1.37)
	Non-smoker	Non-e-cigarette users	3	0.96 (0.41-1.50)
	Former smoker	Non-e-cigarette users	2	2.52 (1.88-3.16)
Stroke	Overall	Non-e-cigarette users	15	1.05 (0.91-1.19)
	Smoking adjusted	Non-e-cigarette users	11	1.02 (0.89-1.16)
	Non-smoker	Non-e-cigarette users	5	0.97 (0.58-1.36)
	Former smoker	Non-e-cigarette users	3	1.73 (1.30-2.15)

Fifth. It is probably not even possible to draw conclusions about vaping risk from studies where the subject has already smoked for many years - the smoking effects "contaminate" any data about vaping. Cardiovascular disease is progressive, involving prolonged deterioration of the circulatory system over many years. To reuse the example above, it is not possible to take an exposure of three decades of smoking followed by three years of vaping, measure the effect on CVD, and then draw conclusions about vaping in isolation (i.e. the risk of three decades of vaping without ever having smoked). Most of the exposures in these studies are a combination of prolonged smoking followed by vaping, not exclusive vaping.

Sixth. A further problem is the counterfactual: in attributing a risk to vaping, the authors implicitly assume that the alternative would be abstinence. But for many people who smoke and vape late in life, the alternative would be continued smoking rather than abstinence. For those smokers, a switch to vaping would create a risk reduction (a negative risk) compared to continuing smoking, even if that risk reduction was not as large as moving to complete abstention. The risk reduction may not be as large, but

it may be more likely to be realised. (And to reiterate, this study does not and cannot show a causal link between vaping and MI or stroke).

Conclusion

Unsurprisingly, this study has led to some irresponsible and misleading media coverage [1]. What purpose is served by publishing a study where the public and media are likely to misunderstand the findings as causal (encouraged by the inappropriate framing of the conclusion), yet the most likely explanations for the observed associations (residual confounding by smoking history, and reverse causation) have not been addressed? It does not add useful insights to our knowledge of e-cigarettes. It may degrade public understanding by creating a false narrative and unfounded fears about MI and stroke risk that deter smokers from switching to a safer alternative, as explicitly stated in the cited press coverage [1].

Reference

[1] Smokers switching to e-cigarettes have an increased heart attack risk, says ICMR study: Why quitting smoking is the only way out. Indian Express, 17 December 2025. [link]

Declarations

Potential competing interests: No potential competing interests to declare.