Reviewer’s report

Title: The association between e-cigarette use and asthma among never combustible cigarette smokers: Behavioral Risk Factor Surveillance System (BRFSS) 2016 & 2017

Version: 0 Date: 23 Mar 2019

Reviewer: Riccardo Polosa

Reviewer's report:

MAJOR POINTS

Aim of this cross-sectional analysis is to examine for potential association between self-reported asthma and use of ECs using the BRFSS dataset. I have the following comments:

As noted by the authors, cross-sectional studies cannot demonstrate causation as there is no way to prove temporal relationship. In this specific case, it is unclear whether the diagnosis of asthma is prior or subsequent to the use of ECs. However, considering that the age range of the study respondents is 18-24 yrs old and that onset of asthma occurs mostly during childhood, it is reasonable to argue that EC use has started AFTER the diagnosis - thus discounting causality. This should be noted in the Discussion.

There could be alternative explanation for the observed association between asthma and EC use. For example, the possibility of a selection bias cannot be discounted because individuals with asthma diagnosis might avoid taking up smoking and might self-selecting to EC use instead. Another possible explanation is that self-reported diagnosis of asthma was often confused with report of cough/wheeze that have been reported with vaping (in approx. 20-30% of first-time users), because inhalation of PG / VG mixtures can cause irritation and trigger the (physiological) reflex of the cough/wheeze. This is known to be transitory, as it tends to wane with time; a normal form of adaptation of the organism to inhalation of PG / VG mixtures that has no prognostic value. If a doctor has deemed this transient cough/wheeze to be a symptom for the diagnosis of asthma, then we have a serious problem. This should be mentioned in the Discussion.

Also, it is often noted that replication of cross-sectional studies raise serious issues with findings stability. Hence, the concern of chance findings. This is particularly true, when relevant confounders are not taken into account. In the case of this study, authors have neglected to factor in relevant important key factors in the multifactorial analysis. It is concerning that the analysis was not adjusted for key asthma confounders such as family or personal hx of allergy (such as atopic dermatitis and allergic rhinitis), as well as second hand exposure to smoking or urban pollution. Also, poverty level has been shown to be a factor for asthma and in this study EC solos use seems to be more prevalent among those with lowest federal poverty thresholds.

Authors pooled data from two years (2016 and 2017). How did they use the sampling weight? Did they divide each sampling weight by 2? If not, then the final sample would have twice the
US population (which is wrong). How can you be so sure that there are no subjects that participated in the survey twice? Authors could ask to insert the survey year as a confounding variable together with age, sex, race, income, education and BMI.

The statistical analysis is over-simplistic and more details are should be provided. All results of the model should be presented in a table (ORs of all variables). I suspect younger age would also have higher odds of asthma, and younger age are more likely to use ECs (as shown in table 1).

There is a huge size difference between experimental and control group (0.8% vs 99.2%). Please consider propensity score matching for the secondary analysis of these two study groups.

Participants who answered "YES" when asked: "Have you ever used an e-cigarette or other electronic 'vaping' product, even just one time, in your entire life?" were classified as occasional (reported using ECs "some days") or daily (reported using ECs "every day" EC users. However, among those who respond "YES" there are also those who quit EC use (e.g. individuals who tried EC a few times and not using them anymore). This should be included as a control group in the analysis.

To increase confidence in the study results, the authors should expand their analysis by including (sex- and age-matched; young 18-24 years old) smokers from the BRFSS dataset.

MINOR POINTS

In the Introduction authors state "In 2016, 10.8 million U.S. adults reported current e-cigarette use of which almost 2 million were never smokers of combustible cigarettes". This cannot be right; 2 out of 10.8 millions (i.e. about 20%) US adults current EC users being never smokers is a miscalculation. This is in clear disagreement with their own data (0.8%).


In line with previous reports, it is reassuring that prevalence of EC use (mainly consisting of occasional users) in never smokers is very low. This should be noted in the Discussion.

In the Discussion is stated "Our study reports significantly higher odds of asthma among never combustible smoking e-cigarette users." but no test is shown (they did a multiple logistic regression to arrive at the odds ratios that they declare significantly different, and I do not even see corrections of the Bonferroni-like threshold value).

"The median age group of current e-cigarette users was 18-24 years". But, median is a number not a range!
It is unlikely that many of the respondents had been using ECs for more than 1-2 years. That question the biological plausibility of vaping products causing asthma. Indeed, no asthma epidemics have been reported in countries with high prevalence of EC use (e.g. UK, Greece and France). This should be included in the Discussion.

Are the methods appropriate and well described?  
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?  
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?  
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No

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I recommend additional statistical review

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