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### Title

Author Response

### Permalink

<https://escholarship.org/uc/item/9bd0s0t2>

### Journal

Pediatrics, 141(6)

### ISSN

0031-4005

### Author

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### Publication Date

2018-06-01

### DOI

10.1542/peds.2018-0828b

Peer reviewed

10 March 2018

## **E-cigarettes are safer than cigarettes but not entirely safe**

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Studying the safety of E-Cigarettes on teenagers is extremely important. This study describes the presence of certain metabolites in the urine of adolescents who smoke e-cigarettes. It also tells us many of them are carcinogenic. It concludes by advising the public to warn teenagers about "the potential risk from toxic exposure to carcinogenic compounds." However, it fails to adequately frame the message for cigarette smokers:

1. Authors were very careful to select e-cigarette-only users (they even established their eligibility by measuring the levels of urine NNAL). But they did not recruit a comparison group composed of cigarette-only users. Being able to compare both groups is important because E-Cigarettes are advertised as an alternative to cigarettes--the carcinogenic hazards of cigarette consumption are well established--not as an alternative to dual use. Having measured the levels of volatile organic compounds in cigarette-only users, we would know by how much e-cigarettes reduce the levels of VOC compared with cigarettes in teenagers. The authors cited a study using this design,[1] suggesting they deliberately decided not to have such comparison group.

2. The study does not tell the reader the levels at which these volatile organic compounds start being toxic. This information is crucial to understand the importance of the findings. While a statistical analysis is useful, toxicity can be better assessed by using a population-level measure of toxicity. If such information is not yet available, it should be mentioned.

Even in the absence of these data, we know that a reduced intake of VOC is associated with a reduction of disease risk [2]. It is likely that cigarette smokers would benefit by becoming e-cigarette-only users and this should be emphasized given how lightly scientific articles can be interpreted and how prevalent smoking-related cancer is.

### References

[1] Hecht, Stephen S. et al. "Evaluation of Toxicant and Carcinogen Metabolites in the Urine of E-Cigarette Users Versus Cigarette Smokers." *Nicotine & Tobacco Research* 17.6 (2015): 704-709. PMC. Web. 11 Mar. 2018.

[2] Shahab, Lion et al. "Nicotine, Carcinogen and Toxicant Exposure in Long-Term E-Cigarette and Nicotine Replacement Therapy Users: A Cross-Sectional Study." *Annals of internal medicine* 166.6 (2017): 390-400. PMC. Web. 11 Mar. 2018.

## **E-cigarettes are less dangerous than cigarettes, and not entirely safe**

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We appreciate the interest in our research, but would suggest a title change to **E-cigarettes are less dangerous than cigarettes** since there is nothing safe about Cigarettes. No single study can resolve all questions of interest, and all findings warrant replication. Our focus for this study was examining toxicants in adolescent e-cigarette only users relative to non-users. Since a number of adolescents who enrolled in our

study were found to also have recently smoked combustible cigarettes (dual users), we included them as a comparison group.

As we stated in our article, e-cigarettes do appear to produce lower levels of toxicants than traditional cigarettes, based on the literature and based upon the levels observed among our dual user group. Use of e-cigarettes among adult tobacco smokers was not a focus of our study and we encourage readers interested in that literature to see the references we noted in our article. Again, we chose to focus on adolescents for whom the paradigm is different than the debate that has been characterized as harm reduction among adults. Rather, the focus of interest with adolescents is harm creation. The comparison of interest is not combustibles, but no use of any tobacco product at all. Specifically, adolescents are by and large using e-cigarettes for recreational use, not as a means of switching from traditional cigarettes. This is evidenced by epidemiologic data showing that the number of adolescents using e-cigarettes outnumbers adolescent tobacco smokers (in the U.S.) and use by never smokers is also increasing. Furthermore, studies of adolescents in the U.S. show a reverse trajectory for teens from e-cigarettes to traditional cigarettes. Consequently, for adolescents, the question of interest is: Are these products more dangerous than no use at all (rather than compared to tobacco only smoking)? As such, the most relevant groups for comparison would be those with and without e-cigarette exposure, which was the focus of our study.

The relative toxicity of the products is complex to determine. For this reason, we analyzed exposures in a non-e-cigarette using comparison group. That way, readers can compare baseline environmental exposures, which we point out in the paper were greater than zero. Again, with the perspective that most adolescents are using e-cigarettes for recreational purposes, our findings provide a warning that they are exposing themselves unnecessarily to cancer-causing toxicants. As we point out in the manuscript (and consistent with other exposures such as secondhand tobacco smoke), the harm from these lower levels of VOCs would likely not present for many years and assumes that these adolescents will continue to be exposed over time (something that as yet remains unknown). Assuming adolescents continue using e-cigarettes for many years, there are data available which can provide an estimate of cancer risk for each of the toxicants we examined. A particularly good reference is: Intake of Toxic and Carcinogenic Volatile Organic Compounds from Secondhand Smoke in Motor Vehicles: 10.1158/1055-9965.EPI-14-0548.

Again, we appreciate the interest and hope that our research findings provide the impetus for deeper investigation into the potential harms and benefits of e-cigarettes for both adults and young people.