

Review of: "Population estimates of biomarkers of exposure to carbon monoxide, nicotine, and NNK in smokers and non-smokers"

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Potential competing interests: The author(s) declared that no potential competing interests exist.

I have major concerns about the intended purpose of the population baseline estimates that this article is attempting to establish as a means of quantifying the "...benefits [of] switching to potentially reduced risk tobacco products" such as e-cigarettes.

Firstly, all of the manuscript's co-authors are employees of the tobacco industry, which has over multiple decades has invested heavily in the e-cigarette industry (e.g. see <https://tobaccotactics.org/wiki/e-cigarettes/>). This raises serious concerns about potential conflicts of interest as regards promoting e-cigarettes. Indeed, my main concern with this article is that it cherry-picks only those metabolites of tobacco smoking that are least sensitive to e-cigarette usage or other forms of smokeless/non-combusted nicotine consumption. If these so-called bio-markers of exposure to tobacco smoke were used as recommended in this article as basis for establishing the benefit of e-cigarette usage, it would be misleading as regards the potential harms caused by e-cigarette usage. In particular, the NNK bio-markers being promoted here is entirely specific to nicotine consumed by burning; and the other nicotine-related bio-marker promoted by the authors NEQ also includes these combustion specific forms of nicotine consumption. The authors fail to mention that the most long established and widely used methods of measuring nicotine exposure typically indicate similar levels of nicotine exposure in smokers and e-cigarette users because they do not include metabolites that are derived specifically from burning (e.g. https://journals.sagepub.com/doi/10.1177/1091581815618935#:~:text=The%20observed%20nicotine%20concentrations%20from,from%20a%20tobacco%20cigarette%20smoking.)).

Another concern that I have about the intended purpose of the authors' population estimates of biomarkers for exposure, is that it does not take into account that approximately 39% of tobacco smokers who attempt to switch to using e-cigarettes end up using both chronically with additional harm (e.g.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2771440> and

https://erj.ersjournals.com/content/54/suppl_63/PA4465). Only a minority of tobacco smokers become exclusive e-cigarette users in the long run. It seems likely that this minority have a different profile of tobacco smoking than the majority of smokers (e.g. lower average consumption; <https://www.mdpi.com/2227-9032/9/10/1252/pdf>). As such, comparing former smokers who exclusively use e-cigarette users' against the baseline estimates provided by the authors would most likely further exaggerate the "benefit" for current smokers of attempting to switch to exclusive e-cigarette usage.

