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Letter to the Editor

Response to Commentary on Vaping, Smoking and Lung Cancer Risk

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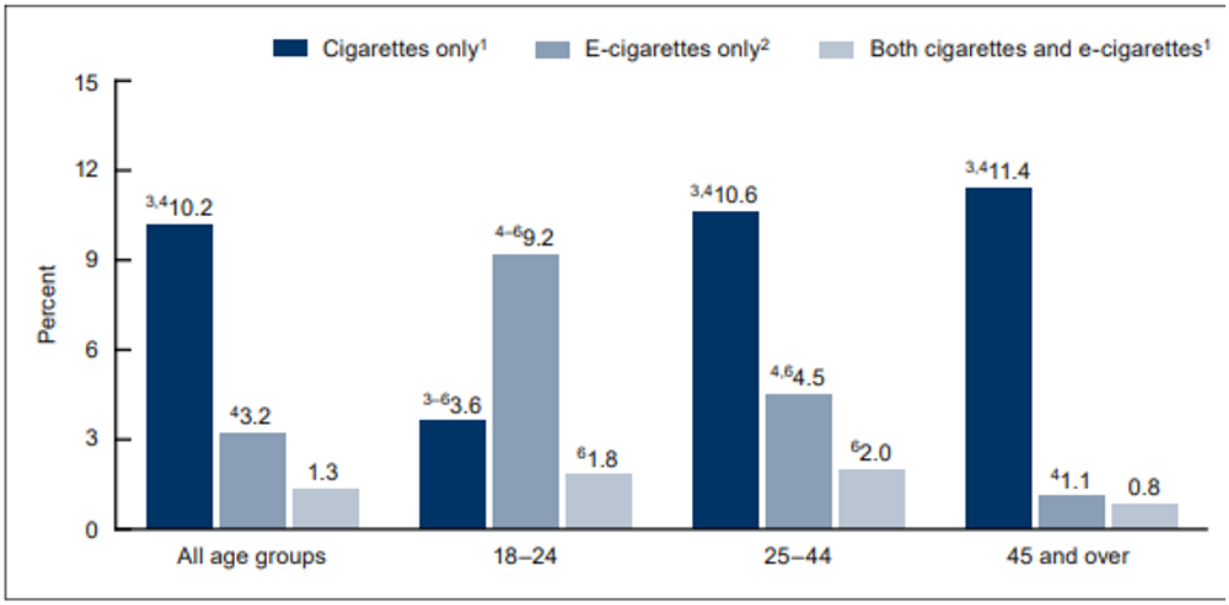
Key words: Vaping; Smoking; Dual Use; Lung Cancer;

We are responding to a commentary [1] regarding our peer-reviewed published journal articles on smoking, vaping and lung cancer risk [2, 3]. We note that the lead author of the critique was submitted by a member of the Rose Research Center of North Carolina, USA, which is funded by Phillip Morris, Inc, JUUL, and other tobacco companies, which constitutes a major conflict of interest.

In brief, our published case control study of 4,975 confirmed cases of lung cancer and 27,294 control subjects matched by age, gender, race, location and year of ascertainment to the cases found that dual smoking and vaping increased the risk of lung cancer four times higher than for smoking alone [2]. Results were consistent with stratification by age, gender, pack-years of smoking and histologic cell type, and adjustment for smoking related comorbidities, chronic obstructive pulmonary disease (COPD) and coronary artery disease (CAD) did not signficantly alter the effect. Pack-years of smoking ranged from 10 to 80 years with a median of 40, and years of vaping ranged from 3 to 9 with a median of 6. A second published study of early onset lung cancer also showed that dual vaping and smoking significantly increased lung cancer risk compared to only smoking cigarettes [3].

In contrast to the commentary, there is no evidence of differential reporting bias in either of our studies. First, the commentary was in error in describing data on controls as being "ascertained from outpatient annual checkups, where documentation of EC use depended on either the patient's self-report or the clinician's asking a forced-choice response regarding current vaping." In contrast, both cases and controls were patients seen in hospital clinics within the James Cancer Medical System at The Ohio State University, which uses standardized questionnaires to collect intake data stored in the electronic medical record (EMR) repository. Trained nurses always ask standard questions about the use and quantity of daily cigarette smoking and vaping, regardless of patient status, which is entered in the EMR. Furthermore, we had complete reports for both cases and controls with potentially contributory risk factors and comorbidities that were also coded into the medical record.

Secondly, and most importantly, the commentary has a major flaw in that it only made comparisons with prevalence estimates of current vaping instead of dual use (smoking in combination with vaping), which was the focus of our study. In the matched control group (n=27,294) of our first study, the average age was 63 years and over 93% of the controls were 45 years of age or older. Indeed, among the controls, the prevalence of daily vaping and chronic smoking (0.8%) was nearly identical to the estimate of dual vaping and smoking for ages ≥45 (0.8%) reported from the US National Center for Health Statistics (NCHS) survey data in 2021 (Figure 1) [4].



[1]Significant quadratic trend by age ($p < 0.05$).
[2]Significant linear trend by age ($p < 0.05$).
[3]Significantly different from e-cigarettes only ($p < 0.05$).
[4]Significantly different from both cigarettes and e-cigarettes ($p < 0.05$).
[5]Significantly different from adults aged 25–44 ($p < 0.05$).
[6]Significantly different from adults aged 45 and over ($p < 0.05$).
NOTES: Current e-cigarette use was based on responses of "every day" or "some days" to the question, "Do you now use e-cigarettes or other electronic vaping products every day, some days, or not at all?" This question was asked of adults who had ever tried an e-cigarette, even one time. Adults were asked if they had smoked at least 100 cigarettes in their lifetime and, if yes, whether they currently smoked cigarettes every day, some days, or not at all. Those who smoked every day or some days were classified as current cigarette smokers. The sum of e-cigarettes only and both cigarettes and e-cigarettes may not equal total e-cigarette use due to rounding. Estimates are based on household interviews of a sample of the U.S. civilian noninstitutionalized population. Access data table for Figure 4 at: https://www.cdc.gov/nchs/data/databriefs/db475-tables.pdf#4.
SOURCE: National Center for Health Statistics, National Health Interview Survey, 2021.

Figure 1: Percentage of adults aged 18 and over who currently smoke cigarettes and use e-cigarettes, by age group: United States, 2021.

In our study, we only observed daily vaping in combination with chronic smoking (dual use) and the reported duration of vaping ranged from 3 to 9 years with a median of 6 years. In most published US national sample data, prevalence estimates of vaping are for any use and any duration with or without dual smoking and thus would be expected to be much higher than our estimates for dual use of vaping and chronic smoking. In fact, when we compared our estimates of dual use with national estimates for dual use, there was little difference.

In our second study of early onset lung cancer, the prevalence of chronic smoking and daily vaping among all 2,291 matched controls under age 50 (1.5%) was similar to the NCHS 2021 estimate for ages 18 and over (1.3%) but slightly lower than the NCHS 2021 estimates for ages 18-24 years (1.8%) or ages 25-44 years (2.0%) (Figure 4 below) [4]; nevertheless, the estimate of dual use for the latter years of our study, 2019-2021 (2.0%), was similar to the NCHS estimates for younger adults from 2021.

Finally, a study by Kim et al [5] provides published evidence of a synergistic effect modification regarding lung cancer risk, which corroborates our findings. Most importantly, a major comprehensive review by Stewart et al was recently published [6], which concluded that nicotine-based e-cigarettes are likely to cause lung cancer, which also complement our results.

Regarding lung cancer trends, though overall lung cancer rates have declined, rising rates of pulmonary adenocarcinoma, the dominant histological cell type in our studies, have recently been observed in non-smokers, particularly among women, not only in the USA but other developed countries [7]. In these studies, vaping is not eliminated from the non-smoking group. Furthermore, recent reports document the early onset of pulmonary adenocarcinoma among cases who vaped on a regular basis [8].

In summary, the similarity of exposure estimates among the controls of our studies with published estimates of dual use from a national NCHS survey strengthens the validity of our findings.

Additional studies have also corroborated our results. We have also acknowledged the need for further well-designed investigations of lung cancer that include more detailed information on smoking and vaping in future research.

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