Cross-Sectional Analyses Can Evaluate the Plausibility of, but Not Validate, Causal Accounts

Alzahrani et al.1 documented a cross-sectional association between survey respondents’ current behavior (daily e-cigarette use) and medical history (having suffered a myocardial infarction [MI]). Robust associations signal the presence of causal forces; they do not identify the nature of the causal model. Imagine if Glantz had not posted to his professional blog, “First evidence of long-term damage from ecigs: Smoking e-cigarettes daily doubles risk of heart attacks,”2 but instead “Health scares push smokers to try ecigs: Smokers who suffered heart attacks overrepresented among e-cigarettes’ regular users.” What if The New York Times had quoted Glantz not as saying, “If you switch it’s almost the same as continuing to smoke,”3 but instead, “Too many smokers are switching too late, only after instead of before suffering smoking-related harm?”

All of these statements are consistent with but none logically follow from the reported association. Without Glantz’s spin, it is unlikely that >190 news outlets would have reported on Alzahrani and colleagues’ with mis-characterizations such as, “They found that vaping leads to an increased risk of heart attack regardless of the user’s other lifestyle choices.”4 Such researcher conduct raises difficult questions for scientific societies and journals whose processes and procedures are better equipped to inspect the quality of research submissions than the accuracy of authors’ public promotions of them.

Glantz5 ignores these issues and instead focuses on our cross-sectional analyses of the 2014–2019 National Health Interview Survey data. We wrote that our analyses have reported on Alzahrani and colleagues1 with mis-reports. Testing for such a dependency helps to evaluate the plausibility of Alzahrani and colleagues’ take that the associations reflect the independent causal contributions of smoking and vaping on MI. Alzahrani et al.4 tested for 1 specific deviation from the independent-effects model. We instead preserved all 4 levels of combustible and e-cigarette use and conducted an omnibus test that rejected the null hypothesis that the independent-effects model was reasonable.

We then moved to stratified analyses that illustrated how the MI—vaping links varied in strength and statistical significance across the 4 levels of smoking status. These analyses showed varied patterns of statistical significance (Table 2) not merely because of the observed variation in the strength of the MI—vaping link (as reflected by the significant interaction) but also because of variation in statistical power that depends on how many respondents fit different vaping—smoking profiles. Glantz7 focuses on the AORs associated with daily e-cigarette use in particular and highlights the aberrantly low MI risk for some-days smokers. Most daily e-cigarette users were former smokers. These former smokers were 57% more likely to have had an MI than those who had never vaped. One possibility is that their switch to daily vaping caused their greater likelihood of having had an MI. But if so, why would daily e-cigarette use show no hint of an association with MI among some-days smokers (AOR=0.53, 95% CI=0.20, 1.39)? One could accommodate this finding by (unreasonably) positing that

Actually, Glantz misreports this AOR as 1.57, which described the association between daily e-cigarette use and MI in former smokers, not never smokers.
smoking on some days serves as a protective factor against the risks of daily e-cigarette use. A more reasonable explanation is that current e-cigarette use is a marker of heavy current (daily) and former smokers who have experienced smoking-related health decline.

We tested whether the primary finding of Alzahrani et al. —the association between daily e-cigarette use and MI—has changed with time. If this association reflected daily e-cigarette use causing MI, it might be expected to strengthen following more years for vaping’s consequences to become clearly observable. Instead, it declined, consistent with the possibility that health-compromised smokers—like the general public—have grown skeptical of e-cigarettes’ harm reduction potential.6,7,9 Glantz5 notes that we tested for 6 secular trends (across the 3 levels of e-cigarette use and 3 levels of cigarette smoking), which increased the chances that any one of those tests would emerge as significant. But none of the other 5 tests addressed whether the central finding reported by Alzahrani and colleagues has varied —finding of Alzahrani et al.'s paper.

Table 1 documents the precise observed trajectory. If Alzahrani et al. had run their analyses not on the 2014 and 2016 data but on the most recent 2018 and 2019 data, they would have found that neither daily e-cigarette use (AOR=0.87, 95% CI=0.49, 1.54) nor some-days e-cigarette use (AOR=1.24, 95% CI=0.76, 2.06) but only former e-cigarette use (AOR=1.43, 95% CI=1.18, 1.75) is associated with ever having had an MI. For those inclined to think that these associations reflect the causal effect of e-cigarette use on MI, they may conclude that e-cigarettes once posed a cardiac risk but no longer do. Instead, we suspect that the disappearance of the MI-vaping association merely reflects the effectiveness with which scientific research on e-cigarettes has been distorted to evoke fear instead of cautious optimism about vaping’s public health potential.10

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