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RESEARCH ARTICLE

Re-examining the Association Between E-Cigarette Use and Myocardial Infarction: A Cautionary Tale

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Introduction: Cross-sectional analyses have suggested that e-cigarette use, independent of combustible cigarette use, elevates the risk of myocardial infarction. Previous researchers confused their own models' assumptions that these risks were independent with the idea that their analyses validated the presence of independent risks. This study avoids this pitfall.

Methods: Cross-sectional analyses of the 2014–2019 National Health Interview Surveys (N=175,546) were conducted in 2020.

Results: Logistic regressions found that e-cigarette use was associated with having had a myocardial infarction, but this association significantly varied on the basis of one's smoking history. With a host of demographic and clinical variables controlled, e-cigarette use was associated with lifetime myocardial infarction occurrence only among current smokers. A counterfactual analysis first removed all (current or former) e-cigarette–using respondents who had suffered a myocardial infarction without a history of smoking. The independent-effects model used in previous research misleadingly indicated that daily vaping increases never smokers' odds of having had a myocardial infarction by 1.55 (95% CI=1.11, 2.15), even though no such myocardial infarction sufferers remained in the analyzed data. The association between myocardial infarction and vaping daily has shown a significant annual decline (AOR=0.81, 95% CI=0.67, 0.98).

Conclusions: There is no reliable evidence that e-cigarette use is associated with ever having had a myocardial infarction among never smokers. Contrary to concerns that the harms associated with e-cigarettes are only now emerging after more years of possible product use, the only evidence of time-dependent variation in the association between e-cigarette use and myocardial infarction ran counter to this possibility. The scientific community must insist that researchers engage in accurate public communication of peer-reviewed findings.

INTRODUCTION

E-cigarettes have been heralded as effective tools for smoking cessation.[1] Cross-sectional analyses[2] and RCTs[3] show that e-cigarettes both are associated with and lead to superior smoking-cessation outcomes. That said, public health organizations and policymakers vary in whether they have embraced or resisted these products, due, in part, to uncertainties about the consequences of prolonged use. Although e-cigarettes are widely considered safer than combustible tobacco cigarettes,[4] some have claimed that vaping increases the risk of various negative health events, including myocardial infarction (MI).[5–7] A better understanding of whether vaping indeed poses risks to cardiovascular health is critical for formulating and evaluating public policy as well as for informing clinical recommendations.

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Crucially, such research has been cross-sectional, documenting a significant association between ever having experienced an MI and being a current e-cigarette user. Furthermore, previous research did not comprehensively test whether the association varies by one's smoking history. At least 3 reasons suggest that it may. Two of these see no causal role for e-cigarettes leading to MIs.

First, e-cigarette use may be a consequence and not a cause of MI. Simulations show that only a small minority of cigarette-smoking MI sufferers adopting e-cigarettes would be sufficient to reproduce the vaping–MI link.[8] In fact, a reanalysis of one of the data sets[6] revealed that significant results required ignoring that many e-cigarette–using MI sufferers initiated vaping after suffering an MI.[9] Second, e-cigarette use may simply identify which smokers are most at risk for smoking-related disease. Smokers who adopt e-cigarettes may have used combustible cigarettes with more frequency and intensity or may have adopted e-cigarettes because they began to experience health problems. For example, smokers diagnosed with respiratory disease are more likely to subsequently initiate e-cigarette use.[10] Third, e-cigarettes might be more harmful to current smokers than to nonsmokers. This evidence is mixed. In one study, smokers—unlike nonsmokers—experienced equally negative acute effects on platelet function from a single vaping as they did a single smoking episode.[11] But in a subsequent experiment, cigarette smokers who actually switched to e-cigarettes experienced significant improvements in endothelial function and vascular stiffness.[12]

Bolstering the plausibility that the e-cigarette–MI link may depend on one's smoking history, e-cigarette use has been found to be associated with cardiovascular disease[13] and having had a stroke[14] among current smokers but not among nonsmokers. Treating cigarette smoking as a confounding variable—the approach taken by previous examinations of the MI–vaping link—rather than as an effect modifier does not address this issue and can cause misleading model output.[15] The present research shows that failing to account for such effect modification is a critical flaw.

PREVIOUS CROSS-SECTIONAL STUDIES LINKING MYOCARDIAL INFARCTION WITH E-CIGARETTE USE

Analyzing the 2014 and 2016 National Health Interview Survey (NHIS), Alzahrani et al.[5] probed the associations between whether one has ever suffered an MI and one's use of combustible cigarettes and e-cigarettes, modeled as 2 independent risk factors. With a host of demographic and health-related variables controlled, current and former smokers as well as daily vapers were all more likely to have suffered a previous MI. Alzahrani and colleagues[5] rightly point out that their models test for and thus demonstrate statistically independent effects of smoking and vaping, but if vaping and smoking are not actually independent contributors to identifying MI occurrence—that is, if the association between e-cigarette use and MI occurrence varies as a function of combustible cigarette use—then the main-effects model cannot be used to draw conclusions about the association between e-cigarette use and MI, independent of (or regardless of) one's history of combustible cigarette use.

Those researchers also claimed that their approach addressed reverse causality: "If someone switched from cigarettes to e-cigarettes in order to quit smoking after an MI and the increased risk was due to being a former smoker, that risk would be captured in the former smoker variable rather than appearing as an artifact in one of the e-cigarette variables" (p. 459).[5] However, former smokers compose a heterogeneous group that includes those who smoked occasionally in their teenage years and those who had a decades-long pack-a-day habit. To the extent that those in the former group are less likely both to have suffered an MI and to have taken up e-cigarettes, then reverse causality is not addressed by the independent-effects model. Finally, Alzahrani et al.[5] acknowledge that some of the MIs may have occurred before the introduction of e-cigarettes but say that these "will bias the OR estimates [of vaping on MI risk] toward the null" (p. 459). That statement's validity depends on the initiation of e-cigarettes being no greater —all else equal—among those who previously suffered an MI than among those who did not.

Bhatta and Glantz[6] replicated the vaping–MI association in Wave 1 of a longitudinal data set. In addition, these authors looked at those who were daily or current smokers at Wave 1 who did not vape. Among those subsets of respondents, those who had had an MI before Wave 1 were not more likely (than those who had not) to have switched to e-cigarettes by Wave 2. From this, they conclude that "reverse causality cannot explain the cross-sectional association between e-cigarette use and MI" (Abstract). But consider who these smokers are: they are people who have suffered a previous MI and chosen to continue to smoke. In other words, they are selected into this analysis precisely because they have demonstrated a particularly strong commitment to combustible cigarette use. It should not be surprising that these persistent smokers were not more likely to switch to vaping than those whose smoking commitment had not been similarly tested.

In fact, another analysis of this data set found that having a new MI in between these 2 waves was associated with 40% increased odds of switching off combusted tobacco (95% CI= −20, 160) and 70% increased odds of adding a noncombusted product (95% CI= −20, 270).[16] Such point estimates are suggestive that the MI −vaping link may be attributable to reverse causation; the width of the CIs speaks to the small number of respondents who suffered a new MI. The focal cross-sectional analyses that show relationships between e-cigarette use and ever having had an MI (not merely in the past few months) do not suffer the same statistical power limitations.

Finally, 2 other aspects of analyses of Bhatta and Glantz[6] call into question whether vaping causes MIs. First, whereas cigarette smoking at Wave 1 predicted a new incidence of MI at Wave 2, e-cigarette use did not. Second, Wave 1 e-cigarette use was significantly associated with MI occurrence only because the researchers included MIs that occurred before vaping could have caused the MI.[6,9] This expression of concern led to the paper of Bhatta and Glantz[6] being retracted by the editors of the *Journal of the American Heart Association*.[17] That said, other details of that paper—including improper statistical reasoning—remain quite relevant in evaluating the existing evidence that e-cigarette use may be an independent risk factor for MI.[5,7]

THE PRESENT ANALYSES

Empirically, this paper builds on previous efforts in 3 ways. First, whereas Alzahrani et al.[5] analyzed the 2014 and 2016 NHIS survey data, the present analyses include survey data from 2015 and 2017−2019 as well. Second, this investigation tests whether the association between e-cigarette use and MI depends on current or past use of combustible cigarettes. Third, this work tests supplemental models to examine whether the relationship between vaping and MI has grown over time. If the cross-sectional association emerges because vaping causes MI, then one might expect these associations to be growing (once there has been more time for e-cigarettes, a relatively new product category, to actually take a toll on cardiac health).

Most centrally, this paper presents a cautionary tale that identifies the shortcomings that have arisen in the investigation and interpretation of related data sets. Such mistakes have taken 2 forms. One issue is a failure to appreciate that model output may reveal more about the assumptions built into a model than about potentially meaningful associations in the analyzed data. A second issue relates to the practice of drawing and broadcasting causal conclusions from correlational data. In some cases, this may reflect underappreciation of what extrapolations actually are premised on causal inference.

At the same time, this study showcases how cross-sectional data can be explored to test for empirical residues that lend more plausibility to certain causal accounts than to others. That said, these efforts must be undertaken with full appreciation that such nuanced analyses remain correlational and thus cannot definitively address causality.

METHODS

Study Population

Administered by the Census Bureau, the NHIS is delivered to a random sample of U.S. adults. These analyses used the 2014−2019 surveys.

Measures

The analyses, conducted in 2020 in SPSS, version 27, included respondents (N=175,546) for whom NHIS offered complete, valid responses for the variables listed in Table 1. These variables were those used by Alzahrani and colleagues[5] in their analysis of 2 years of this data.

Statistical Analysis

Analyses used logistic regressions with MI as the dependent variable, unless stated otherwise. Such models account for NHIS's complex survey design.

RESULTS

In the first model, e-cigarette use was the only predictor (Appendix Table 2, available online). Current vapers were not more likely to have suffered an MI (than never vapers), but former vapers were less likely to have (OR=0.88, 95% CI=0.79, 0.98). The second model added combustible cigarette use as well as its interaction with e-cigarette use. Although independent effects of both e-cigarette and combustible cigarette use emerged ($p<0.001$ for both), an interaction did as well ($\chi^2[9]=111.12$, $p<0.001$). In light of the just-reported interaction, the third set of models examined the relationship between e-cigarette use and MI for each level of combustible cigarette use. Without additional covariates, e-cigarette use was associated with lower MI incidence among 5 of 12 relevant groups (Appendix Table 2, available online). The associations between lifetime MI incidence and e-cigarette use—without adjusting for the covariates—are presented merely to parallel the initial approach taken and thus facilitate a comparison with the analyses reported by Alzahrani et al.[5] These associations show sizable shifts upon the introduction of covariates, with 10 of the 12

Table 1. Measures and Raw (Unweighted) Sample Characteristics

Variables	Measures	% (*n*)
Myocardial infarction	Have you EVER been told by a doctor or other health professional that you had. . . a heart attack (also called a myocardial infarction)?	3.87 (6,788)
E-cigarette use	First question: Have you ever used an e-cigarette EVEN ONE TIME?	
Every-day	If YES, Do you now use e-cigarettes every day, some days, or not at all?	1.29 (2,262)
Some-days	If YES, Do you now use e-cigarettes every day, some days, or not at all?	1.99 (3,499)
Former	If YES, Do you now use e-cigarettes every day, some days, or not at all?	10.94 (19,212)
Never	If NO	85.77 (150,573)
Combustible cigarette use	First question: Have you smoked at least 100 cigarettes in your ENTIRE LIFE?	
Every-day	If YES, Do you NOW smoke cigarettes every day, some days, or not at all?	12.07 (21,190)
Some-days	If YES, Do you NOW smoke cigarettes every day, some days, or not at all?	3.67 (6,450)
Former	If YES, Do you NOW smoke cigarettes every day, some days, or not at all?	24.30 (42,650)
Never	If NO	59.96 (105,256)
Hypertension	Have you EVER been told by a doctor or other health professional that you had. . . Hypertension, also called high blood pressure?	34.91 (61,288)
High cholesterol	Have you EVER been told by a doctor or other health professional that you had high cholesterol?	30.14 (52,907)
Diabetes	Have you EVER been told by a doctor or other health professional that you have diabetes or sugar diabetes?	10.68 (18,745)
Sex (male)	Are you male or female?	45.99 (80,742)
Age, mean (SD)		50.58 (18.46)
BMI, mean (SD)	(calculated from height and weight)	27.99 (6.26)
Race/ethnicity		
Hispanic	If did not select "Not Hispanic/Spanish origin"	13.78 (24,195)
White	If not Hispanic and selected "White only"	66.69 (117,074)
Black	If not Hispanic and selected "Black / African American only"	11.61 (20,380)
Asian	If not Hispanic and selected "Asian only"	5.21 (9,145)
Other	If none of the above Race/ethnicity conditions met	2.71 (4,752)
N		175,546

Note: To match Alzahrani et al. (2018),[5] those who responded to the diabetes question by answering borderline were coded as not having diabetes. For age and BMI, the final column displays the mean and SD instead of a sample percentage and raw frequency count. Descriptive statistics by combustible cigarette use are provided in Appendix Table 1 (available online).

associations at least directionally strengthening and all 5 significant protective effects being eliminated. Such shifts serve as reminders that observed associations between e-cigarette use and MI are quite sensitive to model specifications.

The fourth model returned to Model 2 but added all covariates. This yielded main effects of e-cigarette (p=0.009) and combustible cigarette (p<0.001) use as well as an interaction between them (χ^2[9]=17.94, p=0.036). To interpret the interaction, the fifth set of models probed the associations between e-cigarette use and MI (controlling for the covariates) for each of the 4 levels of smoking status. Patterns of e-cigarette use were associated with MI among every-day (χ^2[3]=9.41, p=0.024) and some-days (χ^2[3]=15.97, p=0.001) smokers but not among former (χ^2[3]=6.50, p=0.090) or never (χ^2[3]=4.21, p=0.240) smokers (Table 2). These analyses allowed the associations with the covariates to vary by the level of combustible cigarette use. This model specification is most consistent with the spirit of the present investigation, which emphasizes that associations with MI may vary by combustible cigarette use. An alternate specification, which estimated the associations with the covariates when collapsing across all the levels of combustible cigarette use, returned substantively similar conclusions (Appendix Table 3, available online).

One possibility is that e-cigarettes do not contribute to MIs, but smokers who have suffered an MI or are already experiencing negative health effects from smoking may switch (or have attempted to switch) to e-cigarettes. Some may have tried e-cigarettes before reverting to daily smoking (former vaper/every-day smoker). Others may have become dual users—using both products daily (every-day vaper/every-day smoker) or alternating between the 2 across days (some-days vaper/some-days smoker)—in an effort to reduce combustible cigarette use. Some may entirely replace cigarettes with e-cigarettes (every-day vaper/former smoker). These 4 groups were the only ones for whom e-cigarette use was consistently associated with having suffered an MI. Had

Table 2. Associations With Lifetime Occurrence of MI, by Combustible Cigarette Use (Model 5)

	Combustible cigarette use			
Variables	**Every day**	**Some days**	**Former**	**Never**
E-cigarette use (omnibus test)	**$\chi^2(3)=9.41^{*}$**	**$\chi^2(3)=15.97^{**}$**	$\chi^2(3)=6.50$	$\chi^2(3)=4.21$
Every day	**1.94*** **(1.07, 3.50)**	0.53 (0.20, 1.39)	**1.57*** **(1.07, 2.30)**	1.65 (0.51, 5.32)
Some days	1.33 (0.96, 1.86)	**2.58***** **(1.48, 4.50)**	1.22 (0.65, 2.29)	2.55 (0.77, 8.51)
Former	**1.23*** **(1.02, 1.47)**	1.50 (0.99, 2.27)	1.13 (0.90, 1.41)	0.76 (0.46, 1.27)
Never	ref	ref	ref	ref
Hypertension	**2.52***** **(2.04, 3.13)**	**3.32***** **(2.23, 4.93)**	**1.87***** **(1.64, 2.14)**	**2.43***** **(2.12, 2.79)**
High cholesterol	**2.57***** **(2.11, 3.12)**	**2.52***** **(1.78, 3.59)**	**2.47***** **(2.19, 2.78)**	**2.20***** **(1.95, 2.48)**
Diabetes	**2.08***** **(1.71, 2.53)**	1.47 (0.97, 2.22)	**1.93***** **(1.71, 2.18)**	**1.95***** **(1.71, 2.22)**
Sex (male)	**1.99***** **(1.67, 2.38)**	**1.89***** **(1.33, 2.68)**	**1.97***** **(1.77, 2.19)**	**2.08***** **(1.84, 2.33)**
Age, mean (SD)	**1.05***** **(1.04, 1.06)**	**1.06***** **(1.05, 1.07)**	**1.06***** **(1.05, 1.06)**	**1.06***** **(1.05, 1.07)**
BMI, mean (SD)	1.00 (0.98, 1.01)	1.02 (0.99, 1.05)	1.00 (0.99, 1.01)	**1.02***** **(1.01, 1.03)**
Race/ethnicity (omnibus test)	**$\chi^2(4)=15.90^{**}$**	$\chi^2(4)=8.41$	$\chi^2(4)=9.46$	**$\chi^2(4)=31.18^{***}$**
n	21,190	6,450	42,650	105,256

Note: Boldface indicates statistical significance ($^{*}p<0.05$; $^{**}p<0.01$; $^{***}p<0.001$).
Rows below E-cigarette use and above race/ethnicity contain adjustable ORs (95% CI). Appendix Table 3 (available online) includes estimates of the effects of e-cigarette use for each level of combustible cigarette use without permitting the estimates of the covariates to vary by combustible cigarette use.
MI, myocardial infarction.

the NHIS data identified the timing of MIs with respect to e-cigarette initiation, this also could have helped in evaluating the plausibility of reverse causality (MI encourages e-cigarette initiation) but not that of third-variable causality (smoking-related health deterioration may encourage e-cigarette initiation and foretell MI).

An alternative possibility is that these data do reflect that e-cigarettes causally contribute to subsequent MI, but the relative newness of the vapor product category means that there has been less time for e-cigarettes to cause MIs for those without a history of smoking (and the cardiovascular decline that promotes). By this interpretation of the cross-sectional association, one might expect the vaping–MI association to be increasing from 2014 to 2019, with e-cigarettes' potential negative effects manifesting themselves more clearly over time. The authors returned to the independent-effects model of Alzahrani and colleagues[5] but added in an effect of year (continuous) as well as its interaction with e-cigarette use and combustible cigarette use. The only significant secular trend to emerge was on the MI incidence of every-day e-cigarette users (AOR=0.81, 95% CI=0.67, 0.98, p=0.029). This reflects that the association between daily vaping and MI has not increased but has declined over time. Keep in mind that few secular trends reflect truly linear shifts. Appendix Table 4 (available online) presents the specific associations between MI and both e-cigarette use and combustible cigarette use by year, thereby detailing the more precise trajectory of the secular trend observed in the data.

It is doubtful that this reflects a reduction in e-cigarettes' riskiness. Given the public's growing skepticism toward e-cigarettes,[4,18] this may reflect the most at-risk smokers becoming less likely to switch to e-cigarettes. Some of such smokers quit using other means, whereas others continue to use combustible cigarettes. Indeed, current e-cigarette use has declined among current and former smokers (compared with use among never smokers) as well as among those who have (versus among those who have not) experienced an MI (p<0.002 for all) (Appendix Table 5, available online). Although current e-cigarette use among those who have not suffered an MI has shown a modest annual uptick (AOR=1.04, 95% CI=1.01, 1.07), e-cigarette use among MI sufferers has shown a more precipitous annual decline (AOR=0.78, 95% CI=0.70, 0.88). Such a drop was not observed in these MI sufferers' current combustible cigarette use

(AOR=0.96, 95% CI=0.92, 1.01). Instead of identifying the burgeoning risk posed by e-cigarettes, previous research may simply have helped to shape a public narrative that has discouraged health-compromised smokers from seeing e-cigarettes as a means of harm reduction.

Finally, consider this illustration of how previous researchers' modeling assumptions permitted the (misleading) demonstration that e-cigarette use alone is a risk factor for MI. Table 3 shows the raw frequencies of MI occurrence among e-cigarette users who vary in their smoking history. Among every-day vapers, 90 had suffered an MI. Only 3 of them had not smoked. Only 1 of these 3—a 51-year-old woman who was overweight (BMI>27) and had a history of hypertension and high cholesterol—was in the data set used to justify the conclusion that for users of e-cigarettes alone, the "risk of heart attacks is double for daily e-cigarette users" (Fernandez, press release August 21, 2018).

Given the range of covariates used, is this an appropriate extrapolation? To see why not, consider what happens after the removal of all 25 respondents from the data set who have ever vaped, never smoked, and suffered an MI. By the independent-effects model of Alzahrani et al.,[5] one would still find that even with no history of smoking, vaping every day (AOR=1.55, 95% CI=1.11, 2.15), vaping some days (AOR=1.43, 95% CI=1.11, 1.85), or having formerly vaped (AOR=1.16, 95% CI=1.03, 1.32) all significantly elevate one's risk of having had an MI. The independent-effects model by (improper) design smooths the extent to which e-cigarette use is associated with MI incidence to be equivalent across all 4 smoking status levels.

DISCUSSION AND CONCLUSIONS

Analyzing 6 years (2014–2019) of NHIS data, this study found that the association between e-cigarette use and lifetime history of MI depends on one's history of combustible cigarette use. Among those without a history of smoking, the use of e-cigarettes—past or present—was not associated with MI incidence. Daily e-cigarette use was associated with higher MI incidence only among every-day and former combustible cigarette users. These results are inconsistent with the conclusions of Alzahrani and colleagues[5] that e-cigarette use alone—independent of combustible cigarette use—is associated with MI. Furthermore, the association between every-day e-cigarette use and ever having had an MI is declining. This may reflect health-compromised smokers' growing skepticism toward the relative benefits of vaping, a possibility supported by the shifting patterns of who currently uses e-cigarettes.

Modeling Risks as Independent Does Not Assess Whether Risks Are Independent

In a published reply to Alzahrani et al.,[5] it was argued that it would be important to examine the association between e-cigarette use and MI in never smokers.[19] Two of the original authors (Alzahrani and Glantz) replied that "We do not need to perform this type of analysis. . . because we used multivariable analysis which is adjusted for confounding factors including smoking."[20] This reply reinforced a statement Alzahrani and colleagues[5] wrote in their original paper: "The fact that the use of e-cigarettes and conventional cigarettes are both included in the same logistic regression means that they both independently contribute to the risk of having had an MI" (p. 457).

These statements confuse an assumption that the researchers themselves placed into their model (that e-cigarettes and conventional cigarettes pose independent risks) with the conclusions that their model output permitted. The presently observed e-cigarette use by combustible cigarette use interaction threatens this assumption's validity. That said, Alzahrani and Glantz's point that subsetting the data can "severely limit the sample size and reduce power to detect a true effect" (p. 569)[20] deserves a sympathetic ear. A more dispassionate analysis would acknowledge that because e-cigarettes are both a relatively new product category[21] and are

Table 3. Frequency of MI Occurrence for Respondents, by E-Cigarette and Combustible Cigarette Use

	Combustible cigarette use			
E-cigarette use	**Every day**	**Some days**	**Former**	**Never**
Every day	35/499 (6.55%)	6/278 (2.16%)	46/1,264 (3.64%)	3/186 (1.61%)
Some days	91/1,826 (4.98%)	31/588 (5.27%)	18/569 (3.16%)	3/516 (0.58%)
Former	442/8,442 (5.24%)	67/2,003 (3.34%)	152/4,444 (3.42%)	19/4,323 (0.44%)
Never	612/10,388 (5.89%)	150/3,581 (4.19%)	2,720/36,373 (7.48%)	2,393/100,231 (2.39%)

Note: Appendix Table 6 (available online) provides this information for never-smoking respondents by year.
MI, myocardial infarction.

disproportionately used by current and former smokers, then it is not currently possible to know whether e-cigarette use alone leads to (much less is reliably associated with) MI. Leaning on an independent-effects model—whether in a cross-sectional or in longitudinal design[10]—does not provide the power to detect a true effect but merely the power to document a mis-specified one.

These points encourage a more nuanced discussion about the potential for both Type I and Type II error in this work. The present investigation's model specifications largely deferred to decisions made by Alzahrani et al.[5] (e.g., the selection of covariates) to avoid the post hoc embrace of model specifications, a practice that can inflate Type I error. That said, confidence in the reliability of and explanation for certain novel patterns, such as the declining association between every-day e-cigarette use and MI, would be bolstered by the examination of independent data sets that permit tests of the same associations or the proposed explanations for them. For example, is there other evidence that the associations between regular e-cigarette use and MI (as well as other smoking-related diseases) decline or rise as public perceptions of e-cigarette risk rise or fall, respectively?

The potential for Type II error—for example, with a premature conclusion that current or former e-cigarette use is not associated with higher or lower incidence of MI for never smokers—can arise because of limited statistical power. Such a limitation is, at least in theory, addressable by recruiting larger samples (e.g., of never-smoking current and former e-cigarette users.) Relatedly, even if such an association does not actually exist today, this does not preclude the possibility that it may emerge in the future. Of course, such epistemic honesty about the limits of empirical observation should not become rhetorically misused as fearmongering innuendo. As society seeks out innovative solutions to pressing public health problems (e.g., the coronavirus disease 2019 [COVID-19] pandemic, the tobacco epidemic), it must distinguish what is presently unknown from what is presently unknowable. As an example, vaccine naysayers attempt to exploit the present unobservability of the future to encourage vaccine hesitancy.

Correlation Is Not Causation: Acknowledged but Soon Forgotten

The present results, which cast doubt on the interpretation that e-cigarette use has led to MI, raise a second issue with much broader implications. When researchers report cross-sectional analyses, it is common to acknowledge that such designs do not permit causal conclusions. Alzahrani and colleagues[5] follow this custom: "The NHIS is a cross-sectional study, so it only permits identifying associations rather than causal relationships" (p. 459). But then, the authors leaned on their model output to simulate different counterfactual scenarios—for example, by asking how the "odds of having had a heart attack for an individual who

Table 4. Examples of Authors' Public Communications of Cross-Sectional Vaping–MI Associations They Observed

Researcher	Date	Outlet	Researcher's communication
Stanton A. Glantz	February 24, 2018	UCSF blog[a]	"First evidence of long-term health damage from ecigs: Smoking e-cigarettes daily doubles risk of heart attacks" (Title)
Stanton A. Glantz	August 21, 2018	UCSF press release[b]	"While people may think they are reducing their health risks, we found that the heart attack risk of e-cigarettes adds to the risk of smoking cigarettes. Using both products at the same time is worse than using either one separately. Someone who continues to smoke daily while using e-cigarettes daily increases the odds of a heart attack by a factor of five."
Stanton A. Glantz	June 6, 2019	UCSF blog[c]	"More Evidence That E-cigs Cause Heart Attacks" (Title)
Dharma N. Bhatta	June 7, 2019	Public statement to San Francisco Public Safety and Neighborhood Services Committee accompanying submission of Bhatta and Glantz (2019)[6] as evidence at a public hearing[d]	"I would like to support banning e-cigarettes. E-cigarettes increase the risk of heart attacks."

[a]https://tobacco.ucsf.edu/first-evidence-long-term-health-damage-ecigs-smoking-e-cigarettes-daily-doubles-risk-heart-attacks.
[b]https://tobacco.ucsf.edu/risk-heart-attacks-double-daily-e-cigarette-users.
[c]https://tobacco.ucsf.edu/more-evidence-e-cigs-cause-heart-attacks-time-path.
[d]https://www.youtube.com/watch?v=ilpP_Vc9w3k. All retrieved October 14, 2020.
MI, myocardial infarction; UCSF, University of California, San Francisco.

switched from daily smoking to daily e-cigarette use would change" (p. 457). Note that this is a causal question[22]: if a specific person changes their behavior (from smoking to vaping), what is the resulting likelihood that *that* person would have an MI? By analogy, if one models height as a function of weight, one cannot then use that output to play out counterfactual scenarios to learn how much shorter a person will become upon losing weight. This is in essence what Alzahrani et al.[5] have done, an inferential misstep they recommit themselves to elsewhere.[23] Furthermore, that they drew policy conclusions from their approach ("From these findings... use of e-cigarettes for smoking cessation should not be recommended," p. 460)[5] reflects a continued reliance on their results as causal evidence.

A separately published response criticized Alzahrani and colleagues[5] for blurring correlation with causation by noting that their "'increased risk' claim clearly implies... that e-cigarette use precedes MI and e-cigarette use caused the MI" (p. 626).[24] Alzahrani and Glantz[25] replied that "we clearly only used terms consistent with 'associations' when reporting the findings of our study" (p. 627). This reply is suspect for 2 reasons. First, when A is said to be a risk factor for B, it need not mean that A causes B, but without clarification, it does not imply that B may cause A. After all, malnutrition is a risk factor for premature death. Premature death is not a risk factor for malnutrition. Second, (non-peer-reviewed) public communication of the authors' cross-sectional findings actively promoted the causal interpretation that e-cigarette use causes MI (Table 4).

The scientific community is well aware that press releases, blog posts, and public activism are not subject to peer review. That same community should be wary of its members who speak with one voice when accountable to peer review but then use the legitimizing power of peer review as a credential that assists with the misbroadcasting of their published findings. Sound science, shaped and strengthened by a strong peer-review process, is a valuable contributor to public policy and clinical recommendation. When the integrity of this process is abused, the legitimacy of the scientific community's collective institutions is damaged.

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To facilitate further analyses, the authors of this paper make public the transformed data set and analysis script used in these analyses at the following link: https://osf.io/4pu2m/.

CRC analyzed the data and drafted the Methods, Results, and Discussion. Both CRC and MS drafted the Introduction and provided critical revisions to each other's writing.

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SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at https://doi.org/10.1016/j.amepre.2021.05.003.

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