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Is e-cigarette use associated with coronary heart disease and myocardial infarction? Insights from the 2016 and 2017 National Health Interview Surveys

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Abstract

Background: This study analyzed the National Health Interview Surveys (NHIS) of 2016 ($n = 33,028$) and 2017 ($n = 26,742$) to examine whether e-cigarette use is consistently associated with myocardial infarction (MI) and coronary heart disease (CHD).

Methods: Surveys were examined separately and pooled. Logistic regression analysis was used, with demographics, e-cigarette use, smoking and risk factors for CHD (hypertension, hypercholesterolemia, and diabetes) being independent variables. Former smokers were subclassified according to quit duration (≤ 6 and > 6 years).

Results: For MI, an association was observed with some days e-cigarette (but not daily) use in the 2017 survey (OR: 2.11, 95% CI: 1.14–3.88, $p = 0.017$). No statistically significant association was observed in the pooled analysis (daily e-cigarette use: OR: 1.35, 95% CI: 0.80–2.27, $p = 0.267$). For CHD, an association was observed with daily e-cigarette use in the 2016 survey (OR: 1.89, 95% CI: 1.01–3.53, $p = 0.047$). From the pooled analysis, no association was found between any pattern of e-cigarette use and CHD. In single-year and pooled analysis, both MI and CHD were strongly associated with all patterns of smoking, hypertension, hypercholesterolemia, diabetes, and age.

Conclusions: The pooled analysis of the 2016 and 2017 NHIS showed no association between e-cigarette use and MI or CHD. The associations between established risk factors, including smoking, and both conditions were remarkably consistent. The inconsistent associations observed in single-year surveys and the cross-sectional design of the NHIS cannot substantiate any link between e-cigarette use and an elevated risk for MI or CHD. Longitudinal studies are needed to explore the effects of e-cigarette use on cardiovascular disease.

Keywords: coronary heart disease, electronic cigarettes, myocardial infarction, National Health Interview Survey, smoking

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Introduction

Cigarette smoking is a well-known risk factor for the development of atherosclerosis and cardiovascular disease (CVD).[1] Although the precise mechanisms remain uncertain, several harmful constituents in cigarette smoke have been shown to elicit detrimental responses in the endothelium with resulting alterations of hemostasis and increased platelet activation.[2–4] This could have significant implications for the initiation and development of atherothrombosis, as already extensively demonstrated with other well-known risk factors for coronary heart disease (CHD) such as hypertension and hypercholesterolemia.[5,6] As a consequence, chronic exposure to cigarette smoke can induce a persistent state of activation of the endothelial–coagulative system and abstinence from smoking may result in the

amelioration of several endothelial and coagulative abnormalities.[7]

Electronic cigarettes (e-cigarettes), an emerging alternative to combustible cigarettes, do not contain tobacco, create smoke, or rely on combustion to operate. Although not completely risk free, the level of chemical constituents in e-cigarette aerosol emissions under normal conditions of use have been shown to be substantially lower compared to cigarette smoke.[8–10] However, in laboratory studies of human cell lines, incubation with e-cigarette extracts increased the release of inflammatory mediators.[11] In addition, e-cigarette aerosol emissions elicited platelet activation, aggregation, and adhesion.[12] In mice, chronic whole body exposure to e-cigarette aerosol emissions accelerates aortic stiffness, significantly impairs aortic endothelial function and may lead to impaired cardiac function.[13] In acute clinical studies of healthy smokers, e-cigarettes and combustible cigarettes exhibit similar inhibition of endothelial function as measured by flow-mediated dilation of arteries,[14] enhanced sympathetic activity,[14] and impaired aortic elasticity.[15] While these effects are associated with increased cardiac risk,[16,17] this is relevant when measured in resting conditions and not after acute intake of a stimulant such as nicotine. In fact, similar acute effects have been observed with nicotine replacement therapies or even caffeine.[18–20] The acute sympathetic effects of nicotine could potentially contribute to acute cardiovascular events, especially in those with underlying coronary heart disease.[21]

In light of the well-established adverse effects of smoking and the potential of e-cigarettes to substitute for smoking as part of a harm reduction strategy, it is important to examine the association between e-cigarettes and heart disease. A recent study presented a pooled analysis of the National Health Interview Survey (NHIS) for 2014 and 2016, a large, annual cross-sectional survey of adults in the US.[22] The study found that daily e-cigarette use was associated with having had a myocardial infarction (MI). Well-established risk factors for MI (including hypertension, hypercholesterolemia, diabetes, age, and smoking) were also significantly associated with MI. While the analysis of cross-sectional studies limits the interpretation of association as causation, such studies are valuable considering the time needed to obtain prospective epidemiological data. In addition, consistency is important in establishing associations and causal links between exposure and disease.[23] Therefore, this study used data from the most recent NHIS with publicly available datasets (2016 and 2017) to examine the association between e-cigarette use and MI and CHD. Other well-established risk factors for MI and CHD (including cigarette smoking, hypertension, hypercholesterolemia, and diabetes) were examined for consistency in the NHIS 2016 and 2017 datasets.

Methods

Study sample

The NHIS is a survey conducted by the National Center for Health Statistics (NCHS) since 1960. It is a cross-sectional household interview survey of non-institutionalized US civilians.[24] The 'Sample Adult Public Use Files' of 2016 ($n = 33{,}028$) and 2017 ($n = 26{,}742$) were used in this analysis, which contains the responses of US adults (aged ≥ 18 years). The two datasets were analyzed separately and were also pooled and treated as 1 year with a very large sample size. No ethics committee approval was sought for this study because the datasets were anonymized and are publicly available through the US Centers for Disease Control and Prevention website.

Measures

The survey included demographic data of which age, gender, and race were used in this analysis. For race, participants were classified as White, Black or African American, American Indian or Alaska Native (AIAN), Asian, and Multiple Race. Another response option, 'race group not releasable' was recorded together with Multiple Race due to the small sample size ($n = 157$). Hispanics were included in the 'White' category.

For CHD, participants were asked 'Have you ever been told by a doctor or other health professional that you had coronary heart disease?'. Those responding 'yes' were classified as having CHD. For MI, participants were asked: 'Have you ever been told by a doctor or other health professional that you had a heart attack (also called myocardial infarction)?'. Those responding 'yes' were classified as having had an MI.

Risk factors for MI and CHD recorded in the surveys were hypertension (participants were asked 'Have you ever been told by a doctor or other health professional that you had hypertension, also called high blood pressure?'), hypercholesterolemia (participants were asked: 'Have you ever been told by a doctor or other health professional that you had high cholesterol?') and diabetes (participants were asked 'Have you ever been told by a doctor or other health professional that you have diabetes or sugar diabetes?'). The responses about diabetes were coded as yes, no, and borderline or prediabetes.

Never smokers were defined in the survey based on a cut-off point of using 100 cigarettes in their life (participants were asked 'Have you smoked at least 100 cigarettes in your entire life?'). Those responding 'no' were classified as never smokers. Those responding 'yes' were subsequently asked about current smoking (participants were asked 'Do you now smoke cigarettes every day, some days, or not at all?'). This question was used to define daily and some days smokers, while former smokers were defined as those responding 'yes' to the question about ever smoking and 'not anymore' to the question about current smoking. It is important to note that the duration of smoking cessation is negatively associated with CVD and mortality risk.[25–30] At the same time, e-cigarette use was rare before 2010, and a very small proportion of former smokers who had quit before 2010 were using e-cigarettes in the US.[31,32] To address this, the question 'How long has it been since you quit smoking cigarettes?' was used to subclassify former smokers according to quit duration as former smokers of $\leqslant$6 years and former smokers of $>$6 years. Additional analyses were performed using difference cutoff points (quit duration of 7 years, 8 years, and 10 years).

Ever e-cigarette use was determined by asking: 'Have you ever used an e-cigarette even one time?'. Those responding 'no' were classified as never users. Those responding 'yes' were subsequently asked about current e-cigarette use (participants were asked 'Do you now use e-cigarettes every day, some days, or not at all?'). This question was used to define daily and some days e-cigarette users, while former e-cigarette users were defined as those responding 'yes' to the question about ever e-cigarette use and 'not anymore' to the question about current e-cigarette use.

For all questions, responses coded in the dataset as 'refused,' 'not ascertained,' and 'don't know' were excluded from the analysis.

Statistical analysis

Continuous variables were presented as mean (SD) and categorical variables as a number (%). Comparisons between e-cigarette groups were performed using one-way analysis of variance (ANOVA) or cross-tabulations and chi-squared tests. Logistic regression analyses were performed to examine the association between e-cigarette use and MI and CHD. The independent variables that were included in the models were demographics (age, gender, race/ethnicity, e-cigarette use (classified as daily, few days, former, and never used), smoking (same classification as for e-cigarettes), other established risk factors for CVD (hypertension, hypercholesterolemia, and diabetes) and body-mass index (BMI). The reference condition for both e-cigarette use and cigarette smoking was never use. As mentioned above, the smoking status was classified as daily, some days, former of $\leqslant$6 years, former of $>$6 years, and never smokers, while additional analyses were performing using quit duration cutoff points of 7 years, 8 years, and 10 years.

To further examine the association between e-cigarette use and MI and CHD without considering the effects of smoking, an attempt to perform the same logistic regression analyses among never smokers was performed. This was not successful because of no or a low number of never-smoking daily and some days e-cigarette users who reported having had an MI or having CHD.

All statistical analyses were weighted by primary sampling unit, sampling stratum, and sampling weight, and were performed using Stata v.13.0 (http://www.stata.com) according to recommendations described by the NCHS.[24] It should be emphasized that the years being pooled (2016 and 2017) fall within the same sample design period with the same public use design variables.[23] Thus the two datasets can be pooled into one dataset and treated as 1 year of data with a very large sample size.[24] The pooled analyses were performed to increase the statistical power, considering the low proportion of the population using e-cigarette users (especially daily users). In addition, results were presented separately for each

year to examine the consistency in the observed associations between years. According to the NCHS recommendations, the sample weight in the pooled dataset was divided by the number of years that were being pooled (i.e. by two).[24]

Results

Participant demographics, smoking status, risk factors, and prevalence of MI and CHD are presented from the pooled analysis, separately for each e-cigarette use group, in Table 1. More than 90% of daily and less than 80% of some days e-cigarette users were smokers or former smokers. As observed in previous studies, e-cigarette use, particularly daily e-cigarette use, was far more prevalent in former smokers of ⩽6 years compared with former smokers of >6 years.

Table 2 presents the results of the logistic regression analysis for MI. From the 2016 NHIS, no statistically significant association was observed between MI and any pattern of e-cigarette use (daily, some days, and former e-cigarette use). From the 2017 NHIS, only some days e-cigarette use was associated with having had MI ($p = 0.017$). From the pooled analysis, no statistically significant association was observed between MI and daily ($p = 0.267$), some days ($p = 0.373$), or former e-cigarette use ($p = 0.720$). All regression models showed consistent strong associations between all established risk factors (cigarette smoking, hypertension, hypercholesterolemia, and diabetes) and having had MI ($p < 0.001$ for all). For smoking, all use patterns (daily, some days, and former smoking) were significantly associated with MI ($p \leqslant 0.001$ for all). Compared with former smokers of ⩽6 years, former smokers of >6 years had lower odds of having had an MI (pooled analysis OR: 0.54, 95% CI: 0.43–0.68, $p < 0.001$). A significant consistent association with MI was also observed for age and gender ($p < 0.001$ for both), but not for BMI.

Table 3 presents the results of the logistic regression analysis for CHD. From the 2016 NHIS, daily e-cigarette use was significantly associated with having CHD ($p = 0.047$), while no association was observed for some days and former e-cigarette use. From the 2017 NHIS, no pattern of e-cigarette use was associated with having CHD. From the pooled analysis, no pattern of e-cigarette use was associated with having CHD. All regression models showed consistent strong associations between all established risk factors (cigarette smoking, hypertension, hypercholesterolemia, and diabetes) and having CHD. For smoking, all use patterns (daily, some days, and former smoking) were significantly associated with having CHD ($p \leqslant 0.001$ for all except some days smoking in the 2016 survey where $p = 0.024$). Compared to former smokers of ⩽6 years, former smokers of >6 years had lower odds of having CHD (pooled analysis OR: 0.73, 95% CI: 0.59–0.91, $p = 0.005$). A significant consistent association with CHD was also observed for age and gender ($p < 0.001$ for both), but not for BMI.

Supplementary Table 1 presents the association between e-cigarette use and MI and CHD from the pooled analysis using different cutoff points to subclassify former smokers (7 years, 8 years, and 10 years). The results were almost identical to those using a cutoff value of 6 years, with no statistically significant association between e-cigarette use and CVD conditions.

Discussion

This study examined the association between e-cigarette use and two CVD conditions, MI and CHD, in a large cross-sectional study in the US. All major risk factors for these conditions that were recorded in the surveys were included in the analysis. The main findings of the study were that, while all of the risk factors were consistently and significantly associated with both MI and CHD, inconsistent associations with e-cigarette use were observed, with no association found between any pattern of e-cigarette use and MI or CHD from the pooled analysis. This inconsistency, combined with the inherent limitations of cross-sectional surveys, provides no definite or indirect evidence that e-cigarette use is causally linked with heart disease.

A characteristic of this analysis was the highly consistent and statistically significant positive associations between long-established risk factors, namely smoking, hypertension, hypercholesterolemia, diabetes, and age, and both MI and CHD. Findings were similar in both single-year and pooled analysis. This is expected considering the strong epidemiological data that have established the link between these conditions and heart disease. All patterns of smoking (every day, some

Table 1. Sample characteristics according to e-cigarette use status, NHIS 2016 and 2017 (pooled).

Variable	E-cigarette use, % (*n*)				*p* value
	Daily *n* = 714	Some days *n* = 1009	Former *n* = 7026	Never *n* = 50830	
Age	43.3 (15.7)	41.2 (15.5)	41.0 (15.6)	52.2 (18.6)	<0.001
Gender					
Male	58.2% (387)	56.7% (535)	55.3% (3621)	46.9% (22441)	<0.001
Female	41.8% (327)	43.3% (474)	44.8% (3405)	53.1% (28389)	
BMI, kg/m² mean (SD)	30.6 (14.4)	29.2 (11.5)	29.5 (12.1)	30.4 (14.2)	<0.001
Race					
White	84.8% (617)	82.0% (847)	82.8% (5902)	77.4% (40478)	<0.001
Black/African American	6.2% (35)	10.2% (80)	9.1% (567)	12.9% (5956)	
AIAN	1.7% (13)	1.2% (11)	1.3% (99)	1.1% (539)	
Asian	3.5% (21)	2.5% (26)	3.3% (202)	6.8% (2817)	
Multiple/not releasable	3.8% (28)	4.2% (45)	3.5% (256)	1.9% (1040)	
Smoking					
Daily	19.6% (154)	49.3% (545)	41.6% (3131)	6.0% (3354)	<0.001
Some days	12.0% (88)	16.2% (163)	10.2% (728)	2.3% (1182)	
Former ⩽6 years	54.1% (380)	13.7% (137)	16.9% (1166)	4.1% (2177)	
Former >6 years	5.2% (40)	2.9% (28)	5.3% (405)	17.8% (10316)	
Never	9.1% (52)	17.9% (134)	25.8% (1580)	69.7% (33657)	
Risk factors for CVD					
Hypertension	27.5% (211)	26.1% (280)	25.2% (1941)	31.9% (18567)	<0.001
Hypercholesterolemia	27.1% (206)	21.5% (246)	22.2% (1703)	28.9% (16243)	<0.001
Prediabetes	1.9% (18)	2.4% (25)	2.2% (155)	2.8% (1476)	<0.001
Diabetes	7.6% (53)	7.3% (85)	7.1% (528)	9.8% (5649)	<0.001
MI	4.2% (32)	3.3% (44)	2.7% (232)	3.2% (1993)	0.177
CHD	4.2% (33)	2.9% (38)	2.9% (258)	4.6% (2893)	<0.001

AIAN, American Indian or Alaska Native; BMI, body mass index; CHD, coronary heart disease; CVD, cardiovascular disease; MI, myocardial infarction.

days, and former smoking) were strongly associated with both disease conditions. This is consistent with the already demonstrated causal effect of smoking on heart disease. The association with former smoking is also expected because some smokers may have quit after developing the

Table 2. Logistic regression analyses of the association between e-cigarette use and myocardial infarction, NHIS 2016 and 2017.

Myocardial infarction	2016			2017			2016 and 2017 (pooled)		
	OR	95% CI	*p* value	OR	95% CI	*p* value	OR	95% CI	*p* value
E-cigarette use									
Never (referent)									
Daily	1.51	0.85–2.67	0.157	1.07	0.36–3.16	0.907	1.35	0.80–2.27	0.267
Some days	0.74	0.40–1.36	0.330	2.11	1.14–3.88	**0.017**	1.22	0.78–1.91	0.373
Former	0.89	0.65–1.23	0.491	1.02	0.76–1.39	0.875	0.96	0.77–1.20	0.720
Smoking									
Never (referent)									
Daily	3.09	2.39–4.01	**<0.001**	3.20	2.48–4.14	**<0.001**	3.13	2.63–3.73	**<0.001**
Some days	2.23	1.47–3.37	**<0.001**	2.73	1.79–4.15	**<0.001**	2.47	1.79–3.40	**<0.001**
Former ⩽6 years	3.09	2.24–4.25	**<0.001**	2.54	1.79–3.60	**<0.001**	2.82	2.22–3.57	**<0.001**
Former >6 years	1.41	1.18–1.69	**<0.001**	1.63	1.34–1.99	**<0.001**	1.51	1.32–1.74	**<0.001**
Hypertension	2.09	1.73–2.52	**<0.001**	2.23	1.81–2.76	**<0.001**	2.16	1.87–2.50	**<0.001**
Hypercholesterolemia	2.47	2.05–2.97	**<0.001**	2.55	2.12–3.07	**<0.001**	2.5	2.19–2.85	**<0.001**
Blood glucose									
Prediabetes	1.43	0.97–2.11	0.074	1.08	0.72–1.61	0.716	1.23	0.93–1.62	0.153
Diabetes	1.90	1.56–2.32	**<0.001**	1.84	1.50–2.26	**<0.001**	1.87	1.62–2.15	**<0.001**
Gender									
Male (referent)									
Female	0.45	0.38–0.54	**<0.001**	0.51	0.43–0.60	**<0.001**	0.48	0.43–0.54	**<0.001**
Race									
White (referent)									
Black/African American	0.83	0.65–1.07	0.152	1.19	0.91–1.55	0.195	1.00	0.84–1.20	0.993
AIAN	2.99	1.37–6.50	**0.006**	0.45	0.16–1.22	0.116	1.47	0.77–2.84	0.245
Asian	0.49	0.27–0.86	**0.014**	0.84	0.50–1.40	0.498	0.66	0.45–0.98	**0.038**
Multiple/not releasable	1.54	0.74–3.21	0.252	1.00	0.59–1.68	0.991	1.23	0.77–1.97	0.380
Age (per year)	1.06	1.05–1.07	**<0.001**	1.06	1.05–1.06	**<0.001**	1.06	1.05–1.06	**<0.001**
BMI (per unit)	1.00	0.99–1.01	0.519	1.00	1.00–1.01	0.367	1.00	1.00–1.01	0.923

AIAN, American Indian or Alaska Native; BMI, body mass index.

Table 3. Logistic regression analysis of the association between e-cigarette use and coronary heart disease, NHIS 2016 and 2017.

Coronary heart disease	2016			2017			2016 and 2017 (pooled)		
	OR	95% CI	*p* value	OR	95% CI	*p* value	OR	95% CI	*p* value
E-cigarette use									
Never (referent)									
Daily	1.89	1.01–3.53	**0.047**	0.66	0.29–1.48	0.312	1.31	0.79–2.17	0.286
Some days	0.93	0.51–1.70	0.814	1.48	0.74–2.94	0.268	1.13	0.70–1.83	0.624
Former	1.06	0.79–1.41	0.715	1.00	0.73–1.37	0.978	1.03	0.83–1.28	0.772
Smoking									
Never (referent)									
Daily	1.55	1.23–1.96	**<0.001**	1.94	1.51–2.48	**<0.001**	1.73	1.46–2.05	**<0.001**
Some days	1.57	1.06–2.32	**0.024**	1.96	1.30–2.96	**0.001**	1.75	1.32–2.32	**<0.001**
Former ⩽6 years	1.88	1.42–2.48	**<0.001**	2.06	1.47–2.88	**<0.001**	1.96	1.58–2.44	**<0.001**
Former >6 years	1.34	1.15–1.55	**<0.001**	1.53	1.30–1.80	**<0.001**	1.43	1.28–1.60	**<0.001**
Hypertension	2.53	2.12–3.02	**<0.001**	2.52	2.07–3.07	**<0.001**	2.53	2.22–2.89	**<0.001**
Hypercholesterolemia	2.77	2.37–3.24	**<0.001**	2.43	2.06–2.87	**<0.001**	2.59	2.32–2.90	**<0.001**
Blood glucose									
Prediabetes	1.09	0.80–1.49	0.583	1.18	0.82–1.72	0.368	1.14	0.90–1.45	0.153
Diabetes	1.74	1.46–2.06	**<0.001**	1.67	1.40–1.98	**<0.001**	1.70	1.51–1.93	**<0.001**
Gender									
Male (referent)									
Female	0.56	0.49–0.64	**<0.001**	0.54	0.47–0.62	**<0.001**	0.55	0.50–0.61	**<0.001**
Race									
White (referent)									
Black/African American	0.96	0.77–1.20	0.717	1.03	0.82–1.28	0.819	0.99	0.85–1.15	0.912
AIAN	1.43	0.74–2.75	0.288	0.23	0.07–0.68	**0.009**	0.73	0.43–1.26	0.260
Asian	0.64	0.43–0.97	**0.036**	0.93	0.64–1.36	0.707	0.79	0.59–1.04	0.092
Multiple/not releasable	1.71	0.92–3.18	0.089	1.03	0.62–1.71	0.914	1.31	0.86–2.01	0.213
Age (per year)	1.06	1.06–1.07	**<0.001**	1.07	1.06–1.07	**<0.001**	1.06	1.06–1.07	**<0.001**
BMI (per unit)	1.00	0.99–1.00	0.397	1.00	0.99–1.01	0.878	1.00	1.00–1.00	0.641

AIAN, American Indian or Alaska Native; BMI, body mass index.

disease while quitting smoking is only gradually and over many years reducing the risk of developing heart disease.[25–29] The latter was the main reason for subclassifying smokers according to quit duration in the present study, since e-cigarette use is a recent phenomenon and was rarely observed before 2010.[32,33] This approach probably provides a useful methodological insight for the future assessment of the association between e-cigarette use and CVD in population studies.

The associations between e-cigarette use and CVD were highly inconsistent and were only observed in single-year surveys for some patterns of use. Unlike daily use, low e-cigarette use intensity (i.e. some days use) was found to be associated with MI in the 2017 survey, which could be characterized as a 'paradox'. These inconsistent findings could be related to the high prevalence of current or former smoking among e-cigarette users, especially among daily and some days users. Thus, the association between some days (but not daily) e-cigarette use and MI in the 2017 survey and between daily e-cigarette and CHD in the 2016 survey cannot be considered as strong evidence for a causal link.

Another concern that has been expressed about e-cigarettes is dual use (i.e. both smoking and using e-cigarettes). A recent study analyzed the 2016 and 2017 Behavioral Risk Factor Surveillance System and found a statistically significant association between dual use and CVD.[34] However, an analysis among never smokers found no association between any pattern of e-cigarette use and CVD. The findings suggest that e-cigarette exposure may be harmful only when added to smoking. The study provided no information on the smoking intensity, smoking duration and smoking patterns before e-cigarette use initiation of dual users compared to exclusive smokers. In addition, established risk factors for CVD such as hypertension and hypercholesterolemia were not included in the analysis. Therefore, the study conclusions need to be interpreted with caution.

It is well known that causal inferences cannot be performed with cross-sectional data, in part because temporal sequencing cannot be easily established.[23] In the NHIS surveys, no questions were asked to ascertain when MI or CHD occurred in relation to e-cigarette use initiation. Similarly, no such information was available in the previous study analyzing the 2014 and 2016 datasets.[22] In fact, even if a strong association between e-cigarette use and heart disease was observed, still a causal link would be far from being substantiated. This is relevant to the novelty of the product, being widely available in the US market only after 2010.[31,32] Therefore, it is possible that some of the participants developed heart disease before e-cigarettes were available, before using them, or after a short period of time using them while having a long history of smoking. In fact, misclassifying a small number of participants as being e-cigarette users before developing MI could erroneously result in an association between e-cigarette use and MI.[33] Perhaps an important limitation of the NHIS 2016 and 2017 datasets is that the number of daily e-cigarette users who had MI or CHD was small ($n = 32$ and $n = 33$, respectively). A low number of MI cases among daily e-cigarette users was also observed in the pooled 2014 and 2016 surveys ($n = 47$). This raises the possibility of chance findings that further explain the inconsistent associations. Another limitation is that the classification of participants according to disease status and risk factors for CVD were based on self-report and were not clinically validated. Other factors that are associated with CVD, such as family history, second-hand smoking exposure, and physical activity, were not available or were not clearly defined in the surveys. Finally, it should be mentioned that the study findings do not necessarily suggest that e-cigarette use does not increase the risk of heart disease. E-cigarettes have only been widely available in the past decade, and longer duration of e-cigarette use may affect CVD risk. Therefore, prospective epidemiological studies are needed to comprehensively address this issue, considering the unique characteristic that the vast majority of e-cigarette users are current and former smokers.

In conclusion, no statistically significant association between e-cigarette use and CVD was found from the pooled analysis of the 2016 and 2017 NHIS, and inconsistent associations were observed from the analyses of each year separately. In contrast, strong and consistent associations were observed for all established risk factors for CVD. The results of this study underscore the well-known limitations of cross-sectional observational studies and, combined with the inconsistent associations across different years, suggest that they cannot be relied upon to render sound inferences with regard to any adverse effect of

e-cigarette use on CVD and possibly other outcomes. Prospective epidemiological studies will be needed to address this issue, with particular care taken to examine the complex interactions and temporal associations between smoking and e-cigarette use as well as other risk factors.

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Supplemental material

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References

1. U.S. Department of Health and Human Services. How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease: a report of the surgeon general. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2010.
2. Blann AD, Kirkpatrick U, Devine C, *et al.* The influence of acute smoking on leucocytes, platelets and the endothelium. *Atherosclerosis* 1998; 141: 133–139.
3. Pittilo R. Cigarette smoking, endothelial injury and cardiovascular disease. *Int J Exp Pathol* 2000; 81: 219–230.
4. Cacciola RR, Guarino F and Polosa R. Relevance of endothelial- haemostatic dysfunction in cigarette smoking. *Curr Med Chem* 2007; 14: 1887–1892.
5. Lip GY, Edmunds E and Beevers DG. Should patients with hypertension receive antithrombotic therapy? *J Intern Med* 2001; 249: 205–214.
6. Vogel RA. Coronary risk factors, endothelial function, and atherosclerosis: a review. *Clin Cardiol* 1997; 20: 426–432.
7. Caponnetto P, Russo C, Di Maria A, *et al.* Circulating endothelial-coagulative activation markers after smoking cessation: a 12-month observational study. *Eur J Clin Invest* 2011; 41: 616–626.
8. Farsalinos KE and Polosa R. Safety evaluation and risk assessment of electronic cigarettes as tobacco cigarette substitutes: a systematic review. *Ther Adv Drug Saf* 2014; 5: 67–86.
9. Margham J, McAdam K, Forster M, *et al.* Chemical composition of aerosol from an e-cigarette: a quantitative comparison with cigarette smoke. *Chem Res Toxicol* 2016; 29: 1662–1678.
10. Farsalinos KE and Gillman G. Carbonyl emissions in e-cigarette aerosol: a systematic review and methodological considerations. *Front Physiol* 2018; 8: 1119.

11. Higham A, Rattray NJ, Dewhurst JA, *et al.* Electronic cigarette exposure triggers neutrophil inflammatory responses. *Respir Res* 2016; 17: 56.

12. Hom S, Chen L, Wang T, *et al.* Platelet activation, adhesion, inflammation, and aggregation potential are altered in the presence of electronic cigarette extracts of variable nicotine concentrations. *Platelets* 2016; 27: 694–702.

13. Olfert IM, DeVallance E, Hoskinson H, *et al.* Chronic exposure to electronic cigarette (E-cig) results in impaired cardiovascular function in mice. *J Appl Physiol (1985)* 2018; 124: 573–582.

14. Carnevale R, Sciarretta S, Violi F, *et al.* Acute impact of tobacco vs electronic cigarette smoking on oxidative stress and vascular function. *Chest* 2016; 150: 606–612.

15. Vlachopoulos C, Ioakeimidis N, Abdelrasoul M, *et al.* Electronic cigarette smoking increases aortic stiffness and blood pressure in young smokers. *J Am Coll Cardiol* 2016; 67: 2802–2803.

16. Thijssen DH, Black MA, Pyke KE, *et al.* Assessment of flow-mediated dilation in humans: a methodological and physiological guideline. *Am J Physiol Heart Circ Physiol* 2011; 300: H2–12.

17. Van Bortel LM, Laurent S, Boutouyrie P, *et al.*; Artery Society; European Society of Hypertension Working Group on Vascular Structure and Function; European Network for Noninvasive Investigation of Large Arteries. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. *J Hypertens* 2012; 30: 445–448.

18. Adamopoulos D, Argacha JF, Gujic M, *et al.* Acute effects of nicotine on arterial stiffness and wave reflection in healthy young non-smokers. *Clin Exp Pharmacol Physiol* 2009; 36: 784–789.

19. Mahmud A and Feely J. Acute effect of caffeine on arterial stiffness and aortic pressure waveform. *Hypertension* 2001; 38: 227–231.

20. Vlachopoulos C, Panagiotakos D, Ioakeimidis N, *et al.* Chronic coffee consumption has a detrimental effect on aortic stiffness and wave reflections. *Am J Clin Nutr* 2005; 81: 1307–1312.

21. Benowitz NL and Fraiman JB. Cardiovascular effects of electronic cigarettes. *Nat Rev Cardiol* 2017; 14: 447–456.

22. Alzahrani T, Pena I, Temesgen N, *et al.* Association between electronic cigarette use and myocardial infarction. *Am J Prev Med* 2018. pii: S0749-3797(18)31871–3.

23. Ioannidis JP. Exposure-wide epidemiology: revisiting Bradford Hill. *Stat Med* 2016; 35: 1749–1762.

24. National Center for Health Statistics. National Health Interview Survey, 2017. Public-use data file and documentation, https://www.cdc.gov/nchs/nhis/data-questionnaires-documentation.htm. (2018, accessed 26 August 2018).

25. Cao Y, Kenfield S, Song Y, *et al.* Cigarette smoking cessation and total and cause-specific mortality: a 22-year follow-up study among US male physicians. *Arch Intern Med* 2011; 171: 1956–1959.

26. Kawachi I, Colditz GA, Stampfer MJ, *et al.* Smoking cessation and time course of decreased risks of coronary heart disease in middle-aged women. *Arch Intern Med* 1994; 154: 169–175.

27. Kawachi I, Colditz GA, Stampfer MJ, *et al.* Smoking cessation in relation to total mortality rates in women. A prospective cohort study. *Ann Intern Med* 1993; 119: 992–1000.

28. Iso H, Date C, Yamamoto A, *et al.*; JACC Study Group. Smoking cessation and mortality from cardiovascular disease among Japanese men and women: the JACC Study. *Am J Epidemiol* 2005; 161: 170–179.

29. Honjo K, Iso H, Tsugane S, *et al.* The effects of smoking and smoking cessation on mortality from cardiovascular disease among Japanese: pooled analysis of three large-scale cohort studies in Japan. *Tob Control* 2010; 19: 50–57.

30. Rogot E and Murray JL. Smoking and causes of death among U.S. veterans: 16 years of observation. *Public Health Rep* 1980; 95: 213–222.

31. Farsalinos K and Niaura R. E-cigarettes and smoking cessation in the United States according to frequency of e-cigarette use and quitting duration: analysis of the 2016 and 2017 National Health Interview Surveys. *Nicotine Tob Res* 2019. pii: ntz025. doi: 10.1093/ntr/ntz025.

32. Giovenco DP and Delnevo CD. Prevalence of population smoking cessation by electronic cigarette use status in a national sample of recent smokers. *Addict Behav* 2018; 76: 129–134.

33. Middlekauff HR and Gornbein J. Association of electronic cigarette use with myocardial infarction: persistent uncertainty. *Am J Prev Med* 2019; 56: 159–160.

34. Osei AD, Mirbolouk M, Orimoloye OA, *et al.* Association between e-cigarette use and cardiovascular disease among never and current combustible-cigarette smokers. *Am J Med* 2019. pii: S0002-9343(19)30211–6.