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Adding Data From 2015 Strengthens the Association Between E-Cigarette Use and Myocardial Infarction

Manderski et al. stated that our conclusion that e-cigarette use was associated with having had a myocardial infarction[1] was erroneous because we did not use population weights in our analysis. We did not use weights when presenting the descriptive statistics for the sample (Table 1 in our paper[1]) because we were describing the actual (unweighted) sample characteristics as opposed to presenting population estimates based on the sample (which would have used the weights). The logistic regression analyses of the association between e-cigarette use and having had a myocardial infarction (Table 2 in our paper[1]) used the National Health Interview Survey (NHIS) weights, accounted for the complex survey design, and followed NHIS procedures to combine the 2014 and 2016 data sets.[2] Our multivariable analysis is nationally representative and does not underestimate variance.

There are several differences in the way that Manderski and colleagues did their analysis compared with what we did. (At our request, the editor obtained the SAS code so that we could understand precisely what they did.) First, Manderski et al. used the NHIS "Weight - Final Annual" (WTFA) in their analysis. WFTA is based on design and ratio (including nonresponse and post-stratification) adjustments. This weight was designed mainly for the analysis of the family and person data. By contrast, we used "Sample Adult Weight - Final Annual" (WTFA_SA) because it includes design, ratio, nonresponse, and post-stratification adjustments for sample adults. According to the Centers for Disease Control and Prevention, "National estimates of all sample adult variables can be made using these weights."[2] We used WTFA_SA because all variables that we used in our analysis were from the adult sample except for race/ethnicity. Second, Manderski and colleagues used age as a continuous variable in their logistic regression model, and then used the "ESTIMATE" function to measure the effect of a 10-year interval. We used age in 10-year intervals as a variable (i.e., age/10 years); the resulting roundoff errors in the calculations contribute to the small differences between our results. Third, Manderski et al. treated BMI=99.99 as a missing value, whereas we incorrectly treated this as a real value. We updated the results in this letter, treating BMI=99.99 as a missing value. This change did not substantially alter the results. Most importantly, despite the differences in the analytic approach of Manderski and colleagues, they obtained essentially the same results that we did for the combined data for 2014 and 2016, namely a significant association between daily e-cigarette use and myocardial infarction (OR=1.74, 95% CI=1.14, 2.64 in their analysis; OR=1.79, 95% CI=1.20, 2.66 in ours).

We did not use the 2015 data in our paper because we did not realize that e-cigarette use was available, as it was buried in the cancer control supplement. Table 1 in this letter shows that the 2015 data reveal significantly increased odds of having had a myocardial infarction for both some-day and everyday e-cigarette use. The overall risks including 2015 are higher than we originally reported[1] based on just 2014 and 2016 (OR=1.49 for all 3 years vs 1.16 for 2014 and 2016, for e-cigarette use on some days; OR=2.14 vs 1.78 for everyday e-cigarette use). Moreover, with the additional 2015 data, some-day e-cigarette use became statistically significant.

Manderski et al. argued that an analysis of e-cigarette use among people who never smoke is necessary to assess an independent association between e-cigarettes and myocardial infarction. As we explained in our response to the first letter written about our paper,[3] we do not need to perform this type of analysis to estimate the association between e-cigarette use and having a myocardial infarction because we used multivariable analysis which is adjusted for confounding factors including smoking. Because about two thirds of e-cigarette users also smoke cigarettes (dual users), excluding these people would severely limit the sample size and reduce power to detect a true effect. In addition, because dual use is the dominant pattern for e-cigarette users, it is important to include them in the analysis to obtain the most relevant results.

Similar to the second letter written about our paper, Manderski and colleagues argued that use of the term

Table 1. Multivariable Associations Between E-Cigarette Use and Myocardial Infarction of NHIS 2014, 2015, and 2016

	2014		2015		2016		Combined NHIS 2014–2016	
Characteristics	**OR (95% CI)**	***p*-value**	**OR (95% CI)**	***p*-value**	**OR (95% CI)**	***p*-value**	**OR (95% CI)**	***p*-value**
E-cigarette use								
Never	ref		ref		ref		ref	
Former	1.17 (0.84, 1.61)	0.355	1.44 (1.04, 1.98)	0.028	1.02 (0.74, 1.41)	0.901	1.16 (0.96, 1.40)	0.128
Some days	1.72 (1.03, 2.87)	0.037	2.02 (1.17, 3.50)	0.012	0.76 (0.42, 1.39)	0.371	1.49 (1.06, 2.09)	0.022
Daily	2.06 (0.90, 4.68)	0.086	2.29 (1.26, 4.15)	0.006	2.20 (1.16, 4.17)	0.016	2.14 (1.41, 3.25)	<0.001
Cigarette smoking								
Never	ref		ref		ref		ref	
Former	1.83 (1.51, 2.21)	<0.001	1.46 (1.20, 1.78)	<0.001	1.64 (1.38, 1.95)	<0.001	1.64 (1.48, 1.82)	<0.001
Some days	2.45 (1.56, 3.85)	<0.001	1.89 (1.19, 3.01)	0.007	1.93 (1.27, 2.93)	0.002	2.08 (1.60, 2.70)	<0.001
Daily	3.01 (2.23, 4.06)	<0.001	2.16 (1.63, 2.86)	<0.001	2.81 (2.15, 3.69)	<0.001	2.68 (2.29, 3.13)	<0.001
Hypertension	2.86 (2.28, 3.59)	<0.001	2.05 (1.65, 2.56)	<0.001	1.99 (1.62, 2.46)	<0.001	2.28 (2.01, 2.58)	<0.001
Diabetes mellitus	1.77 (1.44, 2.17)	<0.001	2.28 (1.87, 2.78)	<0.001	1.94 (1.57, 2.40)	<0.001	1.99 (1.76, 2.25)	<0.001
High cholesterol	2.16 (1.77, 2.63)	<0.001	2.66 (2.22, 3.19)	<0.001	2.65 (2.20, 3.20)	<0.001	2.45 (2.20, 2.74)	<0.001
Woman	0.52 (0.43, 0.62)	<0.001	0.50 (0.42, 0.60)	<0.001	0.46 (0.38, 0.55)	<0.001	0.49 (0.44, 0.55)	<0.001
Age (per 10 years)	1.61 (1.51, 1.73)	<0.001	1.81 (1.69, 1.94)	<0.001	1.70 (1.56, 1.86)	<0.001	1.70 (1.63, 1.77)	<0.001
BMI	1.01 (0.99, 1.02)	0.444	1.01 (0.99, 1.02)	0.330	0.99 (0.98, 1.01)	0.402	1.00 (0.99, 1.01)	0.588
Race/ethnicity								
White	ref		ref		ref		ref	
Hispanic	0.68 (0.53, 0.88)	0.003	0.86 (0.65, 1.13)	0.267	0.90 (0.62, 1.29)	0.553	0.81 (0.68, 0.97)	0.025
Black	0.95 (0.72, 1.24)	0.684	0.82 (0.64, 1.05)	0.117	0.81 (0.62, 1.06)	0.123	0.86 (0.73, 1.01)	0.058
Asian	0.68 (0.43, 1.10)	0.114	0.75 (0.44, 1.29)	0.298	0.38 (0.20, 0.72)	0.003	0.58 (0.43, 0.79)	0.001
Other race	1.44 (0.73, 2.82)	0.294	1.35 (0.66, 2.75)	0.414	1.45 (0.64, 3.26)	0.370	1.42 (0.92, 2.18)	0.115
n	35,156		30,752		31,744		97,652	
Population size (weighted size)	229,754,972		220,309,324		235,393,015		228,485,770	

NHIS, National Health Interview Survey.

"risk" implies causation. As we responded before,[4] the term "risk factor" was developed to specifically describe cross-sectional studies.

Finally, three recent studies have confirmed our results. The first study used the data of the Behavioral Risk Factor Surveillance System and found elevated risks for myocardial infarction and stroke,[5] the second used the data of the Population Assessment of Tobacco and Health study,[6] and the third study used NHIS data (2014, 2016, and 2017).[7] All three yielded similar risks as we found in the NHIS.

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