PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	The time-varying association between cigarette and ENDS use on incident hypertension among US adults: a prospective longitudinal study
AUTHORS	Cook, Steven; Hirschtick, Jana; Barnes, Geoffrey; Arenberg, D; Bondarenko, Irina; Patel, Akash; Jiminez Mendoza, Evelyn; Jeon, Jihyoun; Levy, David; Meza, Rafael; Fleischer, Nancy

VERSION 1 – REVIEW

REVIEWER	Kaplan, Robert Albert Einstein College of Medicine
REVIEW RETURNED	19-Apr-2022

GENERAL COMMENTS	The manuscript from the PATH cohort uses time-varying exposure data to conclude that use of traditional cigarettes raises risk of hypertension, while use of ENDS does not. Thus this analysis is presented as a refutation of a prior analysis of PATH data (PMID: 33803457), which attributed a high risk of hypertension to ENDS use, especially when used in combination with cigarettes. Abstract Please add sample sizes of interest (e.g., all participants, ENDS users, traditional cigarette users), average or median length of followup, and source of population. Methods Description of the population is incomplete and impossible to understand for several reasons: What was the source of study participants, e.g., sampling frame? What is the rationale for calling this “nationally representative?” How were study participants recruited? What was the total number of participants at baseline, and what proportion were included in the follow-up phase versus lost-to-followup (presumably this means no follow up information obtained ever)? Please move some of this information from the supplemental figure to the text. What does “no history of any cardiovascular outcome” mean? The flow chart looks strange, in that about one third of the participants had an “existing heart condition.” This is higher than one would expect in a population sample. What was the method of data collection (e.g., phone questionnaire, website, or what)?

	The question about hypertension “within last 12 months” implies or assumes an annual questionnaire. However this would practically be impossible to execute and in fact they explain that some between-wave intervals were two years. Therefore I wonder is their description of the interview approach correct? Also it would be helpful to know, what are summary measures of the duration of time between each wave (median days, lower 25%ile days, upper 25%ile days, for example)? . Results The presentation of weighted data as percentages without giving actual numbers does not give a clear understanding of the sample. Please cite the sample size of ENDS users, 336 exclusive and 570 dual users, in the text and abstract rather than only in the table. Please also provide more detail about the extent of ENDS exposure. Follow-up is no longer than 5 years for each person, thus total person years of ENDS exposed individuals is not large; perhaps total person-years for each exposure category could be given. Accounting for the time-varying nature of ENDS use through the five surveys, they should estimate the cumulative exposure to ENDS within the study cohort on a per-person basis. Explaining the data this way probably would help most readers understand the caveat that this study may not have adequate numbers of ENDS users to identify a risk of hypertension, except if this risk was very extreme. Interpretation and Discussion It appears that traditional cigarettes and ENDS are handled identically in the analysis, but this is not really the case because of the historical facts relating to recent introduction of ENDS into the market. For example, the claim “we found that time-varying cigarette smoking increased the risk of self-reported incident hypertension, but time-varying ENDS use did not” implies that identical data and identical mechanism of action were evaluated for each exposure, and arguably this is not accurate. Related to this, I do not think they completely controlled for past cigarette smoking. It could be expected that hypertension risk may be attributed partly to acute hemodynamic effects of cigarettes or ENDS, and partly to chronic vascular damage which could only be observed with traditional cigarettes because only traditional cigarettes and not ENDS have been available over the long term. Thus the analysis misses their stated goal, namely to examine the relative contribution of exclusive cigarette use versus exclusive ENDS use to hypertension risk (paraphrasing page 5). Something different would be required. This would be to examine incident hypertension risk among two groups of ever smokers, the first being those that continued smoking during the study period without using ENDS, and the second being those who did not continue smoking and used ENDS instead. The minority of ENDS users who never smoked traditional cigarettes could not contribute to this analysis, and arguably they should not because they can’t fairly be compared with users of traditional cigarettes. Never smokers would be the comparison group for this analysis. It is stated (Discussion) that they studied “short-term follow-up of approximately 5 years” for ENDS, but this 5 year interval sounds like the maximal follow-up of the study rather than the actual duration of exposure to ENDS among users. Please clarify and also see comment above regarding the need for a time-based exposure metric.

REVIEWER	Kubozono, Takuro Kagoshima University, Department of Cardiovascular Medicine and Hypertension
REVIEW RETURNED	30-Sep-2022

GENERAL COMMENTS	In this manuscript, the authors investigated that the association between cigarette and electronic nicotine delivery systems (ENDS) use on self-reported incident hypertension. We found that smoking increased the risk of self-reported hypertension but ENDS use did not. This study has some interesting findings but also presents several problems. 1. The greatest problem is the self-reporting of the occurrence of hypertension. It is very difficult to discuss the development of hypertension without measuring blood pressure. Because blood pressure is not measured, the onset of hypertension is misdiagnosed. In addition, even if baseline blood pressure does not reach the criteria for hypertension, if it is high, the possibility of developing hypertension in the future is increased. 2. The number of ENDS cases is too small. Also, the average age of ESDN is young (33.2 years). Therefore, the number of cases with hypertension may have been too small to be significant. 3. The number and frequency of cigarettes and ENDS should be investigated.

VERSION 1 – AUTHOR RESPONSE

Manuscript ID bmjopen-2022-062297

We would like to thank the editor and reviewers for their feedback and comments. We have responded to each point below and believe the manuscript has been strengthened.

The revised manuscript now includes three additional sensitivity analyses, including:

1. a more frequent cigarette/ENDS use exposure (measured as 10+ days in the past 30 days for each product (Table S5)
2. an expanded exposure with adults who reported ‘never established smoking’ as the reference group, with the following use categories: (1) former cigarette, no ENDS; (2) current cigarette, no ENDS; (3) former cigarette, current ENDS; (4) current cigarette and ENDS; (5) exclusive ENDS (see Table S6).
3. an analysis of the association between ENDS use and hypertension among respondents who had never smoked 100 cigarettes in their lifetime (Table S7).

- The statistical analysis section was updated to include the additional sensitivity analyses and the result section was updated to synthesize the results from these sensitivity analyses.

We also did three additional sensitivity analyses for the reviewer response but did not include these sensitivity analyses in the revised manuscript. These include:

1. A sensitivity analysis restricting the analytic sample to respondents who were between 18-54 years old at baseline. The purpose of this sensitivity analysis was to test for the possible of a 'survivorship bias' (Table R1).
2. A sensitivity analysis using the Wave 2 weights. These weights require respondents to participate in the first follow-up interview and adjust for respondents who participated at baseline but did not participate at any follow-up wave. While the 'all-waves weights' do create a nationally representative sample of respondents who participated in all follow-up interviews, we wanted to make sure that the results didn't change for those who participated at wave 2 but were right censored by wave 5 (Table R2).
3. A sensitivity analysis restricting the analysis to hypertension between Wave 1 and Wave 4. The purpose of this sensitivity analysis was to test for the possibility that the unequal time interval between Wave 4 and Wave 5 may be affecting our results (Table R3).

The results of the six additional sensitivity analyses included in this response (and 9 total) did not change the substantive interpretation of our findings. This gives us further confidence in the robustness of our findings.

Responses to individual comments are included below and are in red. We have included a copy of the revised manuscript where changes have been tracked.

Reviewer: 1
Dr. Robert Kaplan, Albert Einstein College of Medicine
Comments to the Author:
The manuscript from the PATH cohort uses time-varying exposure data to conclude that use of traditional cigarettes raises risk of hypertension, while use of ENDS does not. Thus this analysis is presented as a refutation of a prior analysis of PATH data (PMID: 33803457), which attributed a high risk of hypertension to ENDS use, especially when used in combination with cigarettes.

Response: As the reviewer notes, in a study recently published in the journal *Toxics,* Miller et al (2021) examined the cross-sectional association between e-cigarette use and self-reported hypertension among adults aged 18-54 using data from one wave of the PATH longitudinal cohort study. Miller et al. found a "positive albeit weak association between vaping and self-reported hypertension, of similar magnitude to that of cigarette smoking and hypertension" (p. 11). Moreover, the authors found that the highest odds of hypertension were observed among concurrent cigarette and e-cigarette users.

The reviewer is correct to point out that the findings from our study stand in contrast to the findings from the Miller et al. study. There are two main reasons that explain the differences in our findings. First, our study examined the prospective association between time-varying ENDS use on hypertension using data from all 5-waves of data from the PATH study, a prospective longitudinal study. We restructured our data into a longitudinal structure and then examined the incidence of hypertension at follow-up using a robust longitudinal method. Conversely, Miller et al. looked at the

cross-sectional association between e-cigarette use and hypertension using data from wave 3 of the PATH Study. The authors then examined this association using standard logistic regression techniques. Setting aside the fact that Wave 3 of the PATH Study on its own is not meant to be nationally representative, the hypertension outcome used in the Miller et al. study was based on the cross-sectional prevalence of hypertension (i.e., have you ever been diagnosed) rather than the incidence of hypertension. This is an extremely important limitation of the Miller et al. study because they did not consider when the 2,859 respondents who reported hypertension in their study were diagnosed. The timing of the diagnosis is important because e-cigarettes only became widely available in the US marketplace beginning in 2007, with little use until after 2010. Any diagnosis before that time therefore could not be attributable to e-cigarette use. Moreover, for e-cigarettes to increase the risk of hypertension, not only does the outcome need to have occurred after e-cigarettes became available, but the exposure to e-cigarettes also needs to precede the hypertension outcome. This means that current or former cigarette smokers who switched to e-cigarettes after being diagnosed with hypertension would be classified as e-cigarette users and included in the risk set of Miller et al. For these reasons, the results of the Miller et al. study are at high risk of reverse causation, and the results from this study need to be interpreted with caution. As noted by other scholars (see Farsalinos and Niaura, 2019, for example), this is a common issue among cross-sectional studies using prevalence data to examine the health effects of e-cigarettes and was a primary reason why Bhatta and Glantz's (2019) article titled "Electronic cigarette use and myocardial infarction among adults in the US population assessment of tobacco and health" was retracted from the *Journal of the American Heart Association.* Second, in our study we included a continuous cigarette pack-years measure to adjust for lifetime cigarette smoking among current and former cigarette smokers at baseline. This is important because, as Miller et al. note in their study, "most current vapers were current or former smokers" (p. 4). The cigarette smoking history of respondents, in other words, is an important confounder that needs to be considered when trying to understand the potential impact of e-cigarettes on hypertension risk. Miller et al. had a category for former cigarette smoker but did not have any information on cigarette pack-years or on the duration or intensity of cigarette use. By not adjusting for cigarette pack-years Miller et al. did not account for the considerable smoking history of cigarette smokers. Because most 'exclusive' e-cigarette users in the Miller et al. study were former cigarette smokers, this omission is fundamentally important. As you can see from Figure 2 in the results of the Miller et al. paper (p.9), the adjusted odds ratio for exclusive e-cigarette users who were 'never smokers' was not significantly associated with hypertension compared to never smokers (aOR 1.32, 95% CI 0.50, 3.53).

There is a third difference between our study and the Miller et al. study involves the age ranges included in the analysis. In our study, we imposed no age restrictions and included all adults who were aged 18+ at baseline while Miller et al. removed adults 55 or older from their analysis. Miller et al. argued that they restricted their age to young adults and middle-aged respondents to limit potential survivorship bias, which would "disproportionately influence survival among middle and older age smokers" (pp. 10-11). We believe this is a reasonable argument and decided to restrict our analytic sample to adults aged 18-54 as a sensitivity analysis (see results in Table R1 below). As the reviewer can see, the substantive interpretation of our time-varying cigarette/ENDS exposure does not change when the analysis was restricted to include adults aged 18-54 at baseline. Consistent with our main analysis, the association between exclusive cigarette use and incident hypertension was significant in the adjusted model compared to non-use (aHR 1.17, 95% CI: 1.02, 1.34), while exclusive ENDS use (aHR 0.92, 95% CI: 0.61, 1.37) and dual use (aHR 1.12, 95% CI: 0.84, 1.47) were not. The consistency in our findings provides confidence that our results are not biased because of a potential survivorship bias based on including all adult respondents in our main analysis.

References

Bhatta, D. N. and S. A. Glantz (2019). "Electronic cigarette use and myocardial infarction among adults in the US population assessment of tobacco and health." Journal of the American Heart Association **8**(12): e012317.

Farsalinos, K. and R. Niaura (2019). "E-cigarette use and myocardial infarction: association versus causal inference." American journal of preventive medicine **56**(4): 626-627.

Table R1. Discrete time survival analysis predicting incidence of self-reported hypertension among adults aged 18-54 at baseline, Population Assessment of Tobacco and Health Study (Waves 1-5, 2013-2019)

	Unadjusted		Adjusted	
	Hazard	95% CI	Hazard	95% CI
Time varying cigarettes/ENDS use				
Non use	REF	REF	REF	REF
Exclusive cigarette use	1.42***	1.26, 1.59	1.17*	1.02, 1.34
Exclusive ENDS use	0.97	0.66, 1.44	0.92	0.61, 1.37
Dual use	1.16	0.90, 1.51	1.12	0.84, 1.47
Sociodemographic Risk factors				
Age (mean)^	1.04***	1.03, 1.04	1.04***	1.03, 1.04
Sex (Male=1)	1.27**	1.10, 1.44	1.32***	1.15, 1.51
Race/Ethnicity				
NH White	REF	REF	REF	REF
Hispanic	0.77**	0.64, 0.93	0.83*	0.69, 1.0
NH Black	1.48***	1.26, 1.74	1.50****	1.26, 1.78
NH Asian	0.37***	0.22, 0.63	0.49*	0.28, 0.85
NH Other	1.14	0.90, 1.63	1.13	0.78, 1.62
Household Income				
<$50,000	REF	REF	REF	REF
>$50,000	0.87	0.75, 1.0	0.84*	0.72, 0.98
missing	0.56	0.28, 1.10	0.61	0.30, 1.22
Baseline Risk Factors				
Family History of heart attack	1.52***	1.30, 1.78	1.36***	1.15, 1.61
Obesity (BMI>30)	2.26***	1.96, 2.62	2.01***	1.73, 2.33
Diabetes diagnosis	1.93***	1.46, 2.55	1.44*	1.08. 1.93
Binge Drinking	1.46**	1.17, 1.83	1.44**	1.14, 1.81
Smoking History Variables				
Former Established smoker	1.43**	1.13, 1.81	1.19	0.92, 1.53
Pack years (intervals of 10)^	1.18***	1.13, 1.24	1.05	0.99, 1.11

Person N=15,190 ; Risk Period N =51,684

*p<0.05, **p<0.01, ***p<0.001

^cigarette pack-years were rescaled to intervals of 10 packyears

Abstract

Please add sample sizes of interest (e.g., all participants, ENDS users, traditional cigarette users), average or median length of followup, and source of population.

Response: This information has been added to the abstract.

Methods

Description of the population is incomplete and impossible to understand for several reasons:

What was the source of study participants, e.g., sampling frame? What is the rationale for calling this "nationally representative?" How were study participants recruited?

Response: We have added more detailed information on the sampling frame, national representativeness of the study, and on the recruitment of participants into the study. The text of the manuscript now reads:

> The PATH study is an ongoing, nationally representative cohort study of the civilian, non-institutionalized population in the United States. A four-stage stratified area probability sample was used for recruitment at baseline, and a two-staged design was used for sampling the adult cohort.[31]African-Americans and people who use tobacco were oversampled related to population proportions, and weighting procedures adjusted for oversampling and non-response based on US Census Bureau Data. Data were collected from September, 2013 to December, 2014 for Wave 1 (response rate among screened households, 74.0%); October, 2014 to October, 2015 for Wave 2 (response rate, 83.2%); October, 2015 to October, 2016 for Wave 3 (response rate, 78.4%); December, 2016 to January, 2018 for Wave 4 (response rate, 73.5%); and December, 2018 to November 2019 for Wave 5 (response rate, 69.4%). All PATH survey interviews were completed in-person, using Audio Computer-Assisted Self-Interviewing (ACASI) administrations, available in English or Spanish. Data collection protocols were used to ensure that follow-up interviews were close to the anniversary of their participation in the previous wave.[32] Further details about the design and methods of the PATH Study have been published elsewhere.[31-34]

What was the total number of participants at baseline, and what proportion were included in the follow-up phase versus lost-to-followup (presumably this means no follow up information obtained ever)? Please move some of this information from the supplemental figure to the text.

Response: We have updated the text and included information from the supplemental figure to the text. The text (page 7) now reads:

> The analytic sample for the current study was restricted to adult respondents (18+) (Wave 1, n=32,320) with no self-reported heart condition at baseline (n=21,734). A total of 3,203 respondents were excluded as they did not participate at any follow-up interview, and respondents who did not report a hypertension diagnosis were right censored at their last observation point. Respondents with missing variable information (n=992; 5.3%) were excluded from the analysis using listwise deletion. The final analytic sample consisted of 17,539 respondents. A flowchart summarizing the analytic sample is provided in the appendix (Figure A1).

As we state in the text on page 10 of the manuscript:

We compared baseline characteristics for censored and non-censored respondents (Table A2). Because the censored respondents had a slightly different sociodemographic profile than the non-censored respondents, as a sensitivity analysis, we estimated the discrete time models using the 'all waves weights', which account for this type of attrition[31] and restricts the analysis to a longitudinal cohort of respondents who participated in all waves of the PATH study (person n=11,437 risk period n=45,250).

However, the 3203 respondents who did not participate at any follow-up interview were not adjusted for with the baseline weights. As an additional sensitivity analysis, we restricted our analysis to respondents who participated in the second wave of follow-up using the wave 2 weights. These weights are calibrated to adjust for baseline respondents who did not participate in wave 2 of the PATH Study, and some researchers use these weights. The results from this sensitivity analysis using the wave 2 weights are included below (Table R2). The substantive interpretation of our findings using the wave 2 weights was nearly identical to the results from our main results. The hazard estimates only changed by decimal points, giving us further confidence in the robustness of our findings.

Table R2. Discrete time survival analysis predicting incidence of hypertension among adults using 'wave 2 weights', Population Assessment of Tobacco and Health Study (Waves 1-5, 2013-2019)

	Unadjusted		Adjusted	
	Hazard	95% CI	Hazard	95% CI
Time varying cigarettes/ENDS use				
Non use	REF	REF	REF	REF
Exclusive cigarette use	1.30***	1.16, 1.45	1.23**	1.07, 1.42
Exclusive ENDS use	0.87	0.60, 1.25	1.04	0.70, 1.52
Dual use	1	0.76, 1.31	1.16	0.87, 1.56
Sociodemographic Risk factors				
Age (mean)^	1.03***	1.03, 1.04	1.03***	1.03, 1.04
Sex (Male=1)	1.26**	1.09, 1.46	1.32***	1.14, 1.52
Race/Ethnicity				
NH White	REF	REF	REF	REF
Hispanic	0.86	0.72, 1.02	1.02	0.86, 1.22
NH Black	1.47***	1.27, 1.69	1.66***	1.42, 1.93
NH Asian	0.40***	0.24, 0.66	0.58*	0.34, 0.97
NH Other	1.06	0.76, 1.48	1.09	0.77, 1.54
Household Income				
<$50,000	REF	REF	REF	REF
>$50,000	0.80**	0.70, 0.93	0.85*	0.73, 0.98
missing	0.82	0.41, 1.66	0.74	.036, 1.53
Baseline Risk Factors				
Family History of heart attack	1.44****	1.24, 1.66	1.27**	1.08, 1.49
Obesity (BMI>30)	1.92***	1.69, 2.19	1.73***	1.50, 1.99
Diabetes diagnosis	2.53***	2.03, 3.16	1.78***	1.39, 2.27
Binge Drinking	1.22	0.98, 1.52	1.27*	1.08, 1.49
Smoking History Variables				
Former Established smoker	1.44***	1.18, 1.74	1.04	0.84, 1.29
Pack years (intervals of 10)^	1.17***	1.13, 1.21	1.03	0.99, 1.08

Person N=16,687; Risk Period N =56,452

*p<0.05, **p<0.01, ***p<0.001

^cigarette pack-years were rescaled to intervals of 10 packyears

What does “no history of any cardiovascular outcome” mean? The flow chart looks strange, in that about one third of the participants had an “existing heart condition.” This is higher than one would expect in a population sample.

Response: In the baseline PATH interview, the 32,320 adults were asked whether a doctor or other health professional had ever told them they had the following heart conditions: high blood pressure (n=7127 yes), high cholesterol (n=5490 yes), congestive heart failure (n=486 yes), stroke (n=590 yes), heart attack (n=643 yes), or other heart condition (n=1611 yes). Respondents were considered to have no history of a cardiovascular health outcome if they responded ‘no’ to all the questions outlined above. To improve clarity, we changed “no history of any cardiovascular outcome” to “no self-reported heart condition.” One additional point is that as part of the sampling design, the PATH investigators oversampled individuals likely to use tobacco (Hyland et al., 2017). This could also help explain the apparent high (unweighted) number of individuals with a previous cardiovascular outcome. The oversampling of potential people who use tobacco is one of the reasons why weight adjustment is essential when using PATH data to produce nationally representative estimates.

Reference

Hyland A, Ambrose BK, Conway KP, et al. Design and methods of the Population Assessment of Tobacco and Health (PATH) Study. *Tobacco control.* 2017;26(4):371-378.

What was the method of data collection (e.g., phone questionnaire, website, or what)?

Response: All PATH survey interviews were completed in-person, using Audio Computer-Assisted Self-Interviewing (ACASI) administrations, available in English or Spanish. We have added this information to the methods section of the manuscript (see above).

The question about hypertension “within last 12 months” implies or assumes an annual questionnaire. However this would practically be impossible to execute and in fact they explain that some between-wave intervals were two years. Therefore I wonder is their description of the interview approach correct? Also it would be helpful to know, what are summary measures of the duration of time between each wave (median days, lower 25%ile days, upper 25%ile days, for example)?

Response: The PATH questionnaire was completed annually between Wave 1 and Wave 4. The PATH data collection protocols, as outlined in Mahoney 2021, were designed to interview each respondent close to the one-year anniversary of the participation in the prior wave. We have included this information in the revised methods section of the manuscript (see above).

As the reviewer notes, the data collection procedure changed between Wave 4 and Wave 5, as the follow-up period was extended to two years. While this did change the time between the last two

waves, our hypertension outcome remained relatively unaffected as hypertension was measured based on a past 12-month self-report. Importantly, any bias that was introduced by the change in interview timing would apply equally to both ENDS and non-ENDS users.

We spent a lot of time thinking about how the 2-year interval between Wave 4 and Wave 5 affected our analytic plan. In discrete-time models with a logit link function, it is assumed that events can only occur at discrete time points and that the interval lengths between measurements are equal. However, discrete-time models using a complimentary log log (cloglog) link function estimates an underlying proportional hazard model in continuous time, and it is assumed that the model is invariant to interval length. Moreover, as Paul Allison (2010) notes, in models where there are no restrictions placed on the effect of time and when the data is structured so every individual's interval time at time *t* is the same length as very other individual, the separate estimates for each time interval automatically adjust for differences in interval length. We are therefore confident that discrete-time models using a cloglog link function are appropriate for this analysis.

However, to ensure that the unequal time interval between Wave 4 and Wave 5 was not affecting our results, we conducted a sensitivity analysis restricting the hypertension outcome to Wave 1 to 4. The results from this sensitivity analysis are included below (Table R3). The results are consistent with the results from our main analysis as the association between exclusive cigarette use and incident hypertension was significant in the adjusted model compared to non-use (aHR 1.26, 95% CI: 1.07, 1.48), while exclusive ENDS use (aHR 1.16, 95% CI: 0.71, 1.74) and dual use (aHR 1.14, 95% CI: 0.89, 1.61) were not.

References:

Allison, Paul. (2010). Survival Analysis using SAS: A Practical Guide, Second Edition. SAS Institute Inc., Cary NC.

Mahoney MC, Rivard C, Hammad HT, et al. Cardiovascular risk factor and disease measures from the Population Assessment of Tobacco and Health (PATH) Study. *International journal of environmental research and public health.* 2021;18(14):7692.

Table R3. Discrete time survival analysis predicting incidence of self-reported hypertension among adults, PATH W1-W4

	Unadjusted		Adjusted	
	Hazard	95% CI	Hazard	95% CI
Time varying cigarettes/ENDS use				
Non use	REF	REF	REF	REF
Exclusive cigarette use	1.31***	1.16, 1.49	1.26**	1.07, 1.48
Exclusive ENDS use	0.97	0.66, 1.42	1.16	0.77, 1.74
Dual use	0.98	0.70, 1.37	1.14	0.89, 1.61
Sociodemographic Risk factors				
Age (mean)^	1.03***	1.03, 1.04	1.03***	1.03, 1.04
Sex (Male=1)	1.22*	1.04, 1.43	1.26**	1.08, 1.47
Race/Ethnicity				
NH White	REF	REF	REF	REF
Hispanic	0.94	0.80, 1.12	1.1	0.93, 1.31
NH Black	1.36**	1.13, 1.64	1.51***	1.24, 1.83
NH Asian	0.38**	0.20, 0.71	0.57	0.31, 1.05
NH Other	1	0.66, 1.50	1.01	0.67, 1.51
Household Income				
<$50,000	REF	REF	REF	REF
>$50,000	0.74***	0.64, 0.87	0.79*	0.67, 0.95
missing	0.59	0.27, 1.32	0.51	0.22, 1.16
Baseline Risk Fators				
Family History of heart attack	1.44***	1.25, 1.66	1.27**	1.09, 1.47
Obesity (BMI>30)	1.97***	1.71, 2.27	1.78***	1.54, 2.06
Diabetes diagnosis	2.90***	2.28, 3.69	1.96***	1.52, 2.51
Binge Drinking	1.29	0.99, 1.68	1.36*	1.04, 1.78
Smoking History Variables				
Former Established smoker	1.37**	1.08, 1.72	1	0.77, 1.28
Pack years (intervals of 10)^	1.16***	1.12, 1.21	1.03	0.98, 1.08

Notes: Person N=17,539 ; Risk Period N=47,266

*p<0.05, **p<0.01, ***p<0.001

^for interpretation, pack-years were rescaled to intervals of 10 packyears

The presentation of weighted data as percentages without giving actual numbers does not give a clear understanding of the sample. Please cite the sample size of ENDS users, 336 exclusive and 570 dual users, in the text and abstract rather than only in the table.

Response: This information has been added to both the text of the manuscript and the abstract.

Please also provide more detail about the extent of ENDS exposure. Follow-up is no longer than 5 years for each person, thus total person years of ENDS exposed individuals is not large; perhaps total person-years for each exposure category could be given. Accounting for the time-varying nature of ENDS use through the five surveys, they should estimate the cumulative exposure to ENDS within the study cohort on a per-person basis. Explaining the data this way probably would help most readers understand the caveat that this study may not have adequate numbers of ENDS users to identify a risk of hypertension, except if this risk was very extreme.

Our exposure variable, based on the exclusive use of cigarettes and ENDS and the dual use of cigarettes and ENDS was based on time-varying current use of cigarette and/or ENDS products at each wave of follow-up. While we appreciate the reviewer's recommendation to estimate a cumulative exposure for each respondent at each discrete-time interval, we would be assuming that our exposure was capturing an underlying continuous process when it is, in fact, an acute (i.e., current use) exposure at the time of the survey. This is an important limitation of the current study, and we have revised the limitations section of the manuscript to make this point clearer to readers. Moreover, e-cigarette products have changed considerably since their emergence, so it is unclear what cumulative exposure would represent as of now. On page 22, we now state:

> The findings from our study are based on approximately five years of longitudinal follow-up, and longer exposure to ENDS products may be required to more fully understand the role of ENDS use on risk of hypertension. Moreover, ENDS products continue to evolve, and more recent generations of ENDS products have more efficient nicotine delivery. This study did not adjust for cumulative exposure to ENDS or for nicotine level by product type. Future studies should seek to develop valid methods for better understanding exposure to ENDS products, and this analysis will need to be updated as more longitudinal data on long term ENDS use becomes available.

Moreover, while the suggestion of the reviewer is interesting and worth consideration, especially as more data with longer follow-up becomes available, there are other points that are just as important to consider. First, e-cigarettes have not been in/on the market for long, only becoming widely available after 2010, which is not much earlier than Wave 1 (2013). So there aren't many people who use e-cigarettes with long duration of use currently that we would be able to detect an effect of cumulative exposure. Second, most people who use e-cigarettes are current or former smokers who have longer histories of cigarette than e-cigarette use, which is why it is critical to adjust for cigarette pack-years.

Interpretation and Discussion

It appears that traditional cigarettes and ENDS are handled identically in the analysis, but this is not really the case because of the historical facts relating to recent introduction of ENDS into the market. For example, the claim "we found that time-varying cigarette smoking increased the risk of self-reported incident hypertension, but time-varying ENDS use did not" implies that identical data and identical mechanism of action were evaluated for each exposure, and arguably this is not accurate.

Response: We adjust for cigarette pack-years, but we agree that the exposures are not necessarily the same. We have changed the language in the manuscript to make this distinction more obvious. For example, in the last sentence of the first paragraph in the discussion section, we removed the following sentence: "we found that time-varying cigarette smoking increased the risk of self-reported incident hypertension, but time-varying ENDS use did not." We now state: " and in a longitudinal follow-up of approximately five years, we found no evidence that short term and time-varying ENDS use was associated with an increased risk of incident hypertension."

Related to this, I do not think they completely controlled for past cigarette smoking. It could be expected that hypertension risk may be attributed partly to acute hemodynamic effects of cigarettes or ENDS, and partly to chronic vascular damage which could only be observed with traditional cigarettes because only traditional cigarettes and not ENDS have been available over the long term. Thus the analysis misses their stated goal, namely to examine the relative contribution of exclusive cigarette use versus exclusive ENDS use to hypertension risk (paraphrasing page 5). Something different would be required. This would be to examine incident hypertension risk among two groups of ever smokers, the first being those that continued smoking during the study period without using ENDS, and the second being those who did not continue smoking and used ENDS instead. The minority of ENDS users who never smoked traditional cigarettes could not contribute to this analysis, and arguably they should not because they can't fairly be compared with users of traditional cigarettes. Never smokers would be the comparison group for this analysis.

Response: The reviewer raises potential issues with our control for past cigarette use and our comparison group, which includes both former cigarette users (which we adjust for) and never smokers. To address these concerns, we conducted two sensitivity analyses.

First, we restricted our analysis to respondents who reported they had never smoked 100 cigarettes in their lifetime at baseline and examined the association between ENDS use and hypertension among never established smokers (see Table S7, see results below). Because of this restricted analysis, cigarette pack-years was removed, and our exposure was measured as time-varying ENDS use. As the results show, time-varying ENDS use was not associated with incident hypertension in the unadjusted (HR = 0.56, 95% CI 0.28, 1.13) or adjusted models (aHR=0.75, 95% CI 0.37, 1.52).

Second, to address the concern of the reviewer more directly, we created a revised exposure with 'never smoking' as the reference group, with the following categories: (1) former cigarettes, no ENDS;

(2) current cigarettes, no ENDS; (3) former cigarettes, current ENDS; (4) current cigarettes and ENDS; (5) current exclusive ENDS (see Table S6, results presented below). Prior to adjusting for confounders, former cigarette smoking and non-ENDS use (HR 1.43, 95% CI: 1.17, 1.75) and current cigarette smoking and non-ENDS use (HR 1.38, 95% CI: 1.22, 1.56) were associated with an increased risk of incident hypertension relative to never smoking. After adjusting for cigarette pack-years and other confounders, current cigarette smoking and non-ENDS use (aHR 1.20, 95% CI 1.04, 1.38) was the only group associated with an increased risk of incident hypertension relative to never smoking. Compared to never smoking, current ENDS use among respondents who never smoked (aHR 1.01, 95% CI 0.64, 1.60) or among respondents who currently smoked cigarette (aHR 1.13, 95% CI 0.84, 1.52) was not associated with an increased risk of incident hypertension.

Considered together, the results from our sensitivity analyses show that ENDS use was not associated with incident hypertension when the analysis was restricted to never established cigarette smoking or when never established cigarette smoking was the reference group. Further, with never use included as the reference group, ENDS use was not associated with an increased risk of hypertension among people who smoked cigarettes currently or formerly. The only statistically significant association in adjusted models was for cigarette smoking and non-ENDS use (aHR 1.20, 95% CI 1.04, 1.38). These findings provide further evidence that short-term ENDS use was not associated with an increased risk of incident hypertension, with or without cigarette use. We have included this sensitivity analysis in the supplemental material for the manuscript.

Table S7. Discrete time survival analysis predicting incidence of self-reported hypertension among never established cigarette smokers, Population Assessment of Tobacco and Health Study (Waves 1-5, 2013-2019)

	Unadjusted		Adjusted	
	Hazard	95% CI	Hazard	95% CI
Time varying ENDS use	0.56	0.28, 1.13	0.75	0.37, 1.52
Sociodemographic Risk factors				
Age (mean)^	1.04***	1.03, 1.04	1.04***	1.03, 1.04
Sex (Male=1)	1.25*	1.03, 1.52	1.31**	1.07, 1.60
Race/Ethnicity				
NH White	REF	REF	REF	REF
Hispanic	0.84	0.67, 1.05	0.89	0.69, 1.14
NH Black	1.42**	1.17, 1.72	1.56***	1.25, 1.93
NH Asian	0.40**	0.21, 0.77	0.54	0.28, 1.05
NH Other	1.25	0.80, 1.97	1.34	0.81, 2.19
Household Income				
<$50,000	REF	REF	REF	REF
>$50,000	0.75**	0.62, 0.90	0.74**	0.60, 0.90
missing	0.71	0.27, 1.87	0.53	0.19, 1.43
Baseline Risk Factors				
Family History of heart attack	1.41**	1.16, 1.71	1.23	0.99, 1.52
Obesity (BMI>30)	2.09***	1.72, 2.53	1.80***	1.47, 2.20
Diabetes diagnosis	2.59***	1.95, 3.45	1.71**	1.23, 2.36
Binge Drinking	1.09	0.71, 168	1.4	0.89, 2.18

Notes: Person N=9478 ; Risk Period N=32,579

*p<0.05, **p<0.01, ***p<0.001

^cigarette pack-years were rescaled to intervals of 10 packyears

Table S6. Discrete time survival analysis predicting incidence of self-reported hypertension with revised cigarette/ENDS exposure, Population Assessment of Tobacco and Health Study (Waves 1-5, 2013-2019)

	Unadjusted		Adjusted	
	Hazard	95% CI	Hazard	95% CI
Time varying cigarettes/ENDS use				
Never established use	REF	REF	REF	REF
Former cigarettes, no ENDS	1.43**	1.17, 1.75	0.97	0.78, 1.21
Current cigarettes, no ENDS	1.38***	1.22, 1.56	1.20*	1.04, 1.38
Former cigarettes, current ENDS	1	0.64, 1.55	1.01	0.64. 1.60
Current cigarettes and ENDS	1.07	0.80, 1.41	1.13	0.84, 1.52
Exclusive ENDS	0.64	0.31, 1.32	0.86	0.41, 1.82
Sociodemographic Risk factors				
Age (mean)^	1.03***	1.03-1.04	1.03***	1.03, 1.04
Sex (Male=1)	1.28**	1.11-1.48	1.33***	1.15, 1.53
Race/Ethnicity				
NH White	REF	REF	REF	REF
Hispanic	.83*	.71-.98	1	0.85, 1.17
NH Black	1.44***	1.24-1.68	1.61***	1.37, 1.89
NH Asian	.38***	.23-.64	0.56*	0.33, 0.94
NH Other	1.03	.73-1.44	1.05	0.75, 1.47
Household Income				
<$50,000	REF	REF	REF	REF
>$50,000	.80**	.70-.92	0.83*	0.72, 0.96
missing	0.67	.32-1.39	0.58	0.27, 1.24
Baseline Risk Factors				
Family History of heart attack	1.43***	1.24-1.66	1.28**	1.09, 1.49
Obesity (BMI>30)	1.89***	1.66-2.15	1.72***	1.50, 1.98
Diabetes diagnosis	2.48***	2.0-3.06	1.76***	1.39, 2.22
Binge Drinking	1.22	.99-1.50	1.26*	1.01, 1.57
Smoking History Variables				
Pack years (intervals of 10)^	1.17***	1.13-1.21	1.04	0.99, 1.09

Notes: Person N=17,539 ; Risk Period N=59,367

*p<0.05, **p<0.01, ***p<0.001

^cigarette pack-years were rescaled to intervals of 10 packyears

It is stated (Discussion) that they studied “short-term follow-up of approximately 5 years” for ENDS, but this 5 year interval sounds like the maximal follow-up of the study rather than the actual duration of exposure to ENDS among users. Please clarify and also see comment above regarding the need for a time-based exposure metric.

Response: In addition to discussing the need for developing a valid cumulative ENDS exposure, we have clarified our text about our ENDS exposure. The last sentence of the first paragraph in the discussion (page 19) has been revised and now reads:

> In contrast, studies examining the effects of ENDS use on hypertension have only recently been published,[22] and in a longitudinal follow-up of approximately five years, we found no evidence that short term and time-varying ENDS use was associated with an increased risk of incident hypertension.

Reviewer: 2

Dr. Takuro Kubozono, Kagoshima University
Comments to the Author:
In this manuscript, the authors investigated that the association between cigarette and electronic nicotine delivery systems (ENDS) use on self-reported incident hypertension. We found that smoking increased the risk of self-reported hypertension but ENDS use did not. This study has some interesting findings but also presents several problems.

1. The greatest problem is the self-reporting of the occurrence of hypertension. It is very difficult to discuss the development of hypertension without measuring blood pressure. Because blood pressure is not measured, the onset of hypertension is misdiagnosed. In addition, even if baseline blood pressure does not reach the criteria for hypertension, if it is high, the possibility of developing hypertension in the future is increased.

Response: While we agree with the reviewer that it would be ideal to have a direct measure of blood pressure, we do not believe this invalidates our study as research has examined the validity of self-reported hypertension. For example, using NHANES data, Vargas et al (1997) found that self-reported hypertension had acceptable levels of specificity and sensitivity, and concluded that self-reported hypertension was appropriate when measured blood pressure was not available. Wellman et al (2020) found that self-reported hypertension was reasonably accurate, with the caveat that self-reported hypertension was under reported by some respondents. In a recent study also using data from the PATH Study, Mahoney et al (2021) examined the validity of self-reported cardiovascular disease measures, including hypertension, and found evidence of reliability and concurrent validity. Reflecting this, we added the following sentence to the methods section of the manuscript: “The reliability and concurrent validity of self-reported hypertension has been established in a previous study using PATH Study data.”

However, we remain cognizant of potential limitations associated with self-reported hypertension, especially given research showing that self-reported hypertension is underreported in many studies (Gonçalves et al, 2018). To address this, we conducted several different analyses. For the main

analysis, we adopted an inclusive measurement strategy by including all respondents who responded 'yes' to hypertension regardless of whether they reported seeing a doctor during the past year (respondents in W4 and W5 were only asked about hypertension if they saw a doctor). To ensure our results were not affected by this measurement strategy, we did a sensitivity analysis where we only considered respondents to be hypertensive if they self-reported hypertension and seeing a doctor during the past year. Because of potential concerns with measurement, we have added the results from this sensitivity analysis to the appendix in the revised manuscript.

To better approximate clinical hypertension and minimize potential false positive errors in self-reported hypertension, we also included a measure of medicated hypertension as another sensitivity analysis (self-reported hypertension and medication for hypertension). The substantive analysis from this sensitivity analysis, found in Table A4, were similar to the results from the main analysis as we found that exclusive cigarette use was associated with "self-reported incident hypertension and medication use" while ENDS use was not.

Despite evidence of the validity of self-reported hypertension in the PATH Study and our sensitivity analyses, we still highlight the limitation of our measure of self-reported diagnosed hypertension in our manuscript. On page 21, we state:

> Since systolic and diastolic blood pressure measures are not available in the PATH study, the reported incidence may underestimate the true incidence of hypertension,[35,36] particularly for some sociodemographic groups.[35] Future research would benefit from including measured hypertension instead of self-reported hypertension where possible

References:

Gonçalves, V. S., Andrade, K. R., Carvalho, K., Silva, M. T., Pereira, M. G., & Galvao, T. F. (2018). Accuracy of self-reported hypertension: a systematic review and meta-analysis. *Journal of hypertension*, *36*(5), 970-978.

Mahoney MC, Rivard C, Hammad HT, et al. Cardiovascular risk factor and disease measures from the Population Assessment of Tobacco and Health (PATH) Study. *International journal of environmental research and public health.* 2021;18(14):7692.

Vargas, C. M., Burt, V. L., Gillum, R. F., & Pamuk, E. R. (1997). Validity of self-reported hypertension in the National Health and Nutrition Examination Survey III, 1988–1991. *Preventive medicine*, *26*(5), 678-685.

Wellman, J. L., Holmes, B., & Hill, S. Y. (2020). Accuracy of self-reported hypertension: Effect of age, gender, and history of alcohol dependence. *The Journal of Clinical Hypertension*, *22*(5), 842-849.

2. The number of ENDS cases is too small. Also, the average age of ESDN is young (33.2 years). Therefore, the number of cases with hypertension may have been too small to be significant.

Response: While we do agree that the number of respondents who use ENDS at baseline was relatively small, one of the advantages of the discrete-time approach is that we use ENDS information from each wave in the analysis. This means that the actual number of respondents who use ENDS is much larger in the restructured person-period data set. The descriptive statistics of our cigarette/ENDS exposure is presented in Table S1 (see below). As the reviewer can see, the percent of respondents in the risk set who reported exclusive ENDS use or dual ENDS/cigarette use increased as the waves progressed. This is a nationally representative survey, so the prevalence of ENDS use is representative of the US population, which remains low among adults.

The hazard estimate for exclusive ENDS use was 1.0 for our main multivariable analysis (Table 4), and was less than 1.0 for medicated hypertension (Table S2, aHR 0.88, 95% CI, 0.51, 1.50), for those under 55 (Table S6, aHR 0.92, 0.61, 1.37), and for those who reported using ENDS 10+ days in the past 30 days (Table S7, aHR 0.95, 0.67, 1.35). In fact, across all analyses, the hazard estimate for exclusive ENDS use never approached statistical significance in any model, and we do not believe that this is due to the small number of respondents who used ENDS as the direction of the hazard estimates and their associated confidence intervals do not suggest that a significant association if there were a larger number of ENDS users.

However, the direction of the hazard estimates for dual ENDS/cigarettes use was positive in most multivariable models, making it possible that the small number of respondents who used ENDS may be a potential reason we are not finding statistically significant differences for dual use versus non-use. In the second paragraph of the discussion section, we state:

> These dual use estimates also had relatively wide confidence intervals, and the small number of respondents who reported dual use may limit the power to detect a statistically significant association.

In addition, we also added a caveat to our limitations section. Specifically, we state:

ENDS use was only reported by a relatively small number of respondents, and it is possible that the small number of respondents using ENDS may have limited power to detect an association between ENDS use and incident hypertension.

Table S1. Descriptive Statistics for Time-Varying Cigarette/ENDS Use, Established Adult Cigarette Smokers, Population Assessment of Tobacco & Health Study

	Follow-Up Interview*							
	Wave 1		Wave 2		Wave 3		Wave 4	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Time varying cigarettes/ENDS use								
Non use	79.2	78.5-79.9	78.6	77.9-79.4	79	78.2-79.7	79.9	79.0-80.6
Exclusive cigarette use	18	17.3-18.7	17.8	17.1-18.5	17.5	16.9-18.3	16.9	16.2-17.7
Exclusive ENDS use	1.1	0.92-1.96	1.3	1.2-1.5	1.4	1.3-1.6	1.5	1.3-1.7
Dual use	1.7	1.6-2.0	2.2	2.0-2.5	2.1	1.8-2.3	1.8	1.6-2.0

*time-varying covariates were lagged by one wave to limit issues with reverse causation

3. The number and frequency of cigarettes and ENDS should be investigated.

We agree with the reviewer that the current study would be strengthened by examining the number and frequency of cigarettes and ENDS used in the analysis. One challenge is that there is no reliable or generally agreed upon way to measure intensity of ENDS use, so we are not able to address that limitation in this response. Regarding frequency of use, we conducted a sensitivity analysis where we changed our cigarette/ENDS exposure by defining use as 10+ days in the past 30 days rather than every day or someday use. This approach allowed us to examine whether a measure of more frequent cigarette/ENDS use was associated with incident hypertension. The results from this sensitivity analysis are included as Table S7 (and pasted below). The substantive results from this sensitivity analysis are nearly identical to the results from the main analysis for our exposure. Compared to non-use, exclusive cigarette use was associated with incident hypertension (10+ days, aHR 1.18, 95% CI 1.05, 1.33 vs Table 4, aHR 1.21, 1.06, 1.38), while exclusive ENDS use (10+ days, aHR 0.95, 95% CI: 0.67, 1.35 vs Table 4, aHR 1.0, 95% CI 0.68, 1.47) and dual use (10+ days, aHR 1.14, 0.80, 1.64 vs Table 4, aHR 1.15, 95% CI 0.87, 1.52) were not.

Table S5. Discrete time survival analysis predicting incidence of self-reported hypertension among adults with ‘regular’ cigarette/ENDS use (10+ days), Population Assessment of Tobacco and Health Study (Waves 1-5, 2013-2019)

	Hazard	95% CI	Hazard	95% CI
Time varying cigarettes/ENDS use				
Non use	REF	REF	REF	REF
Exclusive cigarette use	1.28***	1.15-1.42	1.18**	1.05, 1.33
Exclusive ENDS use	0.84	.58-1.21	0.95	0.67, 1.35
Dual use	1	.77-1.30	1.14	0.80, 1.64
Sociodemographic Risk factors				
Age (mean)^	1.03***	1.03-1.04	1.03***	1.03, 1.04
Sex (Male=1)	1.28**	1.11-1.48	1.33***	1.16,1 .54
Race/Ethnicity				
NH White	REF	REF	REF	REF
Hispanic	.83*	.71-.98	0.99	0.84, 1.17
NH Black	1.44***	1.24-1.68	1.62***	1.39, 1.90
NH Asian	.38***	.23-.64	0.55*	0.33, 0.93
NH Other	1.03	.73-1.44	1.06	0.76, 1.49
Household Income				
<$50,000	REF	REF	REF	REF
>$50,000	.80**	.70-.92	0.83*	0.72, 0.96
missing	0.67	.32-1.39	0.58	0.27, 1.23
Baseline Risk Factors				
Family History of heart attack	1.43***	1.24-1.66	1.27**	1.08, 1.49
Obesity (BMI>30)	1.89***	1.66-2.15	1.71***	1.50, 1.96
Diabetes diagnosis	2.48***	2.0-3.06	1.74***	1.37, 2.20
Binge Drinking	1.22	.99-1.50	1.26*	1.02, 1.57
Smoking History Variables				
Former Established smoker	1.42***	1.18-1.72	1.02	0.83, 1.27
Pack years (intervals of 10)^	1.17***	1.13-1.21	1.04	0.99, 1.09

Notes: Person N=17,539 ; Risk Period N=59,367

*p<0.05, **p<0.01, ***p<0.001

^cigarette pack-years were rescaled to intervals of 10 packyears

VERSION 2 – REVIEW

REVIEWER	Kaplan, Robert Albert Einstein College of Medicine
REVIEW RETURNED	17-Feb-2023

GENERAL COMMENTS	The authors have done an admirable job at addressing the comments, completing a large number of additional analyses and rewriting substantially. The work is essentially in acceptable format. Two additional details were only partially addressed, more details needed still: 1, the manuscript still does not explain how participants were recruited which was a point on the initial critique. For example

	were participants approached door to door, by random digit dialing, by mail, through a medical clinic, etc? What was the sampling frame? 2, The exclusions have been better clarified in the response. However I disagree with their characterization of this criteria as "no self-reported heart condition." Hypertension or high cholesterol for example are not diseases affecting the heart. Please find an accurate short hand term for the medical exclusions, or perhaps it will be better to avoid misleading shortcuts and just describe what was done. Thank you and I commend the investigators for a strong and important study with a balanced interpretation.

VERSION 2 – AUTHOR RESPONSE

Reviewer Comments

1.Two additional details were only partially addressed, more details needed still:
1, the manuscript still does not explain how participants were recruited which was a point on the initial critique. For example were participants approached door to door, by random digit dialing, by mail, through a medical clinic, etc? What was the sampling frame?

Response: We apologize for not clarifying this more clearly in the revised manuscript. The Population Assessment of Tobacco Health (PATH) Study uses an address-based sampling frame to randomly select households based on residential addresses derived from the United States Postal Service. Once households were identified, a two-phase sampling procedure was used to select adults within sampled households for in-person interviews. We have revised the text of the manuscript and have added the following information on page 6 of the manuscript:

> "A stratified area probability design was used to sample geographical segments from 156 geographical primary sampling units. An address-based sampling frame was then used to randomly select households based on residential addresses derived from the United States Postal Service. Once households were identified, a two-phase sampling procedure was used to select adults within sampled households for in-person interviews."

2.The exclusions have been better clarified in the response. However I disagree with their characterization of this criteria as "no self-reported heart condition." Hypertension or high cholesterol for example are not diseases affecting the heart. Please find an accurate short hand term for the medical exclusions, or perhaps it will be better to avoid misleading shortcuts and just describe what was done.

Response: We thank the reviewer for this comment and agree that the short-hand term may be misleading. We have removed this language from the manuscript and changed the description of our medical exclusion in the method section. We now sate (pp 6.-7):

> "The analytic sample for the current study was restricted to adult respondents (18+) (Wave 1, n=32,320) with no self-reported heart condition (e.g., congestive heart failure, heart attack, stroke) or previous diagnosis of hypertension or high cholesterol at baseline (n=21,734)."