Supplemental Information for McClelland, M. L., Sesoko, C., MacDonald, D. A., Davis, L. & McClelland, S. *The immediate physiological effects of e-cigarette use and exposure to second-hand e-cigarette vapor.*

This file is meant to augment information in the aforementioned article, with primary emphasis to providing a fulsome reporting of all aspects of data cleaning, preliminary analyses, main analyses and ancillary analyses.

This file is divided into two main sections. The first section provides a succinct description of what was done with the data and is written akin to a results section in an article. It includes two tables. This provided for readers who want a fairly quick and accessible description of what was done and what was found in the study.

The second section provides extensive details on all aspects of data preparation, data cleaning, and statistical analysis. The information is presented in a step-wise manner with most statistical information given in several tables.

This file should be read in conjunction with the article.

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SECTION 1

Prior to running main analyses, data were examined to identify any problems with missing data points and to determine if any of the physiological variables demonstrated severe non-normality. In addition, we examined variances on all pre- and post-physiological variables between groups to determine if they met the assumption of equality of variances that is necessary to run parametric analyses such as Analysis of Variance (ANOVA) and Analysis of Covariance (ANCOVA). Finally, we did some preliminary analyses to ascertain whether or not the Non-vape and Vape groups could be treated as equivalent in terms of essential demographic and health characteristics and pre-vape levels of physiological functioning.

In terms of missing data, values for Post-vape Heart Rate and Post-vape SpO2 were missing for one participant. Rather than remove the participant from the data set, we elected to use a regression-based imputation strategy to estimate the missing values on these variables.

With respect to assessment of normality, Pre-vape Blood Sugar and Pre- and Post-Vape SpO2 were found to demonstrate problems with severely non-normal distributions (i.e., highly significant skew and/or kurtosis). Closer examination of the distribution for Pre-vape Blood Sugar revealed an extreme outlier value for one participant that, when removed, resulted in this variable no longer demonstrating an issue with non-normality. It was subsequently decided that the participant with the extreme outlying value would be excluded from analyses involving Blood Sugar but included in analyses with all other variables. For SpO2, there were no outlying scores that could be identified as responsible for the non-normality and efforts at transformation did not improve the distribution. As a result, we decided to proceed with parametric analyses with this variable but to also run non-parametric statistics to test for between group and pre-post differences as such statistics are not impacted by non-normality.

Turning to assessment of homogeneity of variances between vape groups, Levene's tests were found to be significant for Pre-and Post-vape Blood Sugar, Pre- and Post-vape Forced Vital Capacity (FVC), and Post-vape Respiratory Frequency. These findings indicate that the vape groups cannot be assumed to have equal variances on these variables. While this was cause for some concern, the facts that (a) vape group is a fixed between groups factor and (b) the two groups are roughly similar in size (e.g., for Non-vape group, n= 73; Vape group n= 76), we concluded that the unequal variances were unlikely to have an overly disruptive influence on our main statistical analyses.

Last, examination of the vape groups on Pre-vape physiological variables revealed one significant finding involving FVC where the Vape group obtained the significantly higher mean score ($F[1,147]= 25.93$, $p<.001$; Non-vape mean = 3.97, Vape mean= 4.79). For demographic and health variables, significant differences between the vape groups were found for Age ($F[1,147]= 8.32$, $p= .005$; Non-vape mean= 23.77, Vape mean= 20.39), Gender ($\chi^2[1]= 23.68$, $p<.001$; Non-vape group had more females, Vape group had more males), Recreational Drug Use ($\chi^2[1]= 17.82$, $p<.001$; Vape group had significantly greater number of drug users), Lung Disease ($\chi^2[1]= 6.14$, $p= .013$; Vape group had significantly greater number of participants reporting lung disease), Smoking ($\chi^2[1]= 4.68$, $p= .031$; Fisher's Exact Test one-tailed p-value= .033; Vape group had significantly greater number of smokers), and Drinking ($\chi^2[1]= 3.92$, $p= .048$; Vape group had significantly greater number of drinkers). Based on these results which suggest that the two vape groups significantly differ on a variety of variables, it was decided that demographic and health variables would be used as covariates. This decision was supported by an ancillary correlational analysis (not reported here due to length considerations) which found several significant correlations between health and demographic variables and physiological variables.

Main Analyses

Given that the study used a 2 (between groups) by 2 (pre-post) experimental design, mixed factorial (also known as split plot) Analyses of Variance (ANOVA) were computed for each of the physiological variables. The results of these analyses can be found in Table 1-1. To evaluate the impact of demographic and health variables on the main results, two sets of mixed factorial Analyses of Covariance (ANCOVA) were also computed. In the first set, age and gender were used as covariates. In the second, all 10 demographic and health variables were used as covariates. These analyses can be found in Table 1-2. The findings for each physiological variable across all sets of analyses can be succinctly described as follows:

Heart Rate. The ANOVA produced non-significant main effects but a significant interaction effect ($F[1,147]= 6.79$, $p= .010$, Partial $eta^2= .04$). This interaction remained significant after controlling for age, gender, and the eight health variables in the ANCOVAs. Inspection of means indicates that exposure to vapor resulted in a reduction in mean heart rate for the Non-vape group while vaping contributed to an increase in mean heart rate for the Vape group.

Mean Arterial Pressure. The between groups main effect was found to be significant ($F[1,147]= 4.22$, $p= .042$, Partial $eta^2= .03$) as was the interaction ($F[1,147]= 6.10$, $p= .015$, Partial $eta^2= .04$). Examination of means across the study conditions indicates that the Non-vape group showed a reduction in mean values at Post-vape while the mean values at Pre- and Post-vape remained similar for the Vape group. When controlling for covariates, the between groups effect became non-significant while the interaction remained significant. Controlling for all demographic and health variables, however, resulted in the interaction becoming non-significant, though the repeated measures main effect emerged as significant ($F[1,134]= 5.79$, $p= .017$, Partial $eta^2=.04$).

Respiratory Frequency. The ANOVA uncovered significant results for both main effects and the interaction effect with all effects remaining significant after the control of

covariates in the ANCOVAs. For the between groups main effect ($F[1,147]= 8.63$, $p= .006$, Partial $eta^2= .05$), the Vape group was found to produce the higher mean value. For the repeated measures main effect ($F[1,147]= 4.29$, $p= .040$, Partial $eta^2= .03$), Post-vape mean values were higher. For the interaction effect, ($F[1,147]= 5.34$, $p= .022$, Partial $eta^2=.04$), the Vape group demonstrated a greater mean increase at Post-vape.

Blood Sugar. ANOVA and ANCOVA results were non-significant.

Forced Vital Capacity. The ANOVA produced a significant between groups main effect ($F[1,147]= 24.55$, $p< .001$, Partial $eta^2= .14$) with the Vape group generating the higher mean score. This finding became non-significant when controlling for covariates.

SpO2. The ANOVA produced a significant repeated measures main effect ($F[1,147]= 6.94$, $p= .009$, Partial $eta^2= .05$) with both vape groups showing a reduction in mean values at Post-vape. This result remained significant after controlling for covariates in the ANCOVAs. Due to the fact that SpO2 was observed to be severely non-normal, non-parametric analyses were also completed. Mann-Whitney tests were used to evaluate between group differences in Pre- and Post-vape values and Wilcoxon tests were used to evaluate Pre-Post differences for the Non-vape and Vape groups separately. Both Mann-Whitney tests emerged non-significant, while the Wilcoxon test was significant for the Vape group only ($z= -2.56$, $p= .011$).

Temperature. The ANOVA generated a significant repeated measures main effect ($F[1,147]= 39.69$, $p< .001$, Partial $eta^2= .21$) with both groups having produced higher mean values at Post-vape. This result remained significant after controlling for covariates in the ANCOVAs.

Table 1-1. Results of Mixed Factorial ANOVAs Examining Physiological Variables as a Function Vape Group (Between Groups) and Pre-post Vaping Conditions (Repeated Measures)

	Non-vape Group		Vape Group		ANOVA		
	Pre-Vape Mean (SD)	Post-Vape Mean (SD)	Pre-Vape Mean (SD)	Post-Vape Mean (SD)	Between Groups Main Effect	Repeated Measures Main Effect	Interaction
Heart Rate	88.81 (18.24)	86.83 (18.01)	84.20 (16.28)	88.12 (15.27)	F= 0.43 p=.514	F= 0.73 p= .393	F= 6.79 p= .010 Partial eta^2= .04
Mean Arterial Pressure	94.03 (10.05)	90.83 (10.29)	95.14 (10.74)	95.84 (10.07)	F= 4.22 p= .042 Partial eta^2= .03	F= 2.49 p= .117	F= 6.10 p= .015 Partial eta^2= .04
Respiratory Frequency	11.18 (1.15)	11.15 (1.10)	11.29 (1.02)	11.79 (1.06)	F= 8.63 p= .006 Partial eta^2= .05	F= 4.29 p= .040 Partial eta^2= .03	F= 5.34 p= .022 Partial eta^2=.04
Blood Sugar	97.53 (19.19)	98.63 (18.05)	94.45 (12.34)	96.01 (14.73)	F= 1.49 p= .223	F= 1.04 p= .310	F= 0.03 p= .858
Forced Vital Capacity	3.97 (0.88)	3.97 (0.89)	4.79 (1.07)	4.73 (1.10)	F= 24.55 p< .001 Partial eta^2= .14	F= 0.80 p= .373	F= 0.79 p= .375
SpO2	97.97 (1.72)	97.37 (2.94)	98.20 (1.06)	97.71 (1.66)	F= 1.33 p= .250	F= 6.94 p= .009 Partial eta^2= .05	F= 0.08 p= .780
Temperature	97.87 (0.75)	98.27 (0.49)	97.72 (0.76)	98.20 (0.75)	F= 1.40 p= .239	F= 39.69 p< .001 Partial eta^2= .21	F= 0.36 p= .548

Note. For Non-Vape Group, n= 73 for all analyses except Blood Sugar where n= 72 due to the exclusion of a case with an extreme value. For Vape Group, n= 76. For all ANOVAs except Blood Sugar, degrees of freedom for both main effects and the interaction is 1, 147. Degrees of freedom for Blood Sugar is 1, 146

Table 1-2. Results of Mixed Factorial ANCOVAs Examining Physiological Variables as a Function Vape Group (Between Groups) and Pre-post Vaping Conditions (Repeated Measures) While Controlling for Covariates

	ANCOVA Controlling for Age and Gender			ANCOVA Controlling for Age and Gender and Eight Health Variables		
	Between Groups Main Effect	Repeated Measures Main Effect	Interaction	Between Groups Main Effect	Repeated Measures Main Effect	Interaction
Heart Rate	F(1,145)= 0.01 p= .920	F(1,147)= 0.73 p= .393	F(1,147)= 6.79 p= .010 Partial eta^2= .04	F(1,124)= 0.01 p= .907	F(1,134)= 0.40 p= .526	F(1,134)= 4.94 p= .028 Partial eta^2=.04
Mean Arterial Pressure	F(1,145)= 1.53 p= .218	F(1,147)= 2.49 p= .117	F(1,147)= 6.10 p= .015 Partial eta^2= .04	F(1,124)= 1.42 p= .236	F(1,134)= 5.79 p= .017 Partial eta^2=.04	F(1,134)= 3.24 p= .074
Respiratory Frequency	F(1,145)= 7.09 p= .009 Partial eta^2= .05	F(1,147)= 4.29 p= .040 Partial eta^2= .03	F(1,147)= 5.34 p= .022 Partial eta^2= .04	F(1,124)= 5.15 p= .025 Partial eta^2=.04	F(1,134)= 5.11 p= .025 Partial eta^2=.04	F(1,134)= 6.27 p= .014 Partial eta^2=.04
Blood Sugar	F(1,144)= 0.11 p= .744	F(1,146)= 1.04 p= .310	F(1,146)= 0.03 p= .858	F(1,123)= 0.01 p= .926	F(1,133)= 1.27 p= .262	F(1,133)= 0.70 p= .406
Forced Vital Capacity	F(1,145)= 2.36 p= .127	F(1,147)= 0.80 p= .373	F(1,147)= 0.79 p= .375	F(1,124)= 1.16 p= .284	F(1,134)= 0.85 p= .359	F(1,134)= 0.92 p= .338
SpO2	F(1,145)= 0.64 p= .427	F(1,147)= 6.94 p= .009 Partial eta^2= .05	F(1,147)= 0.08 p= .780	F(1,124)= 0.62 p= .432	F(1,134)= 7.49 p= .007 Partial eta^2=.05	F(1,134)= 0.16 p= .690
Temperature	F(1,145)= 0.00 p= .948	F(1,147)= 39.69 p< .001 Partial eta^2= .21	F(1,147)= 0.36 p= .548	F(1,124)= 0.06 p= .809	F(1,134)= 40.44 p< .001 Partial eta^2=.23	F(1,134)= 0.54 p= .465

Note. Health variables include Present Health, Recreational Drug Use, Mental Health Treatment (with unsure excluded), Lung Disease, Oral Disease (with unsure excluded), Cardiac Disease, Smoking (with former excluded), and Drinking (with former excluded).

SECTION 2—Detailed Overview of Data Cleaning, Preparation, and Analysis

Step One—Initial Evaluation of Data Quality and Data Cleaning

This step was comprised of three sub-steps.

Sub-step (1)—Inspection of the Data set for Missing Data

Examination of the data indicated that only two data points were missing, with both occurring on the same case (i.e., case ID 2487208742). The specific data points that were missing for this case were Post-vape Heart Rate and Post-vape SpO2.

As cases with missing data would get excluded from any analyses involving variables that have the missing data, it was decided to use a regression-based approach to impute estimated values for the missing data points so as to allow for the use of the case in all analyses.

To estimate the missing data point for *Post-vape Heart Rate*, we first ran a multiple regression where we used Post-vape Heart Rate as the dependent variable and Vape Group, Gender, Age, Present health, and all other post-vape physiological variables (i.e., Respiratory Frequency, Blood Sugar, FVC, Temperature, and Mean Arterial Pressure) except Post-vape SpO2 as predictors. We couldn't use Post-vape SpO2 as a predictor because the case was missing the datum on this variable.

We then examined the output to see which predictors were statistically significant. We then re-ran the regression including only significant predictors. Following this process, the only significant predictor of Post-vape Heart Rate was Post-vape Blood Sugar.

Using the results from the second analysis, we created regression equation that we could use to calculate an estimated Post-vape Heart Rate value for case ID 2487208742. For the sake of thoroughness, the regression equation is as follows:

Post-vape Heart Rate= 68.56 + .19(Post-vape Blood Sugar)

Using this equation, the estimated value for Post-vape Heart Rate for case ID 2487208742 is 94.40. This value was entered into the data set.

Following the same process, we used regression to calculate an estimated value for Post-vape SpO2. The only significant predictor was Post-vape Heart Rate. The regression equation that was devised was as follows:

Post-vape SpO2 = 101.35 + (-.04(Post-vape Heart Rate))

Using this equation, the estimated value for Post-vape SpO2 for case ID 2487208742 is 97.57. Since all SpO2 values in the data set are whole numbers, we rounded this value to 98. This value was entered into the data set.

Sub-step (2)—Examination of Continuous Variables to Assess Normality and Presence of Extreme Outliers

In order to ensure that the data are in a form that meet the assumptions for the kind of statistics we need to run (e.g., univariate normality, absence of extreme outliers defined as any score that is 3 or more standard deviations above or below the mean for a variable), descriptive statistics were run for all continuously measured physiological variables (i.e., the pre- and post-vape variables of Heart Rate, Mean Arterial Pressure, Respiratory Frequency, Blood Sugar, FVC, SpO2, and Temperature). More specifically, we examined descriptive statistics and score distributions. If a variable was found to be sufficiently normal in its distribution (i.e., if it was found to be non-severely non-normal), then we did no further investigation of the variable (e.g., we did not go searching for extreme outliers). Conversely, if a variable was found to be severely non-normal based upon elevated skew and/or kurtosis, then we examined the score distributions closely and looked for extreme outliers. If an extreme outlier was found, then we would exclude that value and re-examine descriptive statistics and score distributions to see whether or not it improved the distributional properties of the variable.

Means, standard deviations, minimum and maximum scores, skew, and kurtosis were computed for age and all physiological variables using the entire pooled sample (N= 149) and for the Non-vape (n= 73) and Vape (n= 76) groups separately. This information is presented in Tables 2-1, 2-2, and 2-3.

Table 2-1

Descriptive Statistics for Age and All Physiological Variables for Entire Sample (N= 149)

	Mean	SD	Minimum	Maximum	Skewness	Kurtosis
Age	**22.05**	**7.31**	**18.00**	**63.00**	**3.73**	**15.43**
Pre-vape Heart Rate	86.46	17.36	53.00	132.00	0.50	-0.44
Pre-vape Mean Arterial Pressure	94.59	10.39	57.67	124.67	0.00	0.74
Pre-vape Respiratory Frequency	11.23	1.08	10.00	14.00	0.04	-0.97
Pre-vape Blood Sugar	**97.01**	**20.64**	**64.00**	**255.00**	**3.53**	**23.38**
Pre-vape FVC	4.39	1.06	2.22	8.00	0.58	0.08
Pre-vape SpO2	**98.09**	**1.42**	**89.00**	**99.00**	**-3.55**	**17.97**
Pre-vape Temperature	97.79	0.75	95.10	99.50	-0.67	0.95
Post-vape Heart Rate	87.49	16.63	42.00	147.00	0.51	1.47
Post-vape Mean Arterial Pressure	93.38	10.45	65.67	120.33	0.19	0.29
Post-vape Respiratory Frequency	11.48	1.12	10.00	16.00	0.25	0.86
Post-vape Blood Sugar	97.91	18.05	58.00	190.00	1.45	4.97
Post-vape FVC	4.36	1.07	2.49	8.34	0.66	0.43
Post-vape SpO2	**97.54**	**2.37**	**81.00**	**99.00**	**-4.11**	**21.21**
Post-vape Temperature	98.23	0.63	94.80	99.80	-1.34	5.90

Note. SD= Standard Deviation; For Skewness, values in excess of 2.0 are indicative of severe non-normality. For Kurtosis, values in excess of 7.0 are indicative of severe non-normality. Variables demonstrating severe non-normality are in **bold** font.

Table 2-2

Descriptive Statistics for Age and All Physiological Variables for Non-Vape Sample (n= 73)

	Mean	SD	Minimum	Maximum	Skewness	Kurtosis
Age	**23.77**	**9.78**	**18.00**	**63.00**	**2.68**	**6.96**
Pre-vape Heart Rate	88.81	18.24	53.00	132.00	0.32	-0.50
Pre-vape Mean Arterial Pressure	94.03	10.05	77.33	124.67	0.67	0.11
Pre-vape Respiratory Frequency	11.18	1.15	10.00	14.00	0.32	-0.77
Pre-vape Blood Sugar	**99.68**	**26.51**	**64.00**	**255.00**	**3.14**	**16.06**
Pre-vape FVC	3.97	0.88	2.22	6.84	0.93	1.62
Pre-vape SpO2	**97.97**	**1.72**	**89.00**	**99.00**	**-3.54**	**15.50**
Pre-vape Temperature	97.87	0.75	95.50	99.50	-0.41	0.36
Post-vape Heart Rate	86.83	18.01	42.00	147.00	0.28	1.24
Post-vape Mean Arterial Pressure	90.83	10.29	65.67	119.67	-0.01	0.43
Post-vape Respiratory Frequency	11.15	1.10	10.00	14.00	0.21	-0.98
Post-vape Blood Sugar	99.88	20.87	58.00	190.00	1.35	3.83
Post-vape FVC	3.97	0.89	2.49	6.58	0.94	1.21
Post-vape SpO2	**97.37**	**2.94**	**81.00**	**99.00**	**-3.66**	**15.52**
Post-vape Temperature	98.27	0.49	96.80	99.20	-0.44	0.53

Note. SD= Standard Deviation; For Skewness, values in excess of 2.0 are indicative of severe non-normality. For Kurtosis, values in excess of 7.0 are indicative of severe non-normality. Variables demonstrating severe non-normality are in **bold** font.

Table 2-3

Descriptive Statistics for Age and All Physiological Variables for Vape Sample (n= 76)

	Mean	SD	Minimum	Maximum	Skewness	Kurtosis
Age	**20.39**	**2.81**	**18.00**	**36.00**	**2.82**	**12.35**
Pre-vape Heart Rate	84.20	16.28	57.00	127.00	0.68	-0.27
Pre-vape Mean Arterial Pressure	95.14	10.74	57.67	117.33	-0.54	1.53
Pre-vape Respiratory Frequency	11.29	1.02	10.00	14.00	-0.30	-1.19
Pre-vape Blood Sugar	94.45	12.34	68.00	144.00	0.88	2.38
Pre-vape FVC	4.79	1.07	2.80	8.00	0.27	-0.19
Pre-vape SpO2	**98.20**	**1.06**	**93.00**	**99.00**	**-2.14**	**7.20**
Pre-vape Temperature	97.72	0.76	95.10	99.20	-0.92	1.44
Post-vape Heart Rate	88.12	15.27	60.00	136.00	0.93	1.73
Post-vape Mean Arterial Pressure	95.84	10.07	76.67	120.33	0.47	-0.17
Post-vape Respiratory Frequency	11.79	1.06	10.00	16.00	0.44	3.15
Post-vape Blood Sugar	96.01	14.73	60.00	165.00	1.24	5.41
Post-vape FVC	4.73	1.10	2.61	8.34	0.39	0.40
Post-vape SpO2	**97.71**	**1.66**	**87.00**	**99.00**	**-3.84**	**22.44**
Post-vape Temperature	98.20	0.75	94.80	99.80	-1.43	5.43

Note. SD= Standard Deviation; For Skewness, values in excess of 2.0 are indicative of severe non-normality. For Kurtosis, values in excess of 7.0 are indicative of severe non-normality. Variables demonstrating severe non-normality are in **bold** font.

For the total pooled sample, four variables were found to produce severely non-normal distributions as reflected in skew greater than 2.0 and/or kurtosis greater than 7.0. These variables are Age, Pre-vape Blood Sugar, Pre-vape SpO2, and Post-vape SpO2.

For the Non-Vape group only, four variables were found to produce severely non-normal distributions. These variables are Age, Pre-vape Blood Sugar, Pre-vape SpO2, and Post-vape SpO2.

For the Vape group only, three variables were found to produce severely non-normal distributions. These variables are Age, Pre-vape SpO2, and Post-vape SpO2.

We took a closer look at the severely non-normal variables.

Age—Examination of the descriptive statistics and distribution for age revealed that for the total pooled sample (N= 149) the variable is severely non-normal (skew= 3.73, kurtosis= 15.43, mean= 22.05, standard deviation= 7.31, minimum= 18, maximum= 63). One-hundred and twenty-seven (141) cases have ages ranging from 18 to 30. Eight cases have an age ranging between 31 and 63. When the cases with ages of 31 or higher are excluded, the variable ceases to be severely non-normal (skew= 1.46, kurtosis= 1.74, mean= 20.54, standard deviation= 2.84, minimum= 18, maximum= 30).

When examined for the Non-vape group only (n=73), age is severely non-normal (skew= 2.68, kurtosis= 6.96, mean= 23.77, standard deviation= 9.78, minimum= 18, maximum= 63). Sixty-six (66) of the cases have an age between 18 and 30. Seven have an age between 31 and 63. Six cases have an age of 40 or above. When cases with ages of 31 or higher are excluded, age is no longer severely non-normal (skew= 1.21, kurtosis= 0.45, mean= 20.94, standard deviation= 3.44, minimum= 18, maximum= 30).

When examined for the Vape group only (n= 76), age is severely non-normal (skew= 2.82, kurtosis= 12.35, mean= 20.40, standard deviation= 2.81, minimum= 18, maximum= 36). Seventy-five (75) cases have an age between 18 and 30. One participant has an age of 36. When the one case with age 36 is excluded, age ceases being severely non-normal (skew= 1.34, kurtosis= 2.15, mean= 20.19, standard deviation= 2.15, minimum= 18, maximum= 28).

If age is a variable known to have an influence on the main physiological variables of interest to the study, then it is a variable that may need to be included in main statistical analyses. As such, the exclusion of extreme outlying ages to improve normality may be worth considering. The primary downside to doing so is that the data for up to eight cases (seven from Non-vape group and one from Vape group) will be dropped from the analyses.

Based on this, attention was given to the extent to which age is associated with other study variables (e.g., all demographic and health variables and all physiological variables) and whether or not the two groups significantly differ on age. Such analyses are described later in this report. Depending on the findings, a decision would be made with respect to whether or not cases with outlying ages would be included in main analyses.

Pre-vape Blood Sugar—Examination of values on Pre-vape Blood Sugar revealed one highly aberrant value for one Non-vape case (i.e., case ID 5866515954). The value is 255. When the value for this case is excluded, the degree of skew and kurtosis improved (i.e., the variable is no longer severely non-normal; for just the Non-vape sample [n= 72], skew= 1.06; kurtosis= 2.50; mean= 97.53, standard deviation= 19.19, minimum score= 64.00, maximum score= 170.00; for the total pooled sample [N= 148], skew= 1.18, kurtosis= 3.51, mean= 95.95, standard deviation= 16.06, minimum score= 64, maximum score= 170.00).

Based on this, it was decided that case ID 5866515954 would be retained in the data set but excluded for analyses using any Blood Sugar variables.

Pre- and Post-SpO2—Examination of the values on the Pre- and Post-SpO2 variables did not reveal any ostensible extreme outliers. However, the range of values as reflected in the minimum and maximum scores showed score range restriction (e.g., values range between 81 and 99 across all participants). We also noted that most values tended to be at the upper end of the score range (e.g., For Pre-vape SpO2, 140 cases have values of 97 to 99 and only 9 cases have values of 96 or lower; For Post-vape SpO2, 132 cases have values of 97 to 99 and only 17 cases have values of 96 or lower). The range restriction combined with most cases having higher values is what is responsible for the extreme non-normality.

One remedy to the extreme non-normality would be to exclude all cases with pre- and post-SpO2 values of 96 or less. If this is done for Pre-vape SpO2, the skew and kurtosis substantially improve (i.e., the variable is no longer extremely non-normal; for the entire sample [N= 140] skew= -0.67, kurtosis= -0.91, mean= 98.35, standard deviation= 0.75, minimum score= 97, maximum score= .99). Similarly, if this is done for Post-vape SpO2, the variable is no longer severely non-normal (for the total sample [N= 132], skew= -0.30, kurtosis= -1.27, mean= 98.17, standard deviation= 0.77, minimum score= 97, maximum score= 99). However, there are some problems with this approach. These problems include (a) the score range becomes even more restricted (e.g., values would only range between 97 and 99), (b) up to 17 cases of data would be excluded from analyses involving SpO2 which would be a loss of a fair amount of data, and (c) both of these problems would substantially reduce the likelihood of finding pre-post differences for SpO2 regardless of the type of statistical analysis completed.

In response, we decided to do the following: (a) use the data from all cases in the same type of statistical analyses as we used for all other physiological variables, noting that SpO2 is severely non-normal and the results should be interpreted with caution, and (b) use non-parametric statistics to test for differences between groups and pre-to-post-vape differences. Non-parametric statistics do not require data to be normally distributed. The downside to them, however, is that they are less "powerful" (i.e., they are less likely to produce statistically significant findings).

Sub-step (3)—Examine Frequencies for Categorical and Ordinal Variables

Sub-step 1 involved examination of the data set for any missing data and, if identified, imputing missing values using a regression-based imputation strategy. Sub-step 2 examined the univariate distributional properties of all continuous quantitative variables including all main physiological variables and age. Sub-step 3 was focused on all remaining variables. These include Gender, Present Health (note that this variable can be

considered ordinal but is included here), Recreational Drug Use, Mental Health Treatment, Lung Disease, Oral Disease, Cardiac Disease, Smoke Cigarettes, and Drink Alcohol. The particular focus of this sub-step was to look at frequencies for all variables to ensure that there were no unusual category codes and to determine that there are sufficient numbers for statistical analysis.

Table 2-4 presents the number of cases in each category on each variable along with the verbatim item from the “Medical History Questionnaire” (MHQ) used to gather these data.

Table 2-4. Frequencies for All Categories on Demographic and Health Variables for Total Sample and Non-vape and Vape Groups Separately

"Variable as stated on MHQ" (Variable in data set)	Total Sample (N= 149)	Non-Vape Group (n= 73)	Vape Group (n= 76)
"Gender" (Gender)			
"M"- Male	69 (46.3%)	19 (26.0%)	50 (65.8%)
"F"- Female	80 (53.7%)	54 (74.0%)	26 (34.2%)
"Other"	0 (0%)	0 (0%)	0 (0%)
"Your statement of present health" (Present Health)			
"Excellent"	63 (42.3%)	35 (47.9%)	28 (36.8%)
"Good"	82 (55.0%)	35 (47.9%)	47 (61.8%)
"Fair"	3 (2.0%)	2 (2.7%)	1 (1.3%)
"Poor"	1 (0.7%)	1 (1.4%)	0 (0%)
"Do you take recreational drugs (marijuana, etc)?" (Recreational Drug Use)			
"Yes"	37 (24.8%)	7 (9.6%)	30 (39.5%)
"No"	112 (75.2%)	66 (90.4%)	46 (60.5%)
"Have you ever been treated for a mental health condition (anxiety, depression, etc)? (Mental Health Treatment)			
"Yes"	31 (20.8%)	13 (17.8%)	18 (23.7%)
"No"	114 (76.5%)	59 (80.8%)	55 (72.4%)
"Unsure"	4 (2.7%)	1 (1.4%)	3 (3.9%)
"Have you ever had or have you now had…Lung disease (Asthma, Chronic Bronchitis, Emphysema, Lung Cancer, etc…)" (Lung Disease)			
"Yes"	26 (17.4%)	7 (9.6%)	19 (25.0%)
"No"	123 (82.6%)	66 (90.4%)	57 (75.0%)
"Unsure"	0 (0%)	0 (0%)	0 (0%)
"Have you ever had or have you now had…oral disease (Thrush, Loose/Missing Teeth, excessive cavities, cancer, etc…)" (Oral Disease)			
"Yes"	6 (4.0%)	2 (2.7%)	4 (5.3%)
"No"	141 (94.6%)	71 (97.3%)	70 (92.1%)
"Unsure"	2 (1.3%)	0 (0%)	2 (2.6%)
"Have you ever had or have you now had…Cardiac Disease (Angina, Heart Attach, Valve Disorders, Cardiomyopathies, etc…)" (Cardiac Disease)			
"Yes"	6 (4.0%)	3 (4.1%)	3 (3.9%)
"No"	143 (96.0%)	70 (95.9%)	73 (96.1%)
"Unsure"	0 (0%)	0 (0%)	0 (0%)
"Do you smoke cigarettes?" (Smoker)			
"Yes"	8 (5.4%)	1 (1.4%)	7 (9.2%)
"No"	133 (89.3%)	69 (94.5%)	64 (84.2%)
"Unsure"	8 (5.4%)	3 (4.1%)	5 (6.6%)
"Do you drink alcohol?" (Drinker)			
"Yes"	89 (59.7%)	38 (52.1%)	51 (67.1%)
"No"	59 (39.6%)	35 (47.9%)	24 (31.6%)
"Unsure"	1 (0.7%)	0 (0%)	1 (1.3%)

Note. Percentages represent the percent of the sample or group that falls in a given response category.

Examination of the frequency data for each variable given in Table 4 provides the following information:

Gender—No participants were in the "other" category. The number of participants in the male and female categories is sufficiently large to permit for the use of these two categories in analyses.

Present Health—The vast majority of participants fall in the "excellent" and "good" categories. Only three participants reported "fair" health and only one reported "poor" health. The number of participants in the fair and poor categories is too small for their use in any forms of analysis. As a result, only the good and excellent categories will be used.

Recreational Drug Use—There are a sufficient number of participants in each category (i.e., yes and no) for the use of this variable in analyses.

Mental Health Treatment—The number of cases in the "yes" and "no" categories is acceptable. The number of cases in the "unsure" category, however, is insufficient for analyses. An additional problem with the "unsure" category relates to ambiguity surrounding its meaning. For example, it is not clear to me how a person who participated in a mental health treatment would be unsure of having done so. We did not consider the unsure response category to be of much use.

Lung Disease—There are no cases in the "unsure" category. The number of participants in the yes and no categories is sufficiently large to permit for the use of these two categories in analyses.

Oral Disease—There are two cases in the "unsure" category. This is not sufficient for analysis purposes. For the Non-vape and Vape groups separately, there are not enough cases in the "yes" and "no" categories to allow for robust analyses to be completed.

Cardiac Disease—There are no cases in the "unsure" category. For the Non-vape and Vape groups separately, there are not enough cases in the "yes" category to allow for robust analyses to be completed.

Smoker—For the total pooled sample, there are 133 cases in the "no" category, eight in the "yes" category, and eight in the "unsure" category. Even though the MHQ used the "unsure" response category, a member of the research team indicated that "unsure" means "former" smoker. We did not know if participants were aware that "unsure" was to be marked by those who were former smokers. As such, we considered this response category ambiguous and not appropriate for use in analysis. For the remaining two categories, there is an insufficient number of cases coded "yes" in the Non-vape group. As a result, this variable may be problematic to use in analyses.

Drinker—There is only one case in the "unsure" category. For the remaining categories, there are sufficient numbers of cases to permit for their use in analyses.

Step Two—Power Analysis

In order to ascertain that our sample size was sufficient to ensure adequate statistical power for our main analyses (i.e., mixed factorial ANOVAs), we did a power analysis using G*Power (Version 3.1.9.2). For the calculation, we used a sample size of 149, beta/alpha ratio of 4, with two groups and two measurement points with a small-to-medium effect size (partial eta-squared of .05). This analysis indicated that the implied power was sufficient to detect a significant interaction effect (power= 0.992).

Step Three—Evaluation of Group Differences on Demographic and Health Variables and Pre-vape Physiological Measurements

The main purpose of the study was to evaluate whether physiological functioning changes as a function of vaping. In order to have confidence that any pre-post vaping differences across the Non-vape and Vape groups are real and are caused by the experimental condition (i.e., vaping and exposure to vapor), we needed to be able to rule out any possibility that the two groups differ in any substantive manner before exposure to the experimental condition.

To determine if the two groups are equivalent (i.e., not statistically significantly different) prior to vaping/exposure to vapor, we completed between group analyses using all demographic and health variables and pre-vape physiological variables. Table 2-5 presents the results for the demographic and health variables. Table 2-6 provides the results for the pre-vape physiological variables.

Results from these analyses revealed that the two vape groups are significantly different on a number of variables and indicates that (a) the two groups are not equivalent in terms of a variety of demographic and health characteristics and (b) the two groups were not equivalent at Pre-vape on all physiological measures. Below is a summary of the significant findings and a description of how the two groups differ.

Age—The Non-vape group is significantly older than the Vape group. This significant difference disappears when extreme outliers (i.e., cases with ages of 31 or greater) were removed.

Gender—The two groups significantly vary in terms of the number of males and females. The Non-vape group has a higher number of females while the Vape group has a higher number of males.

Recreational Drug Use—The Vape group has a significantly higher number of cases that report recreational drug use as compared to the Non-vape group.

Lung Disease—The Vape group has a significantly higher number of cases reporting lung disease as compared to the Non-vape group.

Smoker—The Vape group has a significantly higher number of smokers than the Non-vape group.

Drinker—The Vape group has a significantly higher number of drinkers than the Non-vape group.

Pre-vape FVC—The Vape group produced a significantly higher mean score than the Non-vape group.

Table 2-5. Demographic and Health Variables as a Function of Vape Group

Variable	Non-Vape Group	Vape Group	Statistic (df)	p-value
Age	**n= 73** **Mean= 23.76** **SD= 9.79**	**n= 76** **Mean= 20.39** **SD= 2.81**	**t(83.32)= 2.84**	**.006**
Age with outliers excluded (i.e., cases with ages 31 or greater)	n= 66 Mean= 20.94 SD= 3.44	n=75 Mean= 20.19 SD= 2.15	t(106.53)= 1.58	.128
Gender	**Males=19** **Female= 54**	**Males= 50** **Females= 26**	**χ2(1)= 23.68**	**<.001**
Present Health with "fair" and "poor" categories excluded	Good= 35 Excellent= 35	Good= 47 Excellent= 28	χ2(1)= 2.36	.124
Recreational Drug Use	**No= 66** **Yes= 7**	**No= 46** **Yes= 30**	**χ2(1)= 17.82**	**<.001**
Mental Health Treatment with "unsure" excluded	No=59 Yes= 13	No= 55 Yes= 18	χ2(1)= 0.94	.332
Lung Disease	**No= 66** **Yes= 7**	**No= 57** **Yes= 19**	**χ2(1)= 6.14**	**.013**
Oral Disease with "unsure" excluded	No= 71 Yes= 2	No= 70 Yes= 4	χ2(1)= 0.67	.414 Fisher's Exact Test p=.347
Cardiac Disease	No= 70 Yes= 3	No= 73 Yes= 3	χ2(1)= 0.00	.960 Fisher's Exact Test p= .640
Smoker with "unsure/ former" excluded	**No= 69** **Yes= 1**	**No= 64** **Yes= 7**	**χ2(1)= 4.68**	**.031** **Fisher's Exact Test p= .033**
Drinker with "unsure" excluded	**No= 35** **Yes= 38**	**No= 24** **Yes= 51**	**χ2(1)= 3.92**	**.048**

Note. All results that are statistically significant at p< .05 or lower are in bold font. For age, Levene's test indicated that equal variances between the groups could not be assumed. Statistical results reported involve adjustment to degrees of freedom (df) to correct for non-equality of variances. For Oral Disease and Cardiac Disease, expected frequency for two of the four groups is less than 5. For Smoker, frequency for one category is less than 5. This makes the chi-square analyses for these three variables questionable in terms of their reliability. In response, results for Fisher's Exact Test with one-tailed p-values were also computed and are reported in the table for these variables.

Table 2-6. Pre-Vape Physiological Variables as a Function of Vape Group

Variable	Non-Vape Group (n= 73)	Vape Group (n= 76)	t-test (df)	p-value
Pre-vape Heart Rate	Mean= 88.81 SD= 18.20	Mean= 84.20 SD= 16.28	t(147)= 1.63	.105
Pre-vape Mean Arterial Pressure	Mean= 94.03 SD= 10.05	Mean= 95.14 SD= 10.74	t(147)= -0.65	.517
Pre-vape Respiratory Frequency	Mean= 11.18 SD= 1.15	Mean= 11.29 SD= 1.02	t(147)= -0.63	.531
Pre-vape Blood Sugar	Mean= 99.68 SD= 26.51	Mean= 94.45 SD= 12.34	t(100.89)= 1.54	.128
Pre-vape Blood Sugar with outlier case excluded	Mean= 97.53 SD= 19.19 n= 72	Mean= 94.45 SD= 12.34	t(120.08)= 1.15	.251
Pre-vape FVC	**Mean= 3.97** **SD= 0.88**	**Mean= 4.79** **SD= 1.07**	**t(143.54)= -5.09**	**<.001**
Pre-vape SpO2	Mean= 97.97 SD= 1.72	Mean= 98.20 SD= 1.06	t(147)= -0.97	.335
Pre-vape Temperature	Mean= 97.87 SD= 0.75	Mean= 97.72 SD= 0.76	t(147)= 1.20	.230

Note. All results that are statistically significant at p< .05 or lower are in bold font. For "Pre-vape Blood Sugar with outlier case excluded", case ID 5866515954 with a value of 255 was excluded from the analysis. For all t-tests for which the degrees of freedom (df) is a decimal number, Levene's test indicated that equal variances between the groups could not be assumed. Statistical results reported involve adjustment to degrees of freedom (df) to correct for non-equality of variances.

Step Four—Evaluation of Health and Demographic Variables as Potential Confounds

In order for the main analyses to provide good information about the effects of vaping on physiological functioning, we need to take into account the possible influence of potential confounding variables. Such variables are any factors that have a relationship with the main physiological variables that could be argued to influence or distort physiological functioning. With the phase 3 study, it is the demographic and health variables that may be potential confounds.

To determine if the demographic and health variables are possible confounds, we computed bivariate correlations between each variable and all pre- and post-vaping physiological variables for the total pooled sample and for each vape group separately. Where appropriate, we excluded problematic cases or categories on variables.

Below is a summary of the statistically significant findings organized by demographic and health variable.

Age—(a) For total pooled sample (N= 149): Pre-vape Respiratory Frequency (r= .24, p= .004), Pre-vape Blood Sugar (r= .32, p<.001), Pre-vape SpO2 (r= -.19, p=.022), Post-vape Blood Sugar (r= .27, p= .001); (b) For Non-vape group only (n= 73): Pre-vape Respiratory Frequency= .28, p= .016), Pre-vape Blood Sugar (r= .32, p= .006), Post-vape Blood Sugar (r= .30, p= .009); (c) For Vape group only (n= 76): Pre-vape Respiratory Frequency (r= .30, p= .009), Pre-vape Blood Sugar (r= .24, p= .039).

Age with cases of 31 years or older excluded—(a) For total pooled sample (N= 141): Post-vape Blood Sugar (r= .17, p= .049); (b) For Non-vape group only (n= 66): No significant correlations; (c) For Vape group only (n= 75): Pre-vape FVC (r= .30, p= .009), Post-vape Mean Arterial Pressure (r= .28, p= .016); Post-vape FVC (r= .32, p= .006).

Gender (male coded 0, female coded 1)—(a) For total pooled sample (N= 149): Pre-vape Heart Rate (r= .19, p= .020), Pre-vape Respiratory Frequency (r= -.18, p= .024), Pre-vape FVC (r= -.68, p<.001), Pre-vape Temperature (r= .23, p= .005), Post-vape FVC (r= -.65, p<.001), Post-vape Mean Arterial Pressure (r= -.27, p= .001); (b) For Non-vape group only (n= 73): Pre-vape FVC (r= -.65, p<.001), Post-vape FVC (r= -.60, p<.001); (c) For Vape group only (n= 76): Pre-vape Mean Arterial Pressure (r= -.26, p= .022), Pre-vape FVC (r= -.59, p<.001), Post-vape Mean Arterial Pressure (r= -.32, p= .005), Post-vape FVC (r= -.58, p<.001).

Present Health—(a) For total pooled sample (N= 149): No significant correlations; (b) For Non-vape group only (n= 73): No significant correlations; (c) For Vape group only (n= 76): Post-vape Mean Arterial Pressure (r= -.23, p= .045).

Recreational Drug Use (No coded 0, Yes coded 1)—(a) For total pooled sample (N= 149): No significant correlations; (b) For Non-vape group only (n= 73): Post-vape Temperature (r= -.27, p= .023); (c) For Vape group only (n= 76): Pre-vape SpO2 (r= -.33, p= .004), Pre-vape Temperature (r= .30, p= .008), Pre-vape Mean Arterial Pressure (r= -.26, p= .022).

Mental Health Treatment with "unsure" excluded (No coded 0, Yes coded 1)— (a) For total pooled sample (N= 145): Pre-vape Temperature (r= .20, p= .016), Pre-vape Mean Arterial Pressure (r= -.18, p= .027); (b) For Non-vape group only (n= 72): Pre-vape Temperature (r= .29, p= .014); (c) For Vape-group only (n= 73): No significant correlations.

Lung Disease (No coded 0, Yes coded 1)—(a) For total pooled sample (N= 149): No significant correlations; (b) For Non-vape group only (n= 73): Pre-vape Temperature (r= .25, p= .001); (c) Vape group only (n= 76): No significant correlations.

Oral Disease with "unsure" excluded (No coded 0, Yes coded 1)—(a) For total pooled sample (N= 147): No significant correlations; (b) For Non-vape group only (n= 73): No significant correlations; (c) For Vape group only (n= 74): No significant correlations.

Cardiac Disease (No coded 0, Yes coded 1)—(a) For total pooled sample (N= 149): Pre-vape Blood Sugar (r= .17, p=. 039); (b) For Non-vape group only (n= 73): Pre-vape Blood Sugar (r= .26, p= .024); (c) For Vape group only (n= 76): No significant correlations.

Smoker with "former" excluded (No coded 0, Yes coded 1)—(a) For total pooled sample (N= 141): Post-vape Mean Arterial Pressure (r= .18, p= .031); (b) For Non-vape group only (n= 70): No significant correlations; (c) For vape group only (n= 71): No significant correlations.

Drinker with "unsure/former" excluded (No coded 0, Yes coded 1)—(a) For total pooled sample (N= 148): Pre-vape FVC (r= .19, p= .019), Post-vape Respiratory Frequency (r= .23, p= .005), Post-vape Blood Sugar (r= .18, p= .033), Post-vape FVC (r= .22, p= .007), Post-vape Temperature (r= -.17, p= .035); (b) For Non-vape group only (n= 73): No significant correlations; (c) For Vape group only (n= 75): Post-vape Respiratory Frequency (r= .29, p= .011), Post-vape FVC (r= .24, p= .041).

Summary—Of the 10 demographic and health variables, only Oral Disease did not produce any significant correlations with physiological variables. All other variables produced one or more statistically significant correlations.

When the number and size of significant correlations are taken into consideration and are combined with the tests of group differences on demographic and health variables (reported in Table 2-5), age and gender appear to be serious confounding variables and need to be used as covariates in main analyses. Given the putative importance of the other health variables, it would also be worthwhile to consider using them as covariates as well.

Step Five—Main and Ancillary Statistical Analyses

Preamble—The main purpose of the study was to examine the extent to which vaping and/or exposure to vapor influences physiological functioning. To accomplish this purpose, two groups of participants comprised of self-reported vapers and self-reported non-vapers provided demographic and health information and then were measured on a variety of physiological variables both before (pre-vape) and after (post-vape) vaping/exposure to vapor.

Preliminary analyses and data cleaning reported earlier has addressed problems with missing data and identified a number of factors that need to be considered when running main analyses. These factors include the following:

(a) Pre-vape Blood Sugar is severely non-normal in its distribution. The value for one case (case 5866515954 with a value of 255) was identified as an extreme outlier and as being responsible for the non-normality. This case needs to be excluded from any analyses involving Blood Sugar.

(b) Pre-vape and Post-vape SpO2 were found to be severely non-normal. No ostensible outlier cases could be identified to help improve univariate normality. Rather than transforming these variables, it was decided that both parametric and non-parametric analyses will be run with these variables.

(c) Age was found to be severely non-normal and the two vape groups were found to significantly differ in terms of mean age. When participants with an age of 31 or higher are excluded, problems with non-normality and significant group differences disappear. In addition, age was found to be significantly associated with a number of physiological variables. Based on all of these results, analyses need to be completed that address possible influence of age on study outcomes. More specifically, after running the main analysis with all cases, the analysis needs to be recomputed after excluding participants with outlying age values. The analysis also needs to be redone controlling for age as a covariate.

(d) Gender was found to be significantly different across the two vape groups. Gender was also found to be significantly correlated to a number of the physiological variables. As a result, gender needs to be incorporated into analyses as a covariate.

(e) Additional demographic and health variables were also found to be significantly related to physiological variables. This includes recreational drug use, lung disease, smoking, and drinking.

(f) The two vape groups were found to be significantly different in Pre-vape FVC and on a variety of health variables in addition to age and gender. This suggests that the two groups cannot be treated as equivalent at pre-vape and that the lack of group equivalence needs to be kept in mind when interpreting any results.

With all of this information in mind, below are the results for three separate sets of analyses.

The first set involves a series of Between Group Analyses of Variance (ANOVA), Analyses of Covariance (ANCOVA) and Mann-Whitney tests done to examine each Pre-vape and Post-vape physiological variable as a function of Vape group (Non-vape vs. Vape). These results are reported in Tables 2-7 and 2-8.

The second set involves a series of Repeated Measures ANOVAs and Wilcoxon tests to evaluate pre-to-post differences for all physiological variables for the total sample and each vape group separately. These results are reported in Tables 2-9 and 2-10.

The third set involves mixed factorial ANOVAs and ANCOVAs examining both repeated measures and between groups factors simultaneously for all physiological variables. These results are reported in Tables 2-11 and 2-12. It is important to note that with these analyses, main effects are calculated using marginal means—For between groups, this involves combining the pre- and post vape measurements of a physiological variable and combining them to produce a total mean. For repeated measures, this involves combining the means for the Non-vape and Vape groups at pre-vape and post-vape for each physiological variable.

To summarize the results for each set of analyses.

Set one—One-way ANOVAs examining pre- and post-vape physiological variables as a function of vape group (Non-vape vs. Vape), produced significant results for the following variables (a) Pre-vape FVC (Vape group has significantly higher mean score). This result remained significant when age outliers (i.e., cases with age of 31 or higher) were removed and in the Mann-Whitney test. Result became non-significant in the ANCOVA when controlling for age and gender (gender is a significant covariate). (b) Post-vape FCV (Vape group has significantly higher mean score). The result remained significant when age outliers were removed and in the Mann-Whitney test but became non-significant when controlling for gender. (c) Post-vape Mean Arterial Pressure (Vape group has higher mean score). Remained significant when excluding age outliers, when controlling for age and gender, and in the Mann-Whitney test. However, the result became non-significant when controlling for all demographic and health variables. (d) Post-vape Respiratory Frequency (Vape group has higher mean score). This result remained significant in all secondary analyses (i.e., when excluding age outliers and when controlling for any/all demographic and health variables).

Set two—Repeated measures ANOVAs examining pre-post physiological variable pairs were completed using the total pooled sample and each vape group (Non-vape and Vape) separately. When using the total pooled sample, the following significant results were obtained: (a) Respiratory Frequency (higher post-vape mean score). Result stayed significant when excluding age outliers but was non-significant in the Wilcoxon. (b) SpO2 (higher post-vape mean score). Result remained significant when age outliers excluded and in Wilcoxon. (c) Temperature (higher post-vape mean score). Result remained significant when age outliers were excluded and in Wilcoxon. When using the Non-vape group only, the following significant results were obtained: (a) Mean Arterial Pressure (lower post-vape mean). Result remained significant when excluding age outliers and in Wilcoxon. (b) Temperature (higher post-vape mean score). Result

remained significant after excluding age outliers and in Wilcoxon. When using the Vape group only, the following results were significant: (a) Heart Rate (higher post-vape mean score). Result remained significant when age outliers were excluded and in Wilcoxon. (b) Respiratory Frequency (higher post-vape mean score). Results remained significant when age outliers excluded and in Wilcoxon. (c) SpO2 (lower post-vape mean score). Result remained significant when age outliers excluded and in Wilcoxon. (d) Temperature (higher post-vape mean score). Result remained significant when age outliers excluded and in Wilcoxon. (e) FVC was found to produce a significant Wilcoxon test but all other analyses emerged non-significant.

Set three—Mixed factorial ANOVAs (also known as Split Plot ANOVAs) examining between group (vape groups) and within subjects (pre-post) variables produced the following significant results: (a) Heart Rate—Non-significant main effects but significant interaction effect. Examination of means shows that Non-vape group mean is lower at post-vape while Vape group mean is higher. The interaction remains significant after excluding age outliers and after controlling for covariates. (b) Mean Arterial Pressure—Significant between groups main effect (Vape group mean is higher) which remains significant when excluding age outliers but becomes non-significant when covariates are included. Repeated measures main effect non-significant initially but becomes significant when demographic and health variables treated as covariates. Interaction effect is also significant with the Non-vape group showing lower post-vale mean value while Vape group shows slight increase. Interaction remains significant when age outliers are excluded and when controlling for age and sex but becomes non-significant when health variables included as covariates. (c) Respiratory Frequency—Both between group and repeated measures main effects as well as interaction emerged significant. For between groups main effect, Vape group obtained the higher mean score. For repeated measures main effect, post-vape mean is higher. For interaction, both vape groups similar at pre-vape and means become higher at post-vape. However, Vape group produced greater mean increase at post-vape. Main effects and interaction effect remain significant when excluding age outliers and when controlling for demographic and health variables. (d) Forced Vital Capacity—A significant between groups main effect was found with the Vape group producing the higher mean score. Result stays significant when age outliers excluded but becomes non-significant when controlling for age and gender. (e) SpO2—A significant repeated measures main effect was produced with both groups showing a decreate in mean scores at post-vape. This result remains significant when age outliers are excluded and when demographic and health variables are controlled. (f) Temperature—A significant repeated measures main effect was obtained with both groups showing an increase at post-vape. This result remains significant when age outliers are excluded and when controlling for covariates.

Of all the mixed factorial ANOVA and ANCOVA results, those for Heart Rate, Respiratory Frequency, SpO2 and Temperature appear to be the most robust (i.e., they emerge significant and remain significant when eliminating outliers and controlling for potential confounds).

Table 2-7. Results of One-way Analyses of Variance Examining Pre-and Post-vape Physiological Variables as a Function of Vape Group

	Non-Vape (n= 73)	Vape (n= 76)	One-way ANOVA		
	Mean (SD)	Mean (SD)	$F(df_n/df_d)$	p	eta^2
Pre-vape					
Heart Rate	88.81 (18.24)	84.20 (16.28)	F(1,147)= 2.66	.105	
Mean Arterial Pressure	94.03 (10.05)	95.14 (10.74)	F(1,147)= 0.42	.517	
Respiratory Frequency	11.18 (1.15)	11.29 (1.02)	F(1,147)= 0.39	.531	
Blood Sugar*	97.53* (19.19)	94.45 (12.34)	F(1,146)= 1.36**	.245	
FVC	**3.97 (0.88)**	**4.79 (1.07)**	**F(1,147)= 25.93****	**<.001**	**.15**
SpO2	97.97 (1.72)	98.20 (1.06)	F(1,147)= 0.93	.335	
Temperature	97.87 (0.75)	97.72 (0.76)	F(1,147)= 1.45	.230	
Post-vape					
Heart Rate	86.83 (18.01)	88.12 (15.27)	F(1,147)= 0.22	.637	
Mean Arterial Pressure	**90.83 (10.29)**	**95.84 (10.07)**	**F(1,147)= 9.04**	**.003**	**.06**
Respiratory Frequency	**11.15 (1.10)**	**11.79 (1.06)**	**F(1,147)= 12.99****	**<.001**	**.08**
Blood Sugar*	98.63* (18.05)	96.01 (14.73)	F(1,146)= 0.93**	.335	
FVC	**3.97 (0.89)**	**4.73 (1.10)**	**F(1,147)= 21.63****	**<.001**	**.13**
SpO2	97.37 (2.94)	97.71 (1.66)	F(1,147)= 0.77	.383	
Temperature	98.27 (0.49)	98.20 (0.75)	F(1,147)= 0.39	.536	

Note. Single asterisk (*) for Non-vape Blood Sugar means that extreme outlier case with a Pre-vape value of 255 was removed prior to completing analyses. For Blood Sugar, Non-vape group size is n= 72. Double asterisk (**) beside F statistic means that Levene's test was significant so homogeneity of variance cannot be assumed. Due to evidence of severe non-normality, results for SpO2 should be interpreted with caution. Statistically significant results are in bold font.

Table 2-8a. Results of Different Sets of Analyses Examining Pre-vape Physiological Variables as a Function of Vape Group

	ANOVA with Age Outliers Excluded	ANCOVA with All Cases Controlling for Age and Gender	ANCOVA with Age Outliers Excluded Controlling for Age and Gender	ANCOVA with All Cases Controlling for Age, Gender and Health Variables	Mann-Whitney Tests with All Cases
Heart Rate	F(1,139)= 3.55 p= .062	F(1,145)= 0.97 p= .326	F(1,137)= 1.26 p= .264	F(1,124)= 0.70 p= .403	U= 2344.00 z= -1.63 p= .102
Mean Arterial Pressure	F(1,139)= 0.83 p= .364	F(1,145)= 0.01 p= .915	F(1,137)= 0.02 p= .898	F(1,124)= 0.31 p= .580 Mental Health, Present Health significant covariates	U= 2421.00 z= -1.34 p= .180
Respiratory Frequency	F(1,139)= 0.90** p= .345	F(1,145)= 0.25 p= .616 Age significant covariate	F(1,137)= 0.00 p= .952 Gender significant covariate	F(1,124)= 0.07 p= .793 Age significant covariate	U= 2594.00 z=-0.78 p= .431
Blood Sugar*	F(1,138)= 0.16** p= .688	F(1,144)= 0.06 p= .815 Age significant covariate	F(1,136)= 0.09 p= .762 Age significant covariate	F(1,123)= 0.00 p= .975 Age, Mental Health and Cardiac Disease significant covariates	U= 2479.50 z= -0.98 p= .325
FVC	**F(1,139)= 23.77**** **p<.001** **eta^2= .15** **Vape group higher**	F(1,145)= 2.97 p= .09 Gender significant covariate	F(1,137)= 2.64 p= .107 Gender significant covariate	F(1,124)= 1.54 p= .218 Gender significant covariate	**U= 1534.50** **z= -4.71** **p<.001**
SpO2	F(1,139)= 0.50 p= .483	F(1,145)= 0.61 p= .436 Age significant covariate	F(1,137)= 0.82 p= .368	F(1,124)= 0.78 p= .380 Age, Drinking significant covariates	U= 2687.50 z= -0.36 p= .723
Temperature	F(1,139)= 0.89 p= .348	F(1,145)= 0.20 p= .653 Age and Gender significant covariates	F(1, 137)= 0.04 p= .838 Gender significant covariate	F(1,124)= 0.26 p= .613 Age, Gender, and Recreational Drug Use significant covariates	U= 2497.50 z= -1.05 p= .293

Note. For Blood Sugar, single asterisk (*) means that outlier case on Pre-vape was excluded from the analysis. Double asterisk (**) beside F-statistic means that Levene's test was significant and that equal variances across groups cannot be assumed. ANOVA and ANCOVA results for SpO2 need to be interpreted with caution because of evidence of severe non-normality of these variables. Statistically significant results indicated in bold font.

Table 2-8b. Results of Different Sets of Analyses Examining Post-vape Physiological Variables as a Function of Vape Group

	ANOVA with Age Outliers Excluded	ANCOVA with All Cases Controlling for Age and Gender	ANCOVA with Age Outliers Excluded Controlling for Age and Gender	ANCOVA with All Cases Controlling for Age, Gender and Health Variables	Mann-Whitney Tests with All Cases
Heart Rate	F(1,139)= 0.08 p= .777	F(1,145)= 0.70 p= .406	F(1,137)= 0.49 p= .486	F(1,124)= 0.42 p= .516	U= 2715.00 z= -0.22 p= .823
Mean Arterial Pressure	**F(1,139)= 12.65** **p<.001** **eta^2= .08** **Vape group higher**	**F(1,145)= 4.48** **p= .036** **Partial eta^2= .03** **Gender significant covariate**	**F(1,137)= 5.45** **p= .021,** **Partial eta^2= .04,** **Gender significant covariate**	F(1,124)= 2.43 p= .121	**U= 2064.00** **z= -2.70** **p= .007**
Respiratory Frequency	**F(1,139)= 13.04**** **p<.001** **eta^2= .09** **Vape group higher**	**F(1,145)= 12.27** **p= .001** **Partial eta^2=.08**	**F(1,137)= 10.21** **p= .002** **Partial eta^2= .07**	**F(1,124)= 10.75** **p= .001** **Partial eta^2= .08**	**U= 1992.00** **z= -3.53** **p<.001**
Blood Sugar*	F(1,138)= 0.17 p= .683	F(1,144)= 0.10 p= .750 Age significant covariate	F(1,136)= 0.02 p= .884 Age significant covariate	F(1,123)= 0.01 p= .905 Age, Drinking significant covariates	U= 2581.50 z= -0.59 p= .553
FVC	**F(1,139)= 18.91**** **p<.001** **eta^2= .12** **Vape group higher**	F(1,145)= 1.62 p= .205 Gender significant covariate	F(1,137)= 1.49 p= .225 Gender significant covariate	F(1,124)= 0.72 p= .399 Gender significant covariate	**U= 1617.00** **z= -4.39** **p<.001**
SpO2	F(1,139)= 0.49 p= .486	F(1,145)= 0.29 p= .592	F(1,137)= 0.43 p= .513	F(1,124)= 1.46 p= .629	U= 2648.00 z= -0.50 p= .618
Temperature	F(1,139)= 0.52 p= .473	F(1,145)= 0.17 p= .684	F(1,137)= 0.34 p= .560	F(1,124)= 0.03 p=.865	U= 2694.50 z= -0.30 p= .762

Note. For Blood Sugar, single asterisk (*) means that outlier case on Pre-vape was excluded from the analysis. Double asterisk (**) beside F-statistic means that Levene's test was significant and that equal variances across groups cannot be assumed. ANOVA and ANCOVA results for SpO2 need to be interpreted with caution because of evidence of severe non-normality of these variables. Statistically significant results indicated in bold font.

Table 2-9. Repeated Measures ANOVA Examining Pre-Post Differences for all Physiological Variables for the Total Pooled Sample and Each Vape Group Separately.

	Pre-Vape	Post-Vape	ANOVA		
	Mean (SD)	Mean (SD)	$F(df_n/df_d)$	p	eta^2
Total Pooled Sample (N= 149)					
Heart Rate	86.46 (17.36)	87.49 (16.63)	F(1,148)= 0.80	.374	
Mean Arterial Pressure	94.59 (10.39)	93.38 (10.45)	F(1,148)= 2.25	.135	
Respiratory Frequency	**11.23 (1.08)**	**11.48 (1.12)**	**F(1,148)= 4.36**	**.039**	**.03**
Blood Sugar*	95.95 (16.06)	97.28 (16.43)	F(1,147)= 1.05	.306	
FVC	4.39 (1.06)	4.36 (1.07)	F(1,148)= 0.83	.363	
SpO2	**98.09 (1.42)**	**97.54 (2.37)**	**F(1,148)= 6.96**	**.009**	**.04**
Temperature	**97.79 (0.75)**	**98.23 (0.63)**	**F(1,148)= 40.03**	**<.001**	**.21**
Non-Vape Group (n= 73)					
Heart Rate	88.81 (18.24)	86.83 (18.01)	F(1,72)= 1.39	.242	
Mean Arterial Pressure	**94.03 (10.05)**	**90.83 (10.29)**	**F(1,72)= 8.80**	**.004**	**.11**
Respiratory Frequency	11.18 (1.15)	11.15 (1.10)	F(1,72)= 0.03	.867	
Blood Sugar*	97.53 (19.19)	98.63 (18.05)	F(1,71)= 0.45	.506	
FVC	3.97 (0.88)	3.97 (0.89)	F(1,72)= 0.00	.997	
SpO2	97.97 (1.72)	97.37 (2.94)	F(1,72)= 2.94	.091	
Temperature	**97.87 (0.75)**	**98.27 (0.49)**	**F(1,72)= 18.24**	**<.001**	**.20**
Vape Group (n= 76)					
Heart Rate	**84.20 (16.28)**	**88.12 (15.27)**	**F(1,75)= 6.60**	**.012**	**.08**
Mean Arterial Pressure	95.14 (10.74)	95.84 (10.07)	F(1,75)= 0.37	.542	
Respiratory Frequency	**11.29 (1.02)**	**11.79 (1.06)**	**F(1,75)= 9.83**	**.002**	**.12**
Blood Sugar	94.45 (12.34)	96.01 (14.73)	F(1,75)= 0.60	.440	
FVC	4.79 (1.07)	4.73 (1.10)	F(1,75)= 1.26	.265	
SpO2	**98.20 (1.06)**	**97.71 (1.66)**	**F(1,75)= 4.71**	**.033**	**.06**
Temperature	**97.72 (0.76)**	**98.20 (0.75)**	**F(1,75)= 21.65**	**<.001**	**.22**

Note. Single asterisk (*) for Blood Sugar means that extreme outlier case with a Pre-vape value of 255 was removed prior to completing analyses. For Blood Sugar, Non-vape group size is n= 72 and total pooled sample size N=148. Due to evidence of severe non-normality, results for SpO2 should be interpreted with caution. Statistically significant results are in bold font.

Table 2-10. Results of Different Sets of Analyses Examining Pre-post Changes in Physiological Measures

	Total Pooled Sample		Non-Vape Group Only		Vape Group Only	
	ANOVA with Age Outliers Excluded	Wilcoxon Test	ANOVA with Age Outliers Excluded	Wilcoxon Test	ANOVA with Age Outliers Excluded	Wilcoxon Test
Heart Rate	F(1,140)= 0.83 p= .365	z= -1.41 p= .159	F(1,65)= 1.54 p= .219	z= -1.34 p= .182	**F(1,74)= 7.04** **p= .010** **eta2= .09**	**z= -3.34** **p< .001**
Mean Arterial Pressure	F(1,140)= 2.30 p= .132	z= -1.70 p= .088	**F(1,65)= 9.15** **p= .004** **eta2= .12**	**z= -2.97** **p= .003**	F(1,74)= 0.35 p= .557	z= -0.46 p= .644
Respiratory Frequency	**F(1,140)= 5.58** **p= .020** **eta2= .04**	z= -1.81 p= .071	F(1,65)= 0.03 p= .863	z= -0.15 p= .883	**F(1,74)= 9.84** **p= .002** **eta2= .12**	**z= -2.62** **p= .009**
Blood Sugar*	F(1,139)= 2.07 p= .152	z= -1.04 p= .297	F(1,64)= 1.39 p= .242	z= -0.47 p= .638	F(1,74)= 0.84 p= .363	z= -0.95 p= .344
FVC	F(1,139)= 0.63 p= .427	z= -1.92 p= .055	F(1,65)= 0.09 p= .764	z= -0.12 p= .902	F(1,74)= 1.28 p= .261	**z= -2.48** **p= .013**
SpO2	**F(1,140)= 6.76** **p= .010** **eta2= .05**	**z= -3.09** **p= .002**	F(1,65)= 2.62 p= .110	z= -1.81 p= .071	**F(1,74)= 5.00** **p= .028** **eta2= .06**	**z= -2.56** **p= .011**
Temperature	**F(1,140)= 43.83** **p<.001** **eta2= .24**	**z= -5.83** **p <.001**	**F(1,65)= 21.71** **p<.001** **eta2= .25**	**z= -3.78** **p<.001**	**F(1,74)= 22.23** **p<.001** **eta2= .23**	**z= -4.46** **p< .001**

Note. For Blood Sugar, single asterisk (*) means that outlier case on Pre-vape was excluded from the analysis. For Blood Sugar only, N= 148 for total pooled sample and n= 72 for Non-vape sample. ANOVA and ANCOVA results for SpO2 need to be interpreted with caution because of evidence of severe non-normality of these variables. Statistically significant results indicated in bold font.

Table 2-11. Results of Mixed Factorial ANOVAs Examining Physiological Variables as a Function Vape Group (Between Groups) and Pre-post Vaping Conditions (Within Subjects)

	Non-vape Group		Vape Group		ANOVA		
	Pre-Vape Mean (SD)	Post-Vape Mean (SD)	Pre-Vape Mean (SD)	Post-Vape Mean (SD)	Between Groups Main Effect	Repeated Measures Main Effect	Interaction
Heart Rate	88.81 (18.24)	86.83 (18.01)	84.20 (16.28)	88.12 (15.27)	F(1,147)= 0.43 p=.514	F(1,147)= 0.73, p= .393	**F(1,147)= 6.79 p= .010 eta^2= .04**
Mean Arterial Pressure	94.03 (10.05)	90.83 (10.29)	95.14 (10.74)	95.84 (10.07)	**F(1,147)= 4.22 p= .042 eta^2= .03**	F(1,147)= 2.49 p= .117	**F(1,147)= 6.10 p= .015 eta^2= .04**
Respiratory Frequency	11.18 (1.15)	11.15 (1.10)	11.29 (1.02)	11.79 (1.06)	**F(1,147)= 8.63 p= .006 eta^2= .05**	**F(1,147)= 4.29 p= .040 eta^2=.03**	**F(1,147)= 5.34 p= .022 eta^2=.04**
Blood Sugar	97.53 (19.19)	98.63 (18.05)	94.45 (12.34)	96.01 (14.73)	F(1,146)= 1.49 p= .223	F(1,146)= 1.04 p= .310	F(1,146)= 0.03 p= .858
Forced Vital Capacity	3.97 (0.88)	3.97 (0.89)	4.79 (1.07)	4.73 (1.10)	**F(1,147)= 24.55 p< .001 eta^2= .14**	F(1,147)= 0.80 p= .373	F(1,147)= 0.79 p= .375
SpO2	97.97 (1.72)	97.37 (2.94)	98.20 (1.06)	97.71 (1.66)	F(1,147)= 1.33 p= .250	**F(1,147)= 6.94 p= .009 eta^2= .05**	F(1,147)= 0.08 p= .780
Temperature	97.87 (0.75)	98.27 (0.49)	97.72 (0.76)	98.20 (0.75)	F(1,147)= 1.40 p= .239	**F(1,147)= 39.69 p< .001 eta^2= .21**	F(1,147)= 0.36 p= .548

Note. For Non-Vape Group, N= 73 for all analyses except Blood Sugar where n= 72 due to the exclusion of a case with an extreme value. For Vape Group, N= 76. Statistically significant results in bold font.

Table 2-12a. Results of Different Sets of Mixed Factorial ANOVAs and ANCOVAs Examining Physiological Variables as a Function Vape Group (Between Groups) and Pre-post Vaping Conditions (Within Subjects)

	ANOVA Excluding Age Outliers			ANCOVA Controlling for Age and Gender		
	Between Groups Main Effect	Repeated Measures Main Effect	Interaction	Between Groups Main Effect	Repeated Measures Main Effect	Interaction
Heart Rate	F(1,139)= 0.80 p= .372	F(1,139)= 0.57 p= .451	**F(1,139)= 7.15 p= .008 eta^2= .05**	F(1,145)= 0.01 p= .920	F(1,147)= 0.73 p= .393	**F(1,147)= 6.79 p= .010 eta^2= .04**
Mean Arterial Pressure	**F(1,139)= 6.41 p= .012 eta^2= .04**	F(1,139)= 2.90 p= .091	**F(1,139)= 6.43 p= .012 eta^2= .04**	F(1,145)= 1.53 p= .218	F(1,147)= 2.49 p= .117	**F(1,147)= 6.10 p= .015 eta^2= .04**
Respiratory Frequency	**F(1,139)= 9.91 p= .002 eta^2= .07**	**F(1,139)= 5.09 p= .026 eta^2= .04**	**F(1,139)= 4.00 p= .047 eta^2= .03**	**F(1,145)= 7.09 p= .009 eta^2= .05 Age significant covariate**	**F(1,147)= 4.29 p= .040 eta^2= .03**	**F(1,147)= 5.34 p= .022 eta^2= .04**
Blood Sugar	F(1,138)= 0.23 p= .634	F(1,138)= 2.06 p= .154	F(1,138)= 0.00 p= .957	F(1,144)= 0.11 p= .744 Age significant covariate	F(1,146)= 1.04 p= .310	F(1,146)= 0.03 p= .858
Forced Vital Capacity	**F(1,139)= 21.95 p< .001 eta^2=.14**	F(1,139)= 0.53 p= .469	F(1,139)= 1.14 p= .287	F(1,145)= 2.36 p= .127 Gender significant covariate	F(1,147)= 0.80 p= .373	F(1,147)= 0.79 p= .375
SpO2	F(1,139)= 0.80 p= .372	**F(1,139)= 6.77 p= .010 eta^2= .05**	F(1,139)= 0.07 p= .792	F(1,145)= 0.64 p= .427	**F(1,147)= 6.94 p= .009 eta^2= .05**	F(1,147)= 0.08 p= .780
Temperature	F(1,139)= 1.11 p= .293	**F(1,139)= 43.13 p< .001 eta^2=.24**	F(1,139)= 0.08 p= .780	F(1,145)= 0.00 p= .948 Gender significant covariate	**F(1,147)= 39.69 p< .001 eta^2= .21**	F(1,147)= 0.36 p= .548

Note. For Non-Vape Group, N= 66 for all analyses except Blood Sugar where n= 65 due to the exclusion of a case with an extreme value. For Vape Group, N= 75. Statistically significant results in bold font.

Table 2-12b. Results of Different Sets of Mixed Factorial ANOVAs and ANCOVAs Examining Physiological Variables as a Function Vape Group (Between Groups) and Pre-post Vaping Conditions (Within Subjects)

	ANCOVA Controlling for Age, Gender, and All Eight Health Variables		
	Between Groups Main Effect	Repeated Measures Main Effect	Interaction
Heart Rate	F(1,124)= 0.01 p= .907	F(1,134)= 0.40 p= .526	**F(1,134)= 4.94** **p= .028** **eta^2=.04**
Mean Arterial Pressure	F(1,124)= 1.42 p= .236 Gender, Mental Health significant covariates	**F(1,134)= 5.79** **p= .017** **eta^2=.04**	F(1,134)= 3.24 p= .074
Respiratory Frequency	**F(1,124)= 5.15** **p= .025** **eta^2=.04** **Age significant covariate**	**F(1,134)= 5.11** **p= .025** **eta^2=.04**	**F(1,134)= 6.27** **p= .014** **eta^2=.04**
Blood Sugar	F(1,123)= 0.01 p= .926 Age, Drinker significant covariates	F(1,133)= 1.27 p= .262	F(1,133)= 0.70 p= .406
Forced Vital Capacity	F(1,124)= 1.16 p= .284 Gender significant covariate	F(1,134)= 0.85 p= .359	F(1,134)= 0.92 p= .338
SpO2	F(1,124)= 0.62 p= .432	**F(1,134)= 7.49** **p= .007** **eta^2=.05**	F(1,134)= 0.16 p= .690
Temperature	F(1,124)= 0.06 p= .809 Drinker significant covariate	**F(1,134)= 40.44** **p< .001** **eta^2=.23**	F(1,134)= 0.54 p= .465

Note. For Non-Vape Group, N= 73 for all analyses except Blood Sugar where n= 62 due to the exclusion of a case with an extreme value. For Vape Group, N= 75. Statistically significant results in bold font.