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Comparison of different types of vape products on vital signs following twenty minutes of vaping and exposure to vapor

Abstract

Introduction: Vaping continues to rapidly expand as an alternative to cigarette use and a novel tobacco-free inhalation device. The electronic devices are filled with e-juice which is heated, vaporized, and inhaled. There are a plethora of flavors and nicotine concentrations that can be added to the vegetable glycerin, and propylene glycol base liquid found in e-juice.

Methods: 279 participants were divided into four groups varied according to type of e-juice. Two groups were given e-cigarettes to use, one group had no flavoring or nicotine added to the e-juice, the other group had mint flavoring and 5% nicotine added to the e-juice. The third and fourth groups were exposed to the vapor of the aforementioned types of e-juice. Participants vaped or were exposed to vapor for 20 minutes. A set of vital signs were obtained before and after the vaping sessions.

Results: People vaping with mint-flavored e-juice with 5% nicotine have significant reductions in their oxygen saturation, but significant increases in blood pressure, heart rate and respiratory frequency compared to their non-vaping counterparts, or those vaping without mint flavored nicotine e-juice. Participants exposed to vapor with and without nicotine or mint flavors had significantly reduced blood pressures compared to people vaping mint-flavored e-juice with 5% nicotine.

Conclusion: Vaping with mint-flavored e-juice with 5% nicotine for twenty minutes has a significant negative impact on vital signs. Exposure to vapor does not have the same effect on vital signs regardless of the contents of the e-juice.

Implications: Health care providers should assess for vape use in their patients. Law makers should also be made aware of the physiological impacts of vaping different types of e-juice and exposure to vapor, and make informed policies and decisions regarding vape use. Vaping, especially with certain flavors and nicotine concentrations, is not a safe alternative to cigarette smoking, however, exposure to second-hand vapor does not appear to have significant immediate effects on vital signs.

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Introduction

Vaping continues to expand as an alternative to tobacco use worldwide, however, the full health effects of vape use is not yet fully known, but concerning to many researchers and health care providers (HCPs).[1-4] Additionally, the growing billion-dollar industry offers a plethora of products users can chose from. The plethora of nicotine levels, flavorings, e-juice, temperature, and delivery device options provide a wide array of non-tobacco substances users inhale into their lungs.[1,2,5] Many governmental agencies are imposing regulations on the industry and limiting certain types of vape products without fully understanding the effects of each of these different products.[6-7] The health effects of vaping specific products and exposure to second-hand vapor needs to be much better understood so HCPs can provide evidence-based recommendations to their patients regarding vape use.

Varied user patterns combined with hundreds of different types of vaping devices, amounts of nicotine, flavorings, and temperature levels significantly impact the amount of chemicals inhaled by the user.[8] It would behoove HCPs to understand if some combinations of vaping could be more or less harmful than others. Such information could also be used to guide policies relating to vape use. Additionally, if information could be gleaned on acute physiological responses following vape use or exposure to vapor, acute and chronic health outcomes could be better anticipated.

Research has determined that vaping with nicotine increases heart rate (HR), blood pressure (BP), respiratory frequency (RF), respiratory impedance, and airway flow resistance within a few minutes of use.[9-12] Other adverse physiological effects such as endothelial dysfunction, vascular inflammation, oxidative stress, and platelet disorders have also been noted after short term e-cigarette use with and without nicotine.[13,14]

Additionally, the flavor of e-juice seems to impact nicotine concentration, and can have other concerning health effects. Some e-juice flavors can effect the rate of nicotine aborption in the blood stream leading to increased heart rates.[15,16] Other researchers determined that flavor choices determine the frequency and depth of vape inhalations contributing to nicotine intake.[17] E-juice flavorings are likely dangerous to health as inhalants and have not been approved as safe by the Food and Drug Administration (FDA).[18] Some flavorings, such as butter, caramel and fruit while safe for food consumption can become moderately cytotoxic when inhaled. Interestingly, some e-juice flavors allowed by FDA regulations, including cinnamon and menthol tobacco, were found to have strong cytotoxic effects on endothelial cells when inhaled.[19,20] Some researchers have suggested exhaled flavored vapor could be considered a pollutant because toxins are being expelled into the environment.[18,21] Many popular flavors have been banned by the FDA, and many local government agencies

in early 2020 despite sparse research on its health effects.[22-24] It is imperative that information be gleaned regarding the health, public, and environmental implications of vaping with and without flavored e-juice and with and without added nicotine.

Methods

Research question, hypothesis & purpose

The purpose of this study was to determine if differences exist in vital sign response based on type of vape or exposure to different types of vapor. The research questions were 1.) Does a statistically significant relationship exist in vital sign response between different types of vaping and exposure to vapor and 2.) What vital sign response differences exist with the addition of mint flavoring and 5% nicotine added to e-juice in people vaping, and those exposed to the vapor? The hypothesis was people vaping mint flavored, nicotine products and those exposed to such vapor would have significantly increased HR, BP, RF and blood glucose (BG), but a decrease in blood oxygentation (SpO_2%) following 20 minutes of use (exposure) compared to people vaping non-nicotine, non-flavored products or people exposed to such vapor.

Procedure

Two hundred seventy-three (N=279) adult volunteers participated in the study. Subjects completed a general health questionnaire regarding past medical history including mental health, pulmonary conditions (including tuberculosis, asthma, chronic bronchitis, emphysema, and lung cancer), cardiac conditions, hypertension, head injury/trauma, substance abuse and smoking history. Data gleaned was informational only and not used to eliminate any volunteers.

Subjects were divided into four separate groups; 1.) Participants exposed to the vapor of volunteers using e-cigarettes filled with 5% nicotine and mint flavoring (N=66), 2.) Participants using an e-cigarette filled with 5% nicotine and mint flavoring (N=66), 3.) Participants exposed to the vapor of volunteers using e-cigarettes without nicotine or flavoring (N=74), and 4.) Participants using an e-cigarette without nicotine or flavoring (N=73). Vaping subjects were instructed to use the e-cigarettes ad lib for 20 minutes while the non-vaping subjects sat next to them during the same time. Groups were controlled for type of vape for each session meaning people using e-cigarettes with nicotine and flavor were not in the same sessions as those using e-cigarettes without nicotine or flavoring. Participants self-selected into which study group they were willing to participate in. More male participants chose the vaping groups compared to more females choosing the exposure to vapor (non-vaping) groups. All participants were volunteers over the age of 18. (See Table 1). Mint flavoring with 5% nicotine was chosen because it has been found to be one of the most popular e-juice products among vape users.[1]

The study was approved by the IRB at the institution where the study was conducted. Volunteers were obtained through announcements made on social media outlets (e.g., Snap Chat, Instagram, Facebook), a university participant recruitment website, word-of-mouth, and/or by invitation of the researchers. Participants were asked to not eat, smoke cigarettes, or vape for at least 60 minutes prior to the study. Participants were seated in an enclosed laboratory space, provided informed consent, completed a health questionnaire, and given an e-cigarette for use. A set of vital signs including BP, HR, RF, SpO_2% and BG was taken prior to vaping or exposure to vapor, and again at the completion of the 20-minute vaping session. Participants were instructed to vape ad lib and talk amongst the other participants at will throughout the duration of the study.

Physiological measurements were collected by a registered nurse or trained research assistant. Study variables were measured using the following criteria: (a) BP – determined by automatic blood pressure machine while the participant was seated with both feet on the floor. Systolic blood pressure (SBP), and diastolic blood pressures (DBP) were obtained, and then mean arterial pressure (MAP) was found using the following formula: SBP + 2(DBP)/3: (b) HR – determined by automatic finger monitor; (c) RF – determined via counting respirations for 15 seconds and multiplying by 4 to determine rate per minute; (d) SpO_2% – determined by non-invasive finger clamp and (e) BG – determined via finger prick with glucometer analysis.

Table 1 Age and gender characteristics of each vape group

	Exposure to vapor w/o flavor or nicotine	Exposure to vapor with flavor & nicotine	Vaping w/o flavor or nicotine	Vaping with flavor & nicotine
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Age				
Mean	22.71	23.08	23.76	20.39
SD	8.12	8.81	10.30	2.96
Gender				
Male	22	17	41	45
Female	48	49	30	21
Missing	4	0	2	0

Note. One-way ANOVA examining age as a function of group emerged non-significant (F[3,271]= 2.19, p= .089). Chi-square test of independence examining gender as a function of group emerged significant (Chi-square= 33.91, p<.001). More females are in Non-vape groups while more males are in Vape groups

Results

Between Group Analysis of Variance (ANOVA) examining pre-vape and post-vape physiological variables separately as a function of vape group demonstrated several significant differences between the groups relating to the MAP and RF. MAP was significantly lower in group 3, (participants exposed to non-flavored vapor without nicotine) compared to participants in group 2 (participants vaping mint-flavored e-juice with 5% nicotine) prior to exposure or vape use suggesting non-vapers have lower blood pressures at baseline compared to their vaping counterparts.

MAP was also significantly different following 20 minutes of vape use for groups 2 and 4 (both vaping groups) compared to group 3 (participants exposed to non-flavored vapor without nicotine). Participants exposed to vapor both with and without flavoring and nicotine experienced a decrease in MAP after twenty minutes. Participants vaping non-flavored e-juice without nicotine had a slight increase in blood pressure although not statistically significant while those vaping with flavored nicotine experienced a significant increase in blood pressure suggesting vaping mint flavored e-juice with 5% nicotine contributes to elevated blood pressure.

Respiratory frequency was also found to be statistically significant between the groups pre and post vaping or exposure to vapor. Participants exposed to flavored vapor with nicotine (group one) and those vaping with mint flavored e-juice containing nicotine (group two) differed from the participants vaping non-flavored e-juice

without nicotine (group four) in the pre-study respiratory frequency assessment. Following twenty mintues of vape use or exposure to vapor, respiratory frequency significantly differed between group one (participants exposed to vapor with mint flavoring and nicotine) compared to people exposed to non-flavored, non-nicotine vapor (group three) and those vaping non-nicotine, non-flavored e-juice (group four). (See Table 2)

Table 2 Between group analysis of variance (ANOVA) examining pre-vape and post-vape physiological variables separately as a function of vape group

	GROUP ONE Exposure to vapor with flavor & nicotine (n= 66)	**GROUP TWO Vaping with flavor & nicotine (n= 66)**	**GROUP THREE Exposure to vapor w/o flavor or nicotine (n= 74)**	**GROUP FOUR Vaping w/o flavor or nicotine (n= 73)**	**ANOVA Results F(3, 275)**		
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**F**	**p**	**eta²**
Pre-Vape							
Heart Rate	88.89 (18.54)	83.33 (16.44)	85.55 (16.49)	86.62 (17.90)	1.18	.312	
Mean Arterial Pressure	**94.44 (10.21)**	**95.03^{a} (10.91)**	**89.99^{a} (9.00)**	**93.78 (10.73)**	**3.54**	**.015**	**.04**
Respiratory Frequency	**11.18^{a} (1.16)**	**11.30^{b} (1.02)**	**11.84 (1.68)**	**12.05^{ab} (1.63)**	**6.06**	**<.001**	**.06**
Blood Glucose	98.09 (25.57)	94.55 (12.78)	98.88 (18.46)	98.82 (23.58)	0.69	.572	
O2 Saturation	97.92 (1.77)	98.26 (1.03)	98.15 (1.18)	97.77 (1.30)	1.89	.131	
Post-Vape							
Heart Rate	87.10 (18.55)	86.64 (14.66)	82.78 (13.91)	82.77 (16.43)	1.54	.205	
Mean Arterial Pressure	**91.19^{c} (10.22)**	**96.09^{bc} (9.79)**	**86.85^{ab} (8.65)**	**91.59^{a} (10.79)**	**10.18**	**<.001**	**.10**
Respiratory Frequency	**11.18^{ab} (1.11)**	**11.82 (0.91)**	**12.36^{a} (2.52)**	**12.19^{b} (1.60)**	**6.64**	**<.001**	**.07**
Blood Glucose	99.17 (21.37)	95.67 (15.13)	99.27 (17.84)	98.93 (21.93)	0.54	.654	
O2 Saturation	97.36 (3.06)	97.88 (1.03)	97.93 (1.29)	97.74 (1.14)	1.37	.252	

Note. Evaluation of equality of variances across groups was done using Levene test. Equality of variances can be assumed for all variables except Post-vape Respiratory Rate and Post-vape O2 Saturation for which the Levene test emerged significant. Statistically significant ANOVA results are in bold font. For significant ANOVA results, post-hoc pair-wise comparisons of means were computed using the Scheffe test. Groups sharing the same superscript letter (e.g., a, b, c) are significantly different from each other at p<.05 or lower

Repeated Measures Analysis of Variance (ANOVA) tests were also conducted revealing several significant findings. Participants exposed to vapor with and without flavoring or nicotine (groups 1 and 3) had significantly reduced MAP following 20 minutes of exposure compared to pre-test findings. Participants vaping without flavoring or nicotine (group 4) also demonstrated significantly lower HRs and MAPs at the post-vape assessment compared to pre-vape findings. However, participants who vaped with mint-flavored e-juice and 5% nicotine (group 2) experienced significantly higher HR and RF following 20 minutes of vape use while their oxygen saturation was significantly lower. (See Table 3)

Table 3 Repeated measures analysis of variance (ANOVA) examining pre-vape and post-vape variables as a function of vape group

	Pre-Vape	**Post-Vape**	**ANOVA Results**		
	Mean (SD)	**Mean (SD)**	**F**	**p**	**eta²**
Group 1 - Exposure to vapor with mint flavoring and 5% nicotine (n= 66)					
Heart Rate	88.89 (18.54)	87.10 (18.55)	1.06	.308	
Mean Arterial Pressure	**94.44 (10.21)**	**91.19 (10.22)**	**7.67**	**.007**	**.11**
Respiratory Rate	11.18 (1.16)	11.18 (1.11)	0.00	1.00	
Blood Glucose	98.09 (25.57)	99.17 (21.37)	0.33	.570	
O_2 Saturation	97.92 (1.77)	97.36 (3.06)	2.09	.153	
Group 2 - Vape use with mint flavoring and 5% nicotine (n= 66)					
Heart Rate	**83.33 (16.44)**	**86.64 (14.66)**	**4.00**	**.050**	**.06**
Mean Arterial Pressure	95.03 (10.91)	96.09 (9.79)	0.73	.397	

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Table Continued...

	Pre-Vape	Post-Vape	ANOVA Results		
	Mean (SD)	**Mean (SD)**	**F**	**p**	**eta²**
Respiratory Rate	**11.30 (1.02)**	**11.82 (0.91)**	**10.69**	**.002**	**.14**
Blood Glucose	94.55 (12.78)	95.67 (15.13)	0.27	.608	
O2 Saturation	**98.26 (1.03)**	**97.88 (1.03)**	**4.35**	**.041**	**.06**
Group 3 – Exposure to vapor without flavor or nicotine (n= 74)					
Heart Rate	85.55 (16.49)	82.78 (13.91)	2.78	.100	
Mean Arterial Pressure	**89.99 (9.00)**	**86.85 (8.65)**	**12.18**	**.001**	**.14**
Respiratory Rate	11.84 (1.68)	12.36 (2.52)	2.57	.113	
Blood Glucose	98.88 (18.46)	99.27 (17.84)	0.04	.844	
O_2 Saturation	98.15 (1.18)	97.93 (1.29)	1.66	.202	
Group 4 - Vape use without flavor or nicotine (n= 73)					
Heart Rate	**86.62 (17.90)**	**82.77 (16.43)**	**5.45**	**.022**	**.07**
Mean Arterial Pressure	**93.78 (10.73)**	**91.59 (10.79)**	**5.57**	**.021**	**.07**
Respiratory Rate	12.05 (1.63)	12.19 (1.60)	0.33	.567	
Blood Glucose	98.82 (23.58)	98.93 (21.93)	0.00	.956	
O_2 Saturation	97.77 (1.30)	97.74 (1.14)	0.03	.874	

Note. For Vape exposure without nicotine or flavoring group, df= 1, 73. For vape use without nicotine or flavoring, df= 1, 72. For Vape exposure with nicotine and flavoring, df= 1, 65. Statistically significant results in bold font

Finally, a Mixed Factorial ANOVA was run on the data. All physiological variables except blood glucose were implicated in at least one significant result. Results that emerged significant in the initial ANOVA remained significant in the ANCOVA after controlling for age and gender. Specifically, the interaction of groups is significant for HR, and MAP, meaning that the change in heart rate, and mean arterial pressures from pre- to post-vape varies across the groups. Repeated measures main effect emerged as significant for HR, MAP, and RF meaning when the values were averaged across all groups, a significant difference emerged with the post-vape assessments. Between groups main effect emerged as significant for MAP, and RF indicating at least one of the four vape groups significantly differed from the others on the average of pre-and-post-vape scores combined. (See table four).

Table 4 Results of mixed factorial ANOVAs and ANCOVAs examining physiological variables as a function vape group (between groups) and pre-post vaping conditions (within subjects)

	ANOVA			**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(3, 275)=0.88 p= .451	F(1, 275)=2.31 p= .129	**F(3, 275)=3.47 p= .017 Partial eta²=.04**	F(1,263)= 1.35 p= .259	F(1,265)= 1.32 p= .252	**F(3,265)= 2.89 p= .036 Partial eta²=.03**
Mean Arterial Pressure	**F(3,275)= 7.52 p<.001 Partial eta²=.08**	**F(1,275)= 12.60 p<.001 Partial eta²=.04**	**F(3,275)= 3.50 p= .016 Partial eta²=.04**	**F(3,263)= 5.94 p= .001 Partial eta²=.06**	**F(1,265)= 12.28 p= .001 Partial eta²= .04**	**F(3,265)= 3.59 p= .014 Partial eta²= .04**
Respiratory Rate	**F(3,275)= 10.13 p< .001 Partial eta²=.10**	**F(1,275)=5.95 p=.015 Partial eta²=.02**	F(3,275)= 1.21 p= .307	**F(3,263)= 9.26 p<.001 Partial eta²= .10**	**F(1,265)= 5.70 p= .018 Partial eta²= .02**	F(2,265)= 1.52 p= .211
Blood Sugar	F(3,275)= 0.73 p= .537	F(1,275)= 0.45 p= .503	F(3,275)= 0.06 p= .979	F(3,263)= 0.63 p= .597	F(1,265)= 0.27 p= .606	F(3,265)= 0.10 p= .959
O2 Saturation	F(3,275)= 1.98 p= .117	**F(1,275)= 6.10 p= .014 Partial eta²=.02**	F(3,275)= 0.90 p= .441	F(3, 263)= 1.61 p= .187	**F(1,265)= 5.38 p= .021 Partial eta²= .02**	F(3,265)= 1.02 p= .383

Note. Consult earlier tables to see means for groups for each physiological variable. Significant results in bold font

Discussion

There appear to be significant differences in physiological response following twenty minutes of vape use or exposure to vapor which varies according to the type of e-juice. People exposed to vapor had no significant effects on their HR, RF, BG or SpO_2% following 20 minutes of exposure to vapor with or without mint flavor and nicotine. However, both of the exposure to vapor groups demonstrated significantly lower MAP's following 20 mintues of vapor exposure. This finding suggests that vapor, regardless of the contents of the e-juice, does not seem to have an acutely negative impact on vital signs. Additionally, blood pressure reduces as expected during times of rest in this population. This finding suggests that people in close proximity to persons who are vaping may not be at high risk for negative health effects associated with vital signs in the acute phase.

Similarly, people vaping without mint flavor or nicotine had significantly lower MAPs, and also experienced significantly lower HRs at post-vape assessment. It was interesting to note the group vaping non-flavored, non-nicotine e-juice experienced a significant reduction in both MAR, and HR unlike the non-vapers who did not experience a significant reduction in HR. The reason participants vaping non-flavored, non-nicotine participants HRs decreased more so than the non-vape groups is unclear. One explanation is the satisfaction vapers experience when vaping and its calming effects.

This study revealed non-vapers have lower blood pressures and respiratory frequency rates compared to their vaping counterparts at baseline. Additional research is warranted to determine if other pre-exsiting conditions could be contributing to the variations in baseline BP, and RF between groups but these findings suggest vaping with nicotine and mint flavoring could be a contributory factor to sustained elevated blood pressures.

The participants in group 2, those vaping with mint flavoring and 5% nicotine, had the most concerning results. Vaping with e-juice containing mint flavor and nicotine causes increased HR, and RF following 20 minutes of vaping while their oxygen level is significantly reduced. Additionally, their MAP did not significantly reduce compared to the other three groups following 20 minutes of being seated and vaping. These findings suggest there are serious health implications for people vaping with mint flavoring and nicotine. People often begin vaping in their youth, continue throughout adulthood, and find the ability to quit vaping extremely difficult due to the addictive nature of nicotine.[25,26] Sustained HR, and BP with associated oxygen reduction caused by vaping with mint flavor and nicotine can contribute to a plethora of medical conditions including cardiac strain, fatigue, hypoexmia, mood disorders, respiratory diseases, gastrointestinal disorders, reduction in immune response, reproductive complications, and malignancies.[27,28] Health care providers should be screening for vape use, determine the type of e-juice used, and provide education on the health outcomes associated with the various vape products.

Perhaps one method to assist persons wanting to quit vaping would be to suggest they try vaping without nicotine or flavoring. Doing so would provide the familiar hand to mouth inhaling pattern vapers are used to without the harmful physiologial effects noted when vaping with mint flavored nicotine e-juice. Additionally, exposure to vapor with or without mint flavoring and nicotine does not seem to have an immediate impact on vital signs. This is especially significant for patient populations not directly vaping but exposed to the vapor of those who are. Although inhaled vapor can not be considered safe[10,14,21] it does not appear to have the acute physiological response on vital signs that actual vaping does.

Conclusion

Much more research is needed to determine the health responses of vaping the many different combinations of e-juice and exposure to the vapor. This growing trend, once thought to be a safe alternative to cigarette smoking, is rapidly becoming the new challenge for health care professionals and researchers to address. Emerging research is clearly demonstrating vaping does have negative health implications. Specifically, vaping with mint flavored e-juice with 5% nicotine is acutley detrimental to patients, and if sustained is likely to lead to long-term health complications.

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Declaration of interests

All authors declare no conflicts of interest. Data is not publically available, and was destroyed at the conclusion of the study per IRB agreement to maintian anonymity of the participants.

References

1. Leventhal A, Miech R, Barrington-Trimis J, et al. Flavors of e-cigarettes used by youths in the United States. *JAMA.* 2019;322(21):2132−2134.
2. Miech R, Johnston L, O'Malley PM,et al. Trends in Adolescent Vaping, 2017-2019. *N Engl J Med.* 2019;381(15):1490−1491.
3. NIDA. Vaping Devices (Electronic Cigarettes) DrugFacts. *National Institute on Drug Abuse website.* 2020.
4. Pourchez J, Forest V. E-cigarettes: from nicotine to cannabinoids, the French situation. *Lancet Respir Med.* 2018 ;6(5):e16.
5. NIDA. Teen e-cigarette use doubles since 2017. *National Institute on Drug Abuse website*. 2019.
6. Health and Human Services. FDA Finalizes enforcement policy on unauthorized flavored cartridge-based e-cigarettes that appeal to children, including fruit and mint. 2020.
7. Cai K. Juul and rivals, given 10 months to submit FDA application, face battle to keep selling E-cigs. [New York: Forbes]. 2019.
8. DeVito EE, Jensen KP, O'Malley SS, et al. Modulation of "protective" nicotine perception and use profile by flavorants: preliminary findings in e-cigarettes. *Nicotine Tob Res*. 2020;22(5):771−781.
9. Biondi-Zoccai G, Sciarretta S, Bullen C, et al. Acute effects of heat-not-burn, electronic vaping, and traditional tobacco combustion cigarettes: the sapienza university of rome-vascular assessment of proatherosclerotic effects of smoking (sur - vapes) 2 randomized trial. *J Am Heart Assoc.* 2019;8(6):e010455.
10. Lechasseur A, Jubinville É, Routhier J, et al. Exposure to electronic cigarette vapors affects pulmonary and systemic expression of circadian molecular clock genes. *Physiol Rep*. 2017;5(19):e13440.
11. Vardavas CI, Anagnostopoulos N, Kougias M,et al. Short-term pulmonary effects of using an electronic cigarette: impact on respiratory flow resistance, impedance, and exhaled nitric oxide. *Chest*. 2012;141(6):1400−1406.
12. Vlachopoulos C, Ioakeimidis N, Abdelrasoul M, et al. Electronic cigarette smoking increases aortic stiffness and blood pressure in young smokers. *J Am Coll Cardiol*. 2016;67(23):2802−2803.
13. Antoniewicz L, Bosson JA, Kuhl J, et al. Electronic cigarettes increase endothelial progenitor cells in the blood of healthy volunteers. *Atherosclerosis*. 2016;255:179−185.
14. Caporale A, Langham MC, Guo W, et al. Acute effects of electronic cigarette aerosol inhalation on vascular function detected at quantitative MRI. *Radiology.* 2019;293(1):97−106.

15. St Helen G, Dempsey DA, Havel CM, et al. Impact of e-liquid flavors on nicotine intake and pharmacology of e-cigarettes. *Drug Alcohol Depend*. 2017;178:391−398.

16. Voos N, Smith D, Kaiser L, et al. Effect of e-cigarette flavors on nicotine delivery and puffing topography: results from a randomized clinical trial of daily smokers. *Psychopharmacology (Berl).* 2020;237(2):491−502.

17. St Helen G, Shahid M, Chu S, et al. Impact of e-liquid flavors on e-cigarette vaping behavior. *Drug Alcohol Depend*. 2018;189:42−48.

18. Szumilas K, Szumilas P, Grzywacz A, et al. The effects of e-cigarette vapor components on the morphology and function of the male and female reproductive systems: a systematic review. *Int J Environ Res Public Health*. 2020;17(17):6152.

19. Lee WH, Ong SG, Zhou Y, et al. Modeling cardiovascular risks of e-cigarettes with human-induced pluripotent stem cell-derived endothelial cells. *J Am Coll Cardiol*. 2019;73(21):2722−2737.

20. Muthumalage T, Prinz M, Ansah KO,et al. Inflammatory and oxidative responses induced by exposure to commonly used e-cigarette flavoring chemicals and flavored e-liquids without nicotine. *Front Physiol.* 2018;8:1130.

21. Visser WF, Klerx WN, Cremers HWJM, et al. The health risks of electronic cigarette use to bystanders. *Int J Environ Res Public Health*. 2019;16(9):1525.

22. Health and Human Services. FDA Finalizes enforcement policy on unauthorized flavored cartridge-based e-cigarettes that appeal to children, including fruit and mint. 2020.

23. McDonald J. Michigan Gov. Whitmer pushes a permanent flavor ban. 2020.

24. McGinley L. Health. Michigan becomes first state to ban flavored e-cigarettes. *The Washington Post*. 2019.

25. Jones K, Salzman GA. The vaping epidemic in adolescents. *Mo Med*. 2020;117(1):5658.

26. Amato MS, Bottcher MM, Cha S, et al. It's really addictive and i'm trapped: a qualitative analysis of the reasons for quitting vaping among treatment-seeking young people. *Addict Behav* .2021;112: 106599.

27. Mishra A, Chaturvedi P, Datta S,et al. Harmful effects of nicotine. *Indian J Med Paediatr Oncol*. 2015;36(1):24−31.

28. Besson M, Granon S, Mameli-Engvall M, et al. Long-term effects of chronic nicotine exposure on brain nicotinic receptors. *Proceedings of the National Academy of Sciences*. 2007;104(19):8155-8160.