

# The effect of vaping and nicotine-containing liquids to suppress the immune system: A Pilot Study

## KEYWORDS

cigarette smoking; electronic cigarettes; immunosuppression

## ABSTRACT

**AIMS:** We present a pilot study to illustrate how the impact of vaping can be quickly and conclusively documented in a large population and appropriate subpopulations.

**METHODS:** It has been predicted that with longer duration and higher frequency of vaping, there would be a higher frequency of, a longer duration of, and more severe flu and cold symptoms — indicating a negative impact on the immune system. Studies have linked electronic cigarettes and vaping to respiratory and cardiovascular issues, drastic changes in blood pressure, and the reduced function of tissues and cells in the lungs, but only in small populations, making generalization to the entire population less convincing.

A sample of 120, 18–22-year-olds in northern California were asked to complete a 14-question, two-minute, anonymous survey. Those with pre-existing respiratory ailments or a family history of respiratory ailments were excluded from the study along with those who smoke cigarettes or have smoked cigarettes in the past. The survey collected the frequency and time spent vaping and the severity, frequency, and longevity of the flu and cold symptoms. Responses were converted into numerical values and analyzed.

**RESULTS:** Those who vaped more often had more severe flu and cold symptoms ( $p < 0.005$ ). However, no strong trends were present as can be expected from a pilot study. A power analysis based on this pilot data suggests that only 667 subjects would be required to answer the short survey to reach statistical significance.

**CONCLUSION:** A quick survey was created to show the negative effects of vaping on a general population. Showing effects generalizable to the entire population would require a very reasonably sized sample and could easily allow analysis of subpopulations.

## INTRODUCTION

In 2007, electronic cigarettes (e-cigs, vapes) were introduced to the United States. Their use has been an increasing concern of health for the public, especially due to its addictive nature. [1] Vaping's rise in popularity among smokers, non-smokers, pregnant women, and even teens have posed a preventable concern. [2]

In the United States, there was an e-cigarette use-associated acute lung injury (EVALI) outbreak in 2019-2020, with 65 confirmed deaths. [3] Case reports of EVALI have also linked respiratory health problems to vaping as well as limiting the body's defenses by suppressing genes in the airway causing airway resistance; increasing neutrophil activation, aortic stiffness, and blood pressure; altering mucin secretion; impairing neutrophil phagocytosis and ciliary motility. [1,4]

Susceptibility to and severity of infections depend on a variety of factors, which may play a role in the body's response to vaping. [5] Chronic rhinosinusitis (CRS), an inflammatory condition affecting the nose and nasal sinuses, has been linked to the formation of biofilms that can be very resistant to the immune system. [5] LAIV-induced IgA antibody secretions and the cytokine/chemokine release is vital in the innate immune response following influenza infections, both of which are significantly modified by cigarette and e-cigarette exposure. [1] The total absorbance of planktonic cells is depressed in smokers. [6]

Secondary effects are also possible. The nicotine in e-cigarettes enhances physiological hemostasis and increases the risk of thrombosis via modulating platelet function in adult mice. [2] E-cigarette-exposed platelets showed slower activation. [2] Female rats are more sensitive to the effects of nicotine on body weight and the consumption of food and water. [7]

The effects could be mediated by chemicals in vaping besides the nicotine. There are substantial levels of small particles in addition to high levels of metals with toxic materials like aluminum, copper, magnesium, zinc, lead, chromium, manganese, and nickel found in e-cigarettes. Particles could get to the alveolar epithelium in the respiratory membrane, resulting in oxidative stress and a decrease in inflammation. Furthermore, the chemicals found in flavored e-cigarettes have also been shown to be responsible for toxic effects on pulmonary fibroblasts. [4]

Despite the availability of several studies, there is no nationwide survey showing an impact on the population at large, leaving some to argue that the studies to date cannot be generalized to the entire population. In particular, the group of adults between 18 and 22, a population that would have the longest future potential addiction of those legally allowed to vape, has not been studied. In this pilot work, we show how a study can be constructed to quickly and cost-effectively demonstrate, population-wide, the negative effects of vaping.

## **METHODS**

One hundred and twenty, 18–22-year-olds from Northern California were provided a 14-question survey. All subjects were first asked to provide informed consent. This protocol was approved by the institutional review board before commencing.

Participants were recruited by Qualtrics from the general US population via website intercept recruitment, member referrals, targeted email lists, gaming sites, customer loyalty web portals, permission-based networks, and social media. Potential participants' names, addresses and dates of birth were validated via third-party verification measures but not passed to the research team. Among all possible participants, a random sample was requested to complete the survey. Participants were given a small incentive to participate in the form of a gift card or points towards gifts.

Anyone within the age group and in Northern California answering the survey was allowed to participate. For all surveys, nonsensical answers or excessively rapid completion times were disqualified for inclusion in analysis. The first 120 to complete the survey were included. Those with pre-existing health conditions regarding respiration, those with a family history of respiratory conditions, or those who smoke cigarettes or have smoked cigarettes in the past were excluded — participants in this category could have flu/cold symptoms unrelated to their vaping history.

The study questions can be seen in Table 1. Demographic information was collected, including age, gender, and race. Participants were asked about their background with respiratory health issues and their experience with smoking cigarettes, e-cigarettes, and marijuana. Their frequency and time spent smoking were recorded. In addition, questions about flu and cold symptoms were gathered. The severity, frequency and longevity were also asked at the end of the survey.

Responses were converted to numerical values, and a T-test assuming unequal variances was used to determine the relationship between vaping and flu and cold symptoms.

## **RESULTS**

The survey had a total of 120 participants, but only 106 were used for analysis, since those with pre-existing respiratory conditions were excluded from the study. Of the fourteen who were excluded, eleven of those were because of asthma. The remaining three were lung cancer, bronchitis, and sickle-cell disease. In the remaining 106, 42 currently use e-cigarettes or have in the past, and 64 had not used e-cigarettes. Among the 42 users, 22 currently use JUULs, a specific brand of e-cigarettes.

The quick survey provided a rich selection of subpopulations. Among the 42 users, five were eighteen years old, eight were nineteen years old, six were twenty years old, twelve were 21 years old, and eleven were 22 years old. Twelve identified as male, 28 identified as female, and 2 identified as non-binary. Nineteen classified themselves as white, eleven classified themselves as Black/African American, and three classified themselves as Asian. One classified themselves as

American Indian or Alaska Native. The remaining eight preferred not to provide a racial classification response.

Equally diverse were the non-users. Among the 64 participants who had never vaped, eleven were eighteen years old, twelve were nineteen years old, nine were twenty years old, sixteen were 21 years old, and sixteen were 22 years old. Seventeen identified as male and 43 identified as female, while three identified as non-binary. There was one non-disclosure of gender. Twenty participants classified themselves as white. Ten classified themselves as Black/African American. Ten classified themselves as Asian. Four classified themselves as American Indian or Alaska Native, and two classified themselves as Native Hawaiian or Pacific Islander. The remaining 18 preferred not to respond to this question.

The survey was very quick to complete. The average time to complete the survey was under two minutes.

Using a T-test assuming unequal variances, the data indicated that those who use e-cigarettes experience more frequent flu and cold symptoms (1.63 versus 1.79,  $p < 0.25$ ). Although not originally planned as part of this study, we also completed a non-parametric Mann-Whitney test. The non-parametric test confirmed that individuals who vaped had a higher frequency of flu and cold symptoms than did individuals who did not ( $Z = -2.80$ ,  $p < .005$ ). In addition, vaping more often leads to more severe symptoms. However, the differences between each of these variables were not large (Figure 1). For example, for frequency, converting the answers to numerical values showed a difference of 1.63 (non-users) versus 1.79 (users). The severity of symptoms rose from about 1.5 to 2.5 ( $p < 0.17$ ) as the frequency rose from 1 to 5 (Figure 2). A difference of 0.25 is equivalent to moving one-quarter of the way from average to severe symptoms. The severity and frequency indices (shown in Figure 2) were analyzed with linear regression giving a slope of 0.3 ( $r^2 = 0.126$ ).

Subpopulations showed interesting trends that might merit further study. For example, females that identified as black or African American were far heavier users (averaging once per day) but reported more mild symptoms (average 2 severity) than white women (a few times per week with symptoms averaging 2.2 severity). It is not possible to determine if this is a significant difference in this small, pilot study.

The vaping frequency and duration were compared to duration, frequency, and severity of their flu and cold symptoms, but the relationship between these variables showed no strong trends.

## DISCUSSION

Vaping is an emerging habit, especially in younger generations. Some consider vaping a safer alternative to cigarettes, not believing the available science to the contrary. More research, and more convincingly generalizable research, on this topic and its health risks are necessary. An understanding of the effects of vaping on the immune system could change users' perception of vaping on their health. However, it is difficult to conduct a convincing, generalizable study to prove that vaping weakens the immune system. This pilot study shows one way that a quick and

simple study could provide convincing data of the effect of vaping on the immune system in a large population.

Indeed, no previous study offers the ability to probe subgroups as thoroughly or quickly. For example, one recent study used a similar approach but was only able to survey 129 participants [7]. Another study could not limit the age group as succinctly, leading to data ranging from less than 18 to over 60 years of age [6]. Other recent studies have focused on the different types of vaping devices [1] or chemicals in the vaporizers or flavors [4].

This pilot study used a mostly multiple-choice survey that takes less than two minutes to complete. Yet, it provides rich information on vaping history and its relationship with flu and cold symptoms that can be further analyzed along many demographic lines.

Due to the small sample size, this study does not provide conclusive results. However, the sample size required is not insurmountable. For the severity, using a T-Test for the difference in means assuming unequal variance, a power calculation to detect a difference of approximately 0.25 in symptom severity (about one-quarter of the way from average to severe) at an alpha value of .05 with 80% power shows that a sample size of 667 would be sufficient. Thus, a study to examine the differences between immune system responses for those who do and do not vape is not only feasible but would require a relatively small sample size of less than 1000 participants. However, using the non-parametric approach, the study size presented here is sufficient.

## STUDY LIMITATIONS

This is a pilot study whose findings should not be used on their own to draw conclusions. Random electronic sampling tends to favor those with regular, fast-internet access and smart phones. This may not be the population of interest for some future studies. The relatively rapid nature of the study, while advantageous for acquiring responses, limits the amount of internal data validation that is possible. Of particular concern is the symptomatic description, which resulted in multinomial data that can be difficult to analyze using correlations. Perhaps a scale between mild and severe or a checklist of symptoms might permit alternative analysis approaches. Alternatively, a non-parametric test could be planned from the outset and used for the analysis. Using a very quick survey does not allow for extensive definitions or explanations, such as what constitutes a flu and cold symptom. This can lead to variability in interpretation of the answers provided. There can be many confounding factors that are not extracted here like average proximity to people, especially in enclosed areas, BMI, etc.

## CONCLUSIONS

We have shown that a quick and relatively inexpensive study could be conducted in a broad, general population to show that vaping has a negative effect both on the entire population and on

select subgroups. Such a study would more convincingly show that the results are generalizable and that effects seen in the laboratory are not isolated.

**Disclaimer regarding Consent and Ethical Approval:**

As per university standard guideline, participant consent and ethical approval have been collected and preserved by the authors

UNDER PEER REVIEW

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**FIGURES AND TABLES**

UNDER PEER REVIEW

Table 1

Table 1: These questions were used in this survey. The survey took less than 2 minutes to complete and was easily accomplished on a mobile phone.

Questions:	Answer Choices:
1. Age?	
2. Which county do you live in?	
3. Gender?	<ul style="list-style-type: none"> <li>• Male</li> <li>• Female</li> <li>• Non-binary/third gender</li> <li>• Prefer not to say</li> </ul>
4. Race?	<ul style="list-style-type: none"> <li>• White</li> <li>• Black or African American</li> <li>• American Indian or Alaska Native</li> <li>• Asian</li> <li>• Native Hawaiian or Pacific Islander</li> <li>• Other</li> </ul>
5. Do you have any preexisting respiratory conditions and/or a family history of respiratory conditions?	
6. Do/have you smoke/smoked any of the below?	<ul style="list-style-type: none"> <li>• Cigarettes</li> <li>• E-cigarettes</li> <li>• JUULs</li> <li>• Marijuana</li> <li>• None of the above</li> <li>• Other</li> </ul>
7. Have you vaped in the past but don't vape now?	<ul style="list-style-type: none"> <li>• Yes</li> <li>• No</li> </ul>
8. How often do/did you vape?	<ul style="list-style-type: none"> <li>• Everyday or more</li> <li>• Few times a week</li> <li>• Once a week</li> <li>• Few times a month</li> <li>• Once a month or less</li> <li>• N/A</li> </ul>
9. How long (in minutes) are/were your vaping sessions?	<ul style="list-style-type: none"> <li>• 5 minutes or less</li> <li>• 10 minutes</li> <li>• 15 minutes</li> <li>• 20 minutes</li> <li>• 25 minutes</li> </ul>

	<ul style="list-style-type: none"> <li>• 30 minutes or more</li> <li>• N/A</li> </ul>
10. How long (in years) have you been vaping?	<ul style="list-style-type: none"> <li>• Less than six months</li> <li>• Six months – one year</li> <li>• One year</li> <li>• Two years</li> <li>• Three years</li> <li>• Four years</li> <li>• Five years</li> <li>• More than five years</li> <li>• N/A</li> </ul>
11. Have you experienced any flu-like symptoms or conditions before?	<ul style="list-style-type: none"> <li>• Yes</li> <li>• No</li> <li>• Don't know</li> </ul>
12. Last time you experienced cold/flu-like symptoms, how long did the symptoms last?	<ul style="list-style-type: none"> <li>• A day or less</li> <li>• 2 – 3 days</li> <li>• 4 – 6 days</li> <li>• 1 week</li> <li>• 2 – 3 weeks</li> <li>• 1 month</li> <li>• More than 1 month</li> <li>• N/A</li> </ul>
13. Last time you experienced cold/flu-like symptoms, how severe were the symptoms?	<ul style="list-style-type: none"> <li>• Very mild</li> <li>• Mild</li> <li>• Average</li> <li>• Severe</li> <li>• Very severe</li> </ul>
14. How often have you experienced these symptoms?	<ul style="list-style-type: none"> <li>• Once every few years</li> <li>• Once a year</li> <li>• Once every few months</li> <li>• Once a month</li> <li>• Once every few weeks</li> <li>• Once a week or more</li> <li>• N/A</li> </ul>

Figure 1

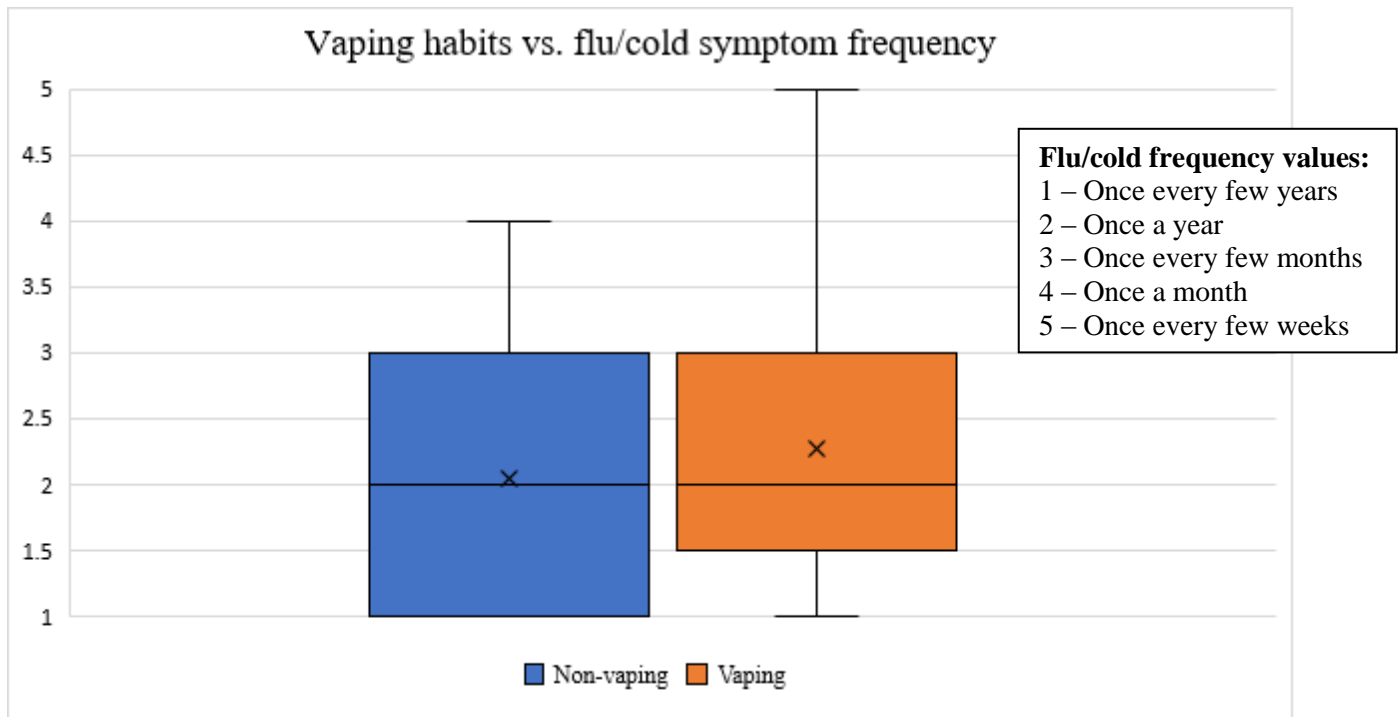


Figure 1: Vaping causes more frequent cold and flu symptoms ( $p < 0.005$ , non-parametric test). While this pilot study was not conclusive, it does demonstrate a quick and effective method to gather data from a large population. In addition, since only about 650 survey respondents would be required per subgroup, it could be used to effectively study population differences and disparities.

Figure 2

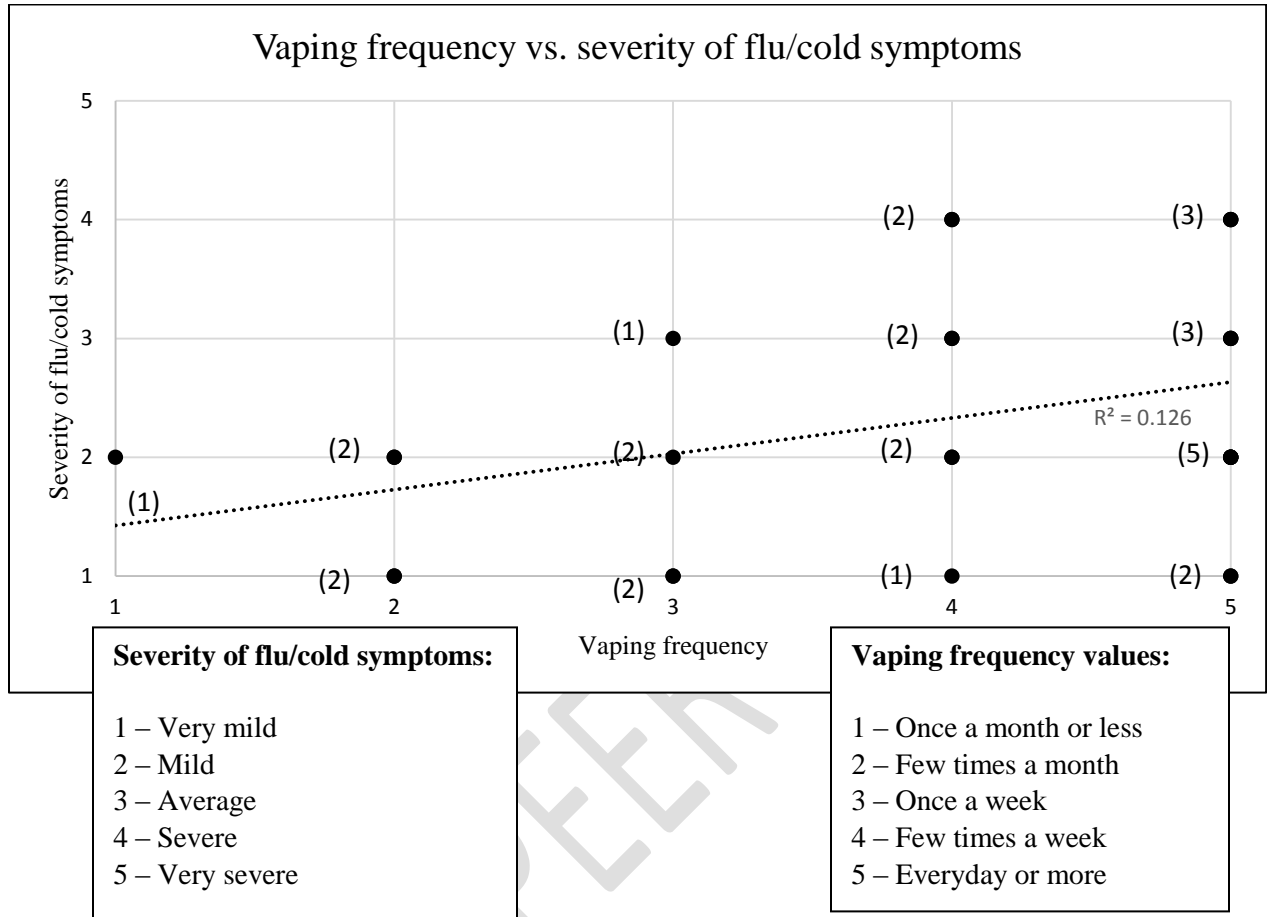


Figure 2: Vaping more often causes more severe cold and flu symptoms. Number in parentheses indicate the number of respondents (not all participants responded to all questions). The multinomial nature of this data is not easily analyzed with a correlation. A future study could consider a numerical rating system between very mild and very severe.