

Vaporized Nicotine (E-Cigarette) and Tobacco Smoking Among People With HIV: Use Patterns and Associations With Depression and Panic Symptoms

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Background: Vaporized nicotine (VN) use is increasing among people with HIV (PWH). We examined demographics, patterns of use, depression, and panic symptoms associated with VN and combustible cigarette (CC) use among PWH.

Methods: We analyzed VN use among PWH in care at 7 US sites. PWH completed a set of patient-reported outcomes, including substance use and mental health. We categorized VN use as never vs. ever with the frequency of use (days/month) and CC use as never, former, or current. We used relative risk regression to associate VN and CC use, depression, and panic symptoms. Linear regression estimated each relationship with VN frequency. Models were adjusted for demographics.

Results: Among 7431 PWH, 812 (11%) reported ever-using VN, and 264 (4%) reported daily use. Half (51%) of VN users concurrently used CC. VN users were more likely than those without use to be

younger, to be White, and to report ever-using CC. PWH reporting former CC use reported ≥ 8.5 more days per month of VN use compared with never CC use [95% confidence interval (95% CI): 5.5 to 11.5 days/month] or current CC use (95% CI: 6.6 to 10.5 days/month). Depression (relative risk: 1.20 [95% CI: 1.02 to 1.42]) and panic disorder (1.71 [95% CI: 1.43 to 2.05]) were more common among PWH ever-using VN. Depression was common among PWH using VN (27%) and CC (22%), as was panic disorder (21% for VN and 16% for CC).

Conclusion: Our study elucidated demographic associations with VN use among PWH, revealed the overlap of VN and CC use, and associations with depression/panic symptoms, suggesting roles of VN in self-medication and CC substitution, warranting further longitudinal/qualitative research.

Key Words: e-cigarette, vaporized nicotine, depression, people with HIV, substance use, tobacco

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INTRODUCTION

In 2007, vaporized nicotine (VN) through electronic cigarettes, “e”-cigarettes (ECs), and alternative nicotine delivery systems became available in the United States, and their use has grown in popularity to reach a prevalence of $\sim 3.2\%$ among adults.^{1–4} In the United States, up to half of those using VN report concurrent use of combustible cigarettes (CCs).¹ Marketing recommendations of VN as a tobacco cessation tool have been persistent since their inception,^{5,6} despite several systematic reviews demonstrating a lack of efficacy of VN for this purpose,^{7,8} with one noting significantly less tobacco cessation among VN users compared with nonusers.⁹ Most VN systems involve vaporization of liquid propylene glycol and glycerol as a vehicle for nicotine and flavoring for inhalation.¹⁰ Nicotine levels and ingredients vary by product,¹¹ with many raising concerns for toxicity,¹² metabolic effects,¹³ and potential carcinogenicity.^{14,15} Other health effects of VN use are not unlike those of CCs: elevated risk for chronic obstructive pulmonary disease/asthma¹⁶ and myocardial infarction.¹⁷

Although VN-related harms are becoming increasingly apparent, data regarding the prevalence and patterns of VN use among people with HIV (PWH) are limited. There is evidence of high rates of concurrent VN and CC use among PWH,¹⁸ which is potentially alarming given that PWH have 2–3 times greater prevalence of smoking CC^{19–26} and report smoking more cigarettes per day and less cessation than the general population.²⁷ Recent analyses among PWH showed more life-years lost to CC use than to HIV infection itself,²⁸ likely related to a significantly increased risk of harmful effects such as smoking-related malignancies²⁹ and cardiovascular complications,^{30,31} as well as greater HIV symptom severity.³² Furthermore, findings have been mixed regarding the association between mental health and CC use among PWH and the general population, ranging from no association to worse depression and anxiety symptoms.^{33–37} Emerging evidence among the general population has suggested a dose-dependent association between VN use and depressive symptoms,³⁸ further highlighting the importance of examining VN use patterns and associations with mental health symptoms among PWH who are at higher risk for these outcomes.³⁹

To address the dearth of knowledge in this area, we examined patterns of VN and CC use among PWH engaged in care in the United States and evaluated associations with demographic characteristics as well as symptoms of depression and panic. To our knowledge, this study is the first to provide a quantitative description of patterns of use of VNs among a large cohort of PWH.

METHODS

Study Setting and Participants

The Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) is a dynamic cohort of PWH aged 18 years and older in care at 8 US academic clinical sites.⁴⁰ PWH at 7 sites who collect data on EC use from September 2017 through July 2021 were included in this study. The CNICS collects and integrates comprehensive clinical data from electronic health records and other sources including laboratory values, diagnoses, medications, and demographic information. PWH also complete a clinical assessment of patient-reported outcomes (PROs) and measures before routine clinic visits, which include measures of substance use (eg, tobacco smoking; VN use, including EC and other alternative nicotine delivery system; and alcohol/drug use), mental health symptoms, and other domains.^{41,42} For PWH who had completed the clinical PRO assessment multiple times, we used data from the most recent assessment. All PWH in the CNICS provided informed consent before cohort entry, and institutional review boards approved CNICS protocols at each site.

Demographics

Demographic characteristics included age, gender (including transgender PWH), race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, or others), and HIV transmission risk factor [men who have sex with

men, heterosexual contact, injection drug use (IDU), or others].

Substance Use

Vaporized nicotine (VN) use was measured in the clinical PRO assessment and dichotomized as never vs. ever use. The frequency of VN use over the past year was also assessed. Response options included never, once or a few times in the past year, once or a few times a month, once or a few times a week, and every day or almost every day. We created a continuous variable from the categorical response options to measure VN use per 30 days, as we have done in previous studies.⁴³ The transformation used 0 for a response of “Never in the past 12 months,” 0.5 for “Once or a few times in the past 12 months,” 1 for “Once or a few times a month,” 4 for “Once or a few times a week,” and 30 for “Every day or almost every day.” CC smoking was measured as never, former, or current use. The Alcohol Use Disorders Identification Test Consumption (AUDIT-C) scale in combination with clinical and self-reported information was used to measure alcohol consumption as no current use, no current use with a prior alcohol use disorder (AUD), current non-hazardous use, and current hazardous use.^{44–46} A prior AUD among those not currently drinking was identified by having had an AUD diagnosis in medical records or self-report of attending alcohol treatment. Hazardous alcohol use was defined by an AUDIT-C score of ≥ 4 for women or ≥ 5 for men.^{45,46}

Depression and Panic Measurements

We also measured self-reported depression and panic symptoms. Depression symptoms were reported using the 9-item Patient Health Questionnaire and dichotomized with a score of ≥ 10 , indicating moderate to severe depression referred to from herein as depression.⁴⁷ Panic symptomology was measured by a 5-item instrument Patient Health Questionnaire that is scored into a 3-level variable that indicates no panic symptoms, some symptoms, or panic disorder.

Statistical Analysis

We evaluated cross-sectional associations between VN use and demographic characteristics, CC smoking, and depression and panic symptoms. First, we use relative risk (RR) regression with a Poisson distribution and robust standard errors to estimate associations between dichotomized VN use (never vs. ever) with demographic characteristics, including age, gender, race/ethnicity, and HIV transmission risk factor. To rule out the possibility that these potentially confounding variables were functioning as mediators, we then separately added the CC and mental health variables into the initial demographic model. We conducted a sensitivity analysis for the model including CC use additionally adjusting for alcohol use. We also used RR regression to estimate associations between current CC use and depression and panic symptoms.

To further characterize VN use among PWH, we excluded anyone reporting never using VN and used linear regression to

model the frequency of VN use per 30 days in a similar manner to the RR regression models. First, we modeled only the demographic characteristics. Then, we separately added CC use and depression/panic symptoms to the linear regression model. Again, we conducted a sensitivity analysis adding an adjustment for alcohol use to the CC model. We also conducted a sensitivity analysis using the original ordinal categories (ie, not transformed into continuous days per month measure) using ordered logistic regression. Analyses were performed using Stata version 16.1 (StataCorp, College Station, TX).

RESULTS

Among 7431 PWH, most (6,619, 89%) reported never using VN products in the past year (Table 1). Daily use was reported among only 4% of the cohort, which was 33% of PWH reporting ever-using VN. Compared with PWH reporting not using, those who used VN were younger and more likely to identify as male, White, and report IDU as their primary HIV transmission risk factor (Table 1). Compared with PWH reporting no VN use, a greater proportion of those reporting VN use also reported depression and panic symptoms, although there were minor differences in mental health symptoms between different frequencies of VN use (Table 1). Depression was common among PWH currently using VN (27%) and CC (22%), as was panic disorder (21% for VN and 16% for CC).

In RR regression models, ever-using VN was associated with younger age [RR: 0.59 per 10 years older, 95% confidence interval (95% CI): 0.56 to 0.62] and HIV transmission risk factor of IDU (RR: 2.03, 95% CI: 1.72 to 2.40) compared with men who have sex with men (Table 2, model 1). In addition, PWH who reported ever-using CC were much more likely to ever use VN: 4.9 times greater among PWH reporting former CC use (RR: 4.89, 95% CI: 3.90 to 6.12) and 7.1 times greater among PWH reporting current CC use (RR: 7.11, 95% CI: 5.70 to 8.86) (Table 2, model 2). We observed similar associations in sensitivity analyses adjusting for alcohol use (Table 5). Mental health symptomatology was also associated with a greater likelihood of reporting VN use. PWH with depression were 1.2 times more likely to have used VN (RR: 1.20, 95% CI: 1.02 to 1.42) (Table 2, model 3). Compared with PWH without any panic symptoms, PWH reporting some symptoms or panic disorder were 1.4 (RR: 1.38, 95% CI: 1.15 to 1.65) and 1.7 (RR: 1.71, 95% CI: 1.43 to 2.05) times more likely to use VN, respectively (Table 2, model 3). Similarly, in models with CC instead of VN, PWH reporting current CC use were more likely to report depressive (RR: 1.25, 95% CI: 1.13 to 1.38) and panic symptomatology (some symptoms: RR: 1.22, 95% CI: 1.09 to 1.37; panic disorder: RR: 1.39, 95% CI: 1.24 to 2.57) (Table 3, model 4).

In linear regression models evaluating the association between demographic characteristics and the frequency of VN use (excluding PWH reporting never using VN), we observed similar patterns to the RR regression models. For

TABLE 1. Demographic and Mental Health Characteristics of PWH From 7 Sites Across the United States by Vaporized Nicotine Use Frequency

Variable	Overall	Never	Ever	Once or a Few Times	Once or a Few Times a Month	Once or a Few Times a Week	Every Day or Almost Every Day
n (%)	7431	6619 (89)	812 (11)	292 (4)	114 (2)	142 (2)	264 (4)
Age*	49 (12)	50 (12)	42 (11)	42 (11)	42 (12)	42 (11)	41 (11)
Female identifying	18%	19%	13%	12%	20%	13%	11%
Race/ethnicity							
White	44%	43%	54%	57%	49%	44%	59%
Black	38%	40%	27%	25%	36%	35%	22%
Hispanic	13%	13%	11%	11%	12%	13%	10%
Others	5%	5%	7%	8%	3%	8%	9%
HIV transmission risk factor							
MSM	63%	63%	65%	67%	57%	65%	65%
Heterosexual	24%	25%	14%	14%	16%	13%	13%
IDU	9%	8%	17%	16%	22%	16%	17%
Others	4%	4%	4%	2%	5%	6%	5%
Depression (PHQ-9 ≥ 10)	16%	15%	26%	30%	29%	27%	21%
Panic symptomatology							
No symptoms	76%	78%	61%	58%	60%	60%	64%
Some symptoms	12%	11%	18%	20%	13%	22%	16%
Panic disorder	10%	9%	21%	22%	27%	18%	20%
CC use							
Never	44%	48%	11%	14%	11%	11%	7%
Former	30%	29%	38%	25%	24%	33%	59%
Current	26%	23%	51%	60%	65%	55%	33%

Data are presented as percentage, unless otherwise noted.

*Data are presented as mean (SD).

MSM, men who have sex with men; PHQ-9, 9-item Patient Health Questionnaire.

TABLE 2. RR Regression Models of Associations Between Demographic Characteristics, CC Use, and Mental Health With Vaporized Nicotine Use (Never vs. Any Frequency of Use) Among PWH From 7 Sites Across the United States

Variable	RR (95% CI)
Age (per decade)	0.59 (0.56 to 0.62)
Female identifying	0.97 (0.76 to 1.24)
Race/ethnicity (White ref)	
Black	0.52 (0.45 to 0.61)
Hispanic	0.60 (0.49 to 0.74)
Others	0.93 (0.73 to 1.19)
HIV transmission risk factor (MSM ref)	
Heterosexual	0.80 (0.62 to 1.04)
IDU	2.03 (1.72 to 2.40)
Others	0.99 (0.73 to 1.35)
CC use (never ref)	
Former	4.89 (3.90 to 6.12)
Current	7.11 (5.70 to 8.86)
Depression	1.20 (1.02 to 1.42)
Panic symptoms (none ref)	
Some symptoms	1.38 (1.15 to 1.65)
Panic disorder	1.71 (1.43 to 2.05)

Adjusted for age, gender, race/ethnicity, and HIV transmission risk factor.
MSM, men who have sex with men; VN, Vaporized nicotine.

example, older PWH and Black PWH (compared with White) vaped fewer days per month (Table 4, model 5). We observed that PWH with former CC use reported VN use on average 8.5 days per month (95% CI: 5.5 to 11.5 days) more than PWH reporting never CC use, whereas PWH with current CC use reported the same frequency of VN use as those reporting never using CC (Table 4, model 6). We conducted an additional analysis using this model, with PWH reporting current CC use as the referent group to estimate the difference in VN use frequency between current and former CC use. Former CC use was associated with 8.6 more days of VN use per month (95% CI: 6.6 to 10.5 days) compared with current use. Sensitivity analyses adding in an adjustment for alcohol use had similar results (Table 5). We also did not observe a difference in the frequency of VN use among PWH with panic symptoms (Table 4, model 7). However, PWH reporting depression used VN about 2 fewer days per month (95% CI: -4.5 to -0.1 days) compared with PWH without

TABLE 3. RR Regression Models of Associations Between Demographic Characteristics and Mental Health With Current CC Use Among PWH From 7 Sites Across the United States

Variable	RR (95% CI)
Depression	1.25 (1.13 to 1.38)
Panic symptoms (none ref)	
Some symptoms	1.22 (1.09 to 1.37)
Panic disorder	1.39 (1.24 to 2.57)

Adjusted for age, gender, race/ethnicity, and HIV transmission risk factor.
VN, Vaporized nicotine.

TABLE 4. Linear Regression Models of Associations Between Demographic Characteristics, CC Smoking, and Mental Health With Vaporized Nicotine Use Frequency Among PWH From 7 Sites Across the United States Excluding Those With No Use

Variable	Days Per Month (95% CI)
Model 5, n = 812	
Age (per decade)	-0.92 (-1.77 to -0.06)
Female	-1.46 (-4.62 to 1.71)
Race/ethnicity (White ref)	
Black	-3.06 (-5.27 to -0.85)
Hispanic	-1.90 (-4.92 to 1.12)
Others	1.02 (-2.86 to 4.91)
HIV transmission risk factor (MSM ref)	
Heterosexual	1.16 (-2.14 to 4.47)
IDU	0.17 (-2.43 to 2.76)
Others	2.15 (-2.57 to 6.87)
CC use (never ref)	
Former	8.52 (5.50 to 11.54)
Current†	-0.31 (-2.85 to 2.79)
Depression	-2.28 (-4.49 to -0.07)
Panic symptoms (none ref)	
Some symptoms	-0.85 (-3.39 to 1.69)
Panic disorder	-0.52 (-3.04 to 2.00)

Adjusted for age, gender, race/ethnicity, and HIV transmission risk factor.
†Wald test of former smoking = current smoking, $P < 0.001$.

MSM, men who have sex with men; VN, Vaporized nicotine.

depression (Table 4, model 7). Finally, sensitivity analysis through ordered logistic regression yielded qualitatively consistent results with the linear regression models, for example, compared with reporting never using CC, former CC use was associated with a greater frequency of VN use, but current smoking was not (data not shown, results consistent with Table 4, model 6).

DISCUSSION

This study offers valuable insights into the currently understudied topic of patterns of VN use among PWH. The majority of our cohort (89%) reported never using VN in the

TABLE 5. Sensitivity Analyses Including Adjustment for Alcohol Use in Vaporized Nicotine and CC Smoking Models Among PWH From 7 Sites Across the United States

Variable	Effect Estimate
Model 2 with alcohol use adjustment, n = 7021*	RR (95% CI)
CC use (never ref)	
Former	4.67 (3.70 to 5.88)
Current	6.81 (5.43 to 8.53)
Model 6 with alcohol use adjustment, n = 808*	Days per month (95% CI)
CC use (never ref)	
Former	8.48 (5.46 to 11.50)
Current	-0.26 (-3.11 to 2.59)

Additionally adjusted for age, gender, race/ethnicity, and HIV transmission risk factor.

past year, with only 4% reporting daily use. Consistent with prior literature among PWH using VN, we observed high rates (51%) of concurrent use of VN and CC. We found that PWH reporting former CC use reported over a week per month more VN use compared with PWH reporting either never or current CC use. These findings are potentially suggestive of people with former CC use intentionally switching to VN as a harm reduction measure. We also observed associations between greater VN use and younger age and White race. The association with IDU as an HIV risk factor warrants further investigation into the relationship between the use of VN and other illicit drugs. Notably, our findings that depression and panic symptoms were associated with a greater prevalence of VN use (although not more frequent use) suggest an important relationship between mental health and nicotine use among PWH.

We found several relationships between the use of CC and VN among PWH. Ever-using CC was associated with a greater likelihood of ever-using VN; this is not surprising given nicotine as the common chemical dependency and the overlap in targeted marketing. Interestingly, those reporting former CC use reported a greater frequency (days/month) of VN use compared with PWH reporting current CC use. The possibility of a substitution effect, whether intentional or not, is an important point. Although our study design did not allow clarification of causality or intent, this finding is consistent with marketing and clinical messaging, endorsing VN as a smoking cessation tool. Furthermore, among PWH who have used VN, most (89%) reported either currently or formerly smoking tobacco cigarettes. This is consistent with studies in the general population showing fairly similar levels of use and acceptability.⁴⁸ The findings presented here may suggest that patterns of VN use among PWH may be affected by the widely held notion of VN as a substitute for cessation aid for CC use, irrespective of evidence.^{49,50}

Although several systematic reviews have found variable evidence supporting the efficacy of VN as a cessation tool for CC use,^{7,8} a recently updated Cochrane review determined a moderate certainty evidence that quit rates were higher in people randomized to VNs compared with nicotine replacement therapy.⁵¹ One study in the general population found that 10.8% of people intentionally substituting VN to reduce CC use without intent to quit ended up completely replacing their CC use with VN use.⁵² Another study, among adults in their 30s who smoked CCs, found that higher vaping frequency relative to CC frequency (presumed indicative of intent to reduce CC use) was associated with more exercise and better physical health.⁵³ There are limited studies regarding substitution among PWH, although 1 study found that transition to VN use among PWH who were not ready to quit CCs was associated with decreased cigarettes per day and increased motivation to quit, with 36.8% of the participants transitioning completely from CCs to VN use.⁵⁴ It is possible that VN substitution may be a proxy correlated with rather than causing overall healthier behaviors. Additional longitudinal studies with greater follow-up time are needed to further elucidate the interplay between co-occurring use, substitution, and health behaviors.

PWH experiencing moderate to severe depression were more likely to use VN. However, current VN users with

depression reported fewer days of VN use per month than current VN users without depression. These findings, coupled with the finding of a greater prevalence of current CC use among people with depression (Table 3), suggest that PWH may use nicotine during times of greater depressive symptoms, and we recommend further investigation of directionality through longitudinal studies. One possibility is that people are reaching for nicotine products in general during these periods but prefer more familiar CCs, as suggested by our recent qualitative research, which found themes of attempting to substitute VN for CC use hampered by failure to replicate the comforting ritual experience of CC use as well as elusive satiety with VN.⁵⁰ This hypothesis of reduced substitution or any possible causative role for VN or CC in triggering or exacerbating depression and anxiety will also require longitudinal investigation. An additional consideration is the perceived or intended effects of nicotine use for symptom management or self-soothing in the context of mental illness, consistent with our prior qualitative work.⁵⁰

Strengths of this study include our large geographically and demographically diverse cohort of PWH engaged in care in the United States. A significant strength is that this is the first description, to our knowledge, of patterns of VN use among a large clinical cohort of PWH and the first quantitative description of the relationship between current and former VN and CC use. Finally, this is the first description of the association between VN use and depression/panic symptoms among PWH.

Limitations of this study include its cross-sectional nature, which does not allow a temporal description of people's changes in status and frequency of VN use over time. However, the association with younger age raises the possibility for increasing the prevalence of use, as more younger patients embrace these delivery methods. By conducting this study in the CNICS that includes PWH older than 18 years in routine clinical care without the many selection criteria of many interval cohorts or trials, we enhance generalizability. However, because of the nature of the CNICS, we are limited by definition to PWH in clinical care and thus do not necessarily generalize to PWH who do not yet know they have HIV or who are not engaged in care. In addition, we are limited by the patient-reported nature of our exposures. Undisclosed nicotine use would result in selection bias through inappropriately categorized participants; however, the use of self-administration through tablet has been shown to greatly reduce social desirability bias and increase the likelihood of accurate reporting of sensitive or potentially stigmatizing information.⁵⁵ The structure of our PROs did not allow a precise determination of days of use or amount of nicotine used, although our shift from categorical to continuous frequency of use is sufficiently robust to infer dose—response and is consistent with results considering the variable with an ordinal parameterization. In addition, although we assessed PWH by gender (and included transgender PWH), this analytic cohort lacked power to further differentiate analyses by transgender status.

The findings described above provide a strong impetus for future studies to further clarify patterns and impact of VN

use among PWH. Specifically, future longitudinal studies would clarify temporal relationships between current and former use of VN and CCs, helping elucidate the extent to whether VN use is used as substitution toward the goal of CC cessation or simply used concurrently with CCs. In addition, a study over a longer period would enable assessment of long-term or more rare clinical outcomes of VN use such as obstructive lung disease, atherosclerotic disease (myocardial infarction, stroke, and cognitive decline), and e-cigarette or vaping use-associated lung injury. Finally, future longitudinal studies could facilitate a step toward mechanistic understanding of the complex relationship between VN/CC use and dynamic changes in mental health symptomatology.

CONCLUSIONS

Among PWH, those using VN are more often young, White, and having IDU as an HIV risk factor. Former or current use of CC was associated with having used VN, and former use of CC was associated with the greatest frequency of current VN use. Finally, PWH experiencing depression, panic symptoms, or panic disorder were more likely to report current VN (and CC) use. Together, these findings provide insights into patterns of VN use among PWH and highlight the interplay between depression, panic symptoms, and VN use, warranting further research to confirm and investigate mechanisms.

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