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Short Communication

Electronic cigarette use and risk of COVID-19 among young adults without a history of cigarette smoking

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ABSTRACT

It is unknown whether use of e-cigarettes increases susceptibility to COVID-19. In a large clinical sample of young adults, we evaluated whether current or ever e-cigarette use was associated with polymerase chain reaction (PCR)-confirmed COVID-19. To address the confounding of combustible smoking, the sample was restricted to never smokers. This retrospective cohort study analyzed data from the electronic health records of 74,853 young adults (aged 18–35 years), without a history of cigarette smoking, who were screened for e-cigarette use (current, former, never) in the Kaiser Permanente Northern California (KPNC) healthcare system from 3/5/2020 (baseline) to 11/30/2020 (pre-vaccine). COVID-19 risk was estimated in time-to-event analyses using multivariable Cox proportional hazard regression models, adjusted for socio-demographics and medical comorbidities. E-cigarette status in the cohort was: 1.6% current, 1.2% former, and 97.2% never. During follow-up, 1965 (2.6%) patients acquired COVID-19. We did not find evidence that current (vs never) e-cigarette use was associated with risk of COVID-19 (aHR = 1.12 95%CI:0.77–1.62). However, we did find suggestive evidence that former (versus never) e-cigarette use may be associated with greater risk of COVID-19 (aHR = 1.39 95%CI:0.98–1.96). While e-cigarette use is associated with health risks for young adults, results from this study suggest that current use of e-cigarettes may not increase susceptibility for COVID-19 among young adults who have never smoked cigarettes.

1. Introduction

Electronic cigarette (e-cigarette) use is associated with respiratory conditions (Xie et al., 2020) and may increase susceptibility to COVID-19 through compromised lung function (Volkow, 2020). Additionally, e-cigarette use could increase COVID-19 risk due to greater contact between the fingers and mouth, removal of one's mask while vaping, or sharing of vape devices with others. Conversely, nicotine could lower risk of COVID-19 through its anti-inflammatory properties or via interactions between COVID-19 and nicotinic acetylcholine receptors (Boutou et al., 2020; Garufi et al., 2020; Lutchman, 2020; Tindle et al., 2020; Usman et al., 2021). To date, four studies have found no association between e-cigarette use and COVID-19 risk among adults (Burnett-Hartman et al., 2022; Jose et al., 2021; Kale et al., 2021; Tattan-Birch et al., 2021), while a fifth reported greater risk associated with ever (but not current) e-cigarette use among adolescents (Gaiha et al., 2020). Two studies have found no association between e-cigarette use and COVID-19

severity (Burnett-Hartman et al., 2022; Gao et al., 2022). Notably, people who vape also may smoke cigarettes, currently or formerly, and may have smoking-related comorbidities (Prakash et al., 2021), making it challenging to identify the independent risk of e-cigarettes.

To inform the literature, we examined the risk of polymerase chain reaction (PCR)-confirmed COVID-19 diagnosis associated with e-cigarette use in a population-based retrospective cohort study. Patient data were from a large healthcare system, and analyses were restricted to young adults (aged 18–35) without a history of cigarette smoking, who had e-cigarette status documented. Understanding whether e-cigarette use is independently associated with COVID-19 susceptibility among young adults is important for guiding public health messaging and prevention guidelines.

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2. Methods

2.1. Setting and population

Data were drawn from Kaiser Permanente Northern California (KPNC), a nonprofit, integrated healthcare delivery system providing comprehensive health services to >4 million racially and socio-demographically diverse members representative of Northern California (Gordon, 2006; Han et al., 2018). We performed a retrospective cohort study of KPNC patients from 3/5/2020 (the day after California declared a state emergency) (Eby, 2022) to 11/30/2020 (when COVID-19 vaccines were introduced). Eligible patients were those without a history of cigarette smoking (based on routine screening for current, former, and never-smoking status by medical assistants during primary care visits while taking vital signs), aged 18–35 years (due to their higher prevalence of e-cigarette use and lower likelihood of cigarette smoking related comorbidities) (Cornelius et al., 2020; Henley et al., 2016), with continuous KPNC health plan enrollment in the prior year, ≥1 in-person outpatient or inpatient non-emergency visit (providing the opportunity to get screened for smoking and e-cigarette status) from 05/18/2019 (when e-cigarette documentation in KPNC began) to 3/5/2020. The KPNC IRB approved the project with a waiver of informed consent.

2.2. Measures

The primary outcome was COVID-19 infection determined by a positive PCR test (Supplement). The test positivity rate was defined as number of positive PCR-tests/number of PCR-tests performed.

E-cigarette use was assessed by medical assistants during a primary care visit while taking the patient's vital signs using the question: "Do you currently use e-cigarettes or vape, even sometimes?" Patients who did not endorse current e-cigarette use were asked an additional question about whether they had ever used e-cigarettes or vaped. Responses were charted in patients' electronic health record (EHR) as: never, former, or current. We obtained the most recent charted status during the 10 months before study start.

Covariates included age, sex, race/ethnicity, any enrollment in a Medicaid insurance plan in the prior year, medical service area, neighborhood deprivation index (NDI) (Messer et al., 2006), body mass index (BMI), and medical comorbidities associated with COVID-19 severity among young adults (Sandoval et al., 2021) (Supplement) documented during the two years before study start.

2.3. Analysis

We summarized patient characteristics and calculated unadjusted COVID-19 incidence rates (per 1000 person-years) and 95% confidence intervals (CIs) by e-cigarette status. Unadjusted and multivariable Cox proportional hazards regression analyses examined the association between e-cigarette status and risk of COVID-19. We used time-to-event modeling rather than logistic regression modeling to allow for censoring and to allow estimation of risk over time while accounting for changes in risk during the first year of the pandemic. Patients were followed until outcome occurrence, with censoring on death, health plan disenrollment, or study end (11/30/2020). Models were fit in steps. Model 1 (minimally-adjusted model) included age, sex, race/ethnicity, medical service area, Medicaid status and NDI quartiles. Model 2 (fully-adjusted) added BMI, cardiovascular conditions and diabetes. Model 3 (extended) further included respiratory conditions that could be mediators rather than confounders, and results represent effects not dependent on potential casual pathways. Analyses were conducted using SAS software, v9.4. Statistical significance was assessed at two-sided $p <$ 0.05.

3. Results

Of the $N = 470,250$ KPNC patients meeting inclusion criteria, we excluded individuals not screened for e-cigarette status ($n = 395,114$; 84%), and those missing sex ($n = 2$; 0.0%), NDI ($n = 112$; 0.0%), and service area ($n = 169$; 0.0%) for a final sample of 74,853. Those screened vs. not screened did not differ on socio-demographics, except women (21%) were more likely to be screened than men (7%; $p < 0.001$). E-cigarette use status was: 1.6% current, 1.2% former, and 97.2% never (Table 1). Compared to never e-cigarette use, current and former use were associated with being male, non-Hispanic White, and not obese.

Table 1

Baseline characteristics of KPNC patients, overall and by e-cigarette use status.

Characteristics	All patients	E-cigarette status		
		Never	Current	Former
	($N = 74,853$)	($N = 72,728$) (97.2%)	($N = 1233$) (1.6%)	($N = 892$) (1.2%)
Age, years				
Mean (SD)	27.6 (4.8)	27.7 (4.8)	24.0 (4.6)	24.9 (4.6)
Sex, n (%)				
Female	62,347 (83.3)	61,070 (84.0)	674 (54.7)	603 (67.6)
Male	12,506 (16.7)	11,658 (16.0)	559 (45.3)	289 (32.4)
Race/ethnicity, n (%)				
Non-Hispanic White	26,970 (36.0)	26,025 (35.8)	581 (47.1)	364 (40.8)
Hispanic	20,680 (27.6)	20,157 (27.7)	261 (21.2)	262 (29.4)
Asian/Pacific Islander	17,181 (23.0)	16,769 (23.1)	250 (20.3)	162 (18.2)
Non-Hispanic Black	5672 (7.6)	5567 (7.7)	50 (4.1)	55 (6.2)
Other/unknown	4350 (5.8)	4210 (5.8)	91 (7.4)	49 (5.5)
Medicaid insurance, n (%)	7864 (10.5)	7676 (10.6)	92 (7.5)	96 (10.8)
NDI 2018 quartiles, n (%)				
Quartile 1 (least deprived)	18,752 (25.1)	18,137 (24.9)	380 (30.8)	235 (26.3)
Quartile 2	18,662 (24.9)	18,098 (24.9)	330 (26.8)	234 (26.2)
Quartile 3	18,700 (25.0)	18,191 (25.0)	297 (24.1)	212 (23.8)
Quartile 4 (most deprived)	18,739 (25.0)	18,302 (25.2)	226 (18.3)	211 (23.7)
BMI category, n (%)				
Underweight (<18.5 kg/m^2)	1589 (2.1)	1504 (2.1)	51 (4.1)	34 (3.8)
Normal (18.5–24.9 kg/m^2)	28,915 (38.6)	27,972 (38.5)	575 (46.6)	368 (41.3)
Overweight (25.0–29.9 kg/m^2)	21,802 (29.1)	21,245 (29.2)	311 (25.2)	246 (27.6)
Obese (≥30.0 kg/m^2)	21,510 (28.7)	21,050 (28.9)	233 (18.9)	227 (25.4)
Missing	1037 (1.4)	957 (1.3)	63 (5.1)	17 (1.9)
Any cardiovascular condition, n (%)[a]	3275 (4.4)	3186 (4.4)	47 (3.8)	42 (4.7)
Diabetes, n (%)	1274 (1.7)	1249 (1.7)	12 (1.0)	13 (1.5)
Any respiratory condition, n (%)[b]	15,155 (20.2)	14,664 (20.2)	274 (22.2)	217 (24.3)

Abbreviations: BMI, body mass index; NDI, Neighborhood Deprivation Index; SD, standard deviation.

Note: Percentages may not add to 100 due to rounding.

[a] Any cardiovascular conditions include atherosclerotic cardiovascular disease, cardiac dysrhythmias, heart failure, and hypertension.

[b] Any respiratory condition includes obstructive lung disease, lung cancer, and other lung diseases.

Those with current (versus never and former) use tended to live in less deprived neighborhoods. Membership was stable, with only 6478 (8.7%) patients censored for disenrollment.

The percentage of patients tested for COVID-19 differed minimally by e-cigarette status (current: 30.0%; former: 35.1%, never: 29.4%). However, the test positivity rate was higher for former (8.1%) versus current (5.8%) and never (6.6%) use.

Current (versus never) e-cigarette use was associated with a lower incidence of COVID-19 (33.43/1000 person-years; Table 2). There were no differences in infection comparing current to never e-cigarette use in unadjusted (hazard ratio [HR] = 0.90; 95%CI:0.63–1.30), fully-adjusted (aHR = 1.12; 95%CI:0.77–1.62) or extended models (aHR = 1.11; 95% CI:0.77–1.61).

Former (versus never) e-cigarette use was associated with a higher COVID-19 incidence (51.07/1000 person-years). Results were suggestive of modestly higher COVID-19 rates associated with former versus never e-cigarette use in unadjusted (HR = 1.38; 95%CI:0.98–1.96; Table 2), fully-adjusted (aHR = 1.39; 95%CI:0.99–1.96) and extended models (aHR = 1.39; 95%CI:0.98–1.97).

4. Discussion

Among young adults without a history of cigarette smoking, current versus never e-cigarette use was not significantly associated with elevated COVID-19 risk. The percentage of patients tested for COVID-19 was similar across e-cigarette status, suggesting that findings are unlikely to be due to testing differences. Results are consistent with studies finding no association between current e-cigarette use and COVID-19 among adults (Jose et al., 2021; Kale et al., 2021; Tattan-Birch et al., 2021), or among adolescents who did not smoke cigarettes (Gaiha et al., 2020). Characteristics of e-cigarette use (e.g., duration, heaviness, frequency, product type) may differ among those who have never used combustible cigarettes, and studies are needed to examine how patterns of use relate to COVID-19.

Results suggesting possible greater risk of COVID-19 associated with former (versus never) e-cigarette use are somewhat similar to findings of increased risk of self-reported COVID-19 associated with ever e-cigarette use among adolescents without a history of cigarette use (Gaiha et al.,

2020). While there is no clear mechanism for this finding, young adults with a history of versus current e-cigarette use may differ on other unmeasured factors that may impact COVID-19 risk (e.g., years of e-cigarette use, children in the home, protective behaviors such as hand washing or social distancing). Our sample of patients with a history of (versus current or never) e-cigarette use was small (*n* = 892), and meta-analyses with greater statistical power are needed to further examine this question.

Study strengths include data from a large, closed healthcare system with PCR COVID-19 testing, evaluations of associations with COVID-19 independent of cigarette smoking, and adjustment for sociodemographic and medical covariates. Our study design allows estimation of risk over time while accounting for changes in risk during the first year of the pandemic.

4.1. Limitations

The study had several limitations. EHR-based screening for e-cigarette use was new and not universal. The study's prevalence of current e-cigarette use was slightly lower than in the US population of young adult never-smokers (1.6% versus 2.0%) (Prakash et al., 2021), and results may not generalize to other healthcare settings. In addition, e-cigarette use frequency, heaviness, and duration were not captured. COVID-19 test results were limited to tests recorded by KPNC (home tests were not yet available), and patients with minor or no symptoms may not have been tested. Our data are limited to the first 9 months of the pandemic and results may not generalize to later periods as the predominant variants shifted. Finally, studies are needed to determine whether other factors (e.g., essential worker status, asymptomatic testing, social distancing) vary with e-cigarette status.

5. Conclusions

While e-cigarette use is associated with health risks for young adults, current use of e-cigarettes was not associated with acquiring COVID-19 during the first year of the pandemic. Future research is needed to replicate these findings.

Data sharing

The data underlying this article cannot be shared publicly as we do not have permission from patients to share their data outside of the Kaiser Permanente Northern California healthcare system.

CRediT authorship contribution statement

Kelly C. Young-Wolff: Conceptualization, Methodology, Writing – original draft. **Natalie E. Slama:** Methodology, Formal analysis, Writing – original draft. **Stacey E. Alexeeff:** Supervision, Methodology, Writing – review & editing. **Judith J. Prochaska:** Methodology, Writing – review & editing. **Renee Fogelberg:** Methodology, Writing – review & editing. **Lori C. Sakoda:** Conceptualization, Methodology, Writing – review & editing.

Table 2

Cox proportional hazard regression results for risk of COVID-19 among KPNC patients aged ≤35 who have never smoked cigarettes, by e-cigarette status (N = 74,853).

E-cigarette status	Never	Current	Former
N (row %)	72,728 (97.2%)	1233 (1.6%)	892 (1.2%)
COVID-19			
N events (row %)	1904 (96.9%)	29 (1.5%)	32 (1.6%)
Incidence rate* (95% CI)	37.05 (37.00, 37.10)	33.43 (33.05, 33.82)	51.07 (50.51, 51.63)
Unadjusted, HR (95% CI)	1.00 (ref)	0.90 (0.63, 1.30)	1.38 (0.98, 1.96)
Model 1, aHR (95% CI)	1.00 (ref)	1.09 (0.75, 1.58)	1.39 (0.98, 1.97)
Model 2, aHR (95% CI)	1.00 (ref)	1.12 (0.77, 1.62)	1.39 (0.98, 1.96)
Model 3, aHR (95% CI)	1.00 (ref)	1.11 (0.77, 1.61)	1.39 (0.98, 1.97)

Notes: aHR = adjusted hazard ratio. BMI = body mass index. CI = confidence interval. HR = hazard ratio. NDI = neighborhood deprivation index. Missing BMI (*n* = 1037, 1.4%) was included as a category in all analyses.
Model 1 (minimally-adjusted): age, sex, race, medical service area, Medicaid, NDI.
Model 2 (fully-adjusted): age, sex, race, medical service area, Medicaid, NDI, BMI, any cardiovascular disease, diabetes.
Model 3 (extended model): age, sex, race, medical service area, Medicaid, NDI, BMI, any cardiovascular disease, diabetes, any respiratory condition.
 * Incidence rate per 1000 person-years.

Declaration of Competing Interest

Judith J. Prochaska, PhD, MPH, has provided consultation to pharmaceutical and technology companies that make medications and other treatments for quitting smoking and has served as an expert witness in lawsuits against the tobacco companies. All other authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2022.107151.

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