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ORIGINAL RESEARCH

Dual Use of Electronic Cigarettes and Cigarettes Elevates Risk of Chronic Obstructive Pulmonary Disease and Mental Health Issues: Insights from a Korean Health Survey

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Purpose: Significant differences exist between the toxicity and adverse outcomes of conventional cigarettes and electronic cigarettes. However, spirometry-based clinical outcome analyses in the general population have not been widely studied. This study aimed to investigate the factors associated with electronic cigarette use among individuals with different smoking status and pulmonary function test results.

Patients and Methods: This study was conducted in Korea using data from the Korean National Health and Nutrition Examination Survey from 2013 to 2019. Participants who reported baseline clinical information, including smoking status, and underwent a pulmonary function test, were included.

Results: In total, 19,356 participants, including current smokers, former smokers, and participants who never smoked, participated in this study. Among the participants who smoked, 5.7% reported current electronic cigarette use, including dual users (who use conventional cigarettes and electronic cigarettes). Factors associated with e-cigarette use included male sex, younger age, higher education level, higher household income, and being current or former heavy smoker. Additionally, cigarette users had the highest prevalence of chronic obstructive pulmonary disease, followed by dual users and electronic cigarette-only users ($P < 0.001$). Furthermore, individuals with anxiety and depression were significantly more prevalent among dual users than among those who had never smoked ($P < 0.001$).

Conclusion: This study indicates an association between e-cigarette use and individual factors, including sex, age, education level, and income level. Electronic cigarette use, including dual use, is associated with chronic obstructive pulmonary disease. Additionally, anxiety and depression were highest among dual users, followed by those among conventional cigarette users.

Keywords: airflow obstruction, chronic obstructive pulmonary disease, depression, E-cigarette, anxiety

Introduction

Since electronic cigarettes (e-cigarettes) were introduced to the United States market in the late 2000s, there has been significant debate about the risks and advantages of these products compared to traditional combustible cigarettes. E-cigarettes, especially the newer pod-based and disposable varieties, contain elevated nicotine levels and youth-attracting flavors, which may contribute to nicotine dependence and elevate the risk of transitioning to combustible tobacco products among adolescents and young adults.[1–4] Additionally, there is increasing evidence of adverse short-term effects on the airways and blood vessels, while the long-term risks remain uncertain.[5,6]

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Recently, e-cigarettes have gained significant popularity as a substitute for conventional tobacco smoking. Tobacco companies have promoted them as safer alternatives and effective tools for quitting smoking. However, e-cigarettes are not as safe as claimed, particularly concerning the percentage of functional respiratory symptoms associated with e-cigarette product use.[7–9]

The aerosol produced by e-cigarettes contains various potentially harmful substances, including volatile organic compounds, heavy metals, and ultrafine particles.[10,11] Exposure to these toxic chemicals has been linked to an increased risk of developing lung diseases, including self-reported asthma or chronic obstructive pulmonary disease (COPD).[12,13] Evaluating the effects of e-cigarettes on the risk of COPD can be challenging owing to the difficulties associated with examining individuals who use e-cigarettes and conventional cigarettes concurrently.[14,15] Moreover, e-cigarettes are relatively new products, and long-term data on their health effects are scarce.[16] Comparing the association between e-cigarettes and COPD based on smoking status can present additional complexities, as most studies define COPD based on self-reported information or misclassification,[13,17,18] rather than relying on spirometry for accurate diagnosis.

This study aimed to investigate the factors associated with e-cigarette use among individuals with different smoking status and pulmonary function test (PFT) results.

Materials and Methods

Study Populations and Data Sources

This study was conducted in Korea using data from the 6th, 7th, and 8th Korean National Health and Nutrition Examination Survey (KNHANES) from 2013 to 2019. The KNHANES is an annual, population-based, cross-sectional health and nutritional survey conducted by the Division of Chronic Disease Surveillance under the Korean Centers for Disease Control and Prevention and the Korean Ministry of Health and Welfare. KNHANES utilizes a multistage, complex sampling method to ensure the representation of non-institutionalized South Koreans. The KNHANES dataset is openly accessible on the website of the Korea Centers for Disease Control and Prevention.[19]

The initial sample for this study comprised 55,327 participants who completed the health interview, behavior surveys, and examination surveys (2013–2015, N = 22,948, response rate 78.3%; 2016–2018, N = 24,269, response rate = 76.7%; 2019, N = 8110, response rate = 74.7).

Exclusion criteria for this study were no reporting of smoking status (N = 4353) and not having undergone a PFT (N = 27,884). In addition, individuals who did not report baseline characteristics regarding basic clinical information were also excluded (N = 3734). Finally, 19,356 participants were included in this study (Figure 1).

PFTs

PFTs were conducted using dry rolling seal spirometers (Model 2130; SensorMedics, Yorba Linda, CA, USA) from 2013 to 2015 and Vyntus Spiro (CareFusion, San Diego, CA, USA) from 2016 to 2019, with an acceptable measure considered valid when the difference between the largest and next largest forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) values were within 0.15 liters; however, only pre-bronchodilator test data were measured, as the KNHANES did not include post-bronchodilator test data. Additionally, spirometry tests were regularly calibrated and subjected to quality control following the guidelines established by the American Thoracic Society.[20] Lung function tests were administered to individuals aged ≥40 years, measuring the FEV1 to FVC ratio. A ratio of < 70% was indicative of COPD.

Classification of Smoking Status and Behaviors

We categorized individuals into five smoking categories based on their smoking behaviors. Participants who never smoked were defined as individuals who have either smoked < 100 cigarettes in their lifetime or have never engaged in smoking or using any tobacco products, including e-cigarettes, throughout their lives. Former smokers were defined as individuals who have smoked ≥100 cigarettes in their lifetime or have a past smoking history but had stopped using cigarettes or e-cigarettes for > 1 year. Cigarette smokers were defined as individuals who have smoked > 100 cigarettes in their lifetime and currently smoke every day or some days but have not used e-cigarettes within the past month. E-cigarette-only users were defined as individuals who have used e-cigarettes within the past month but currently do not

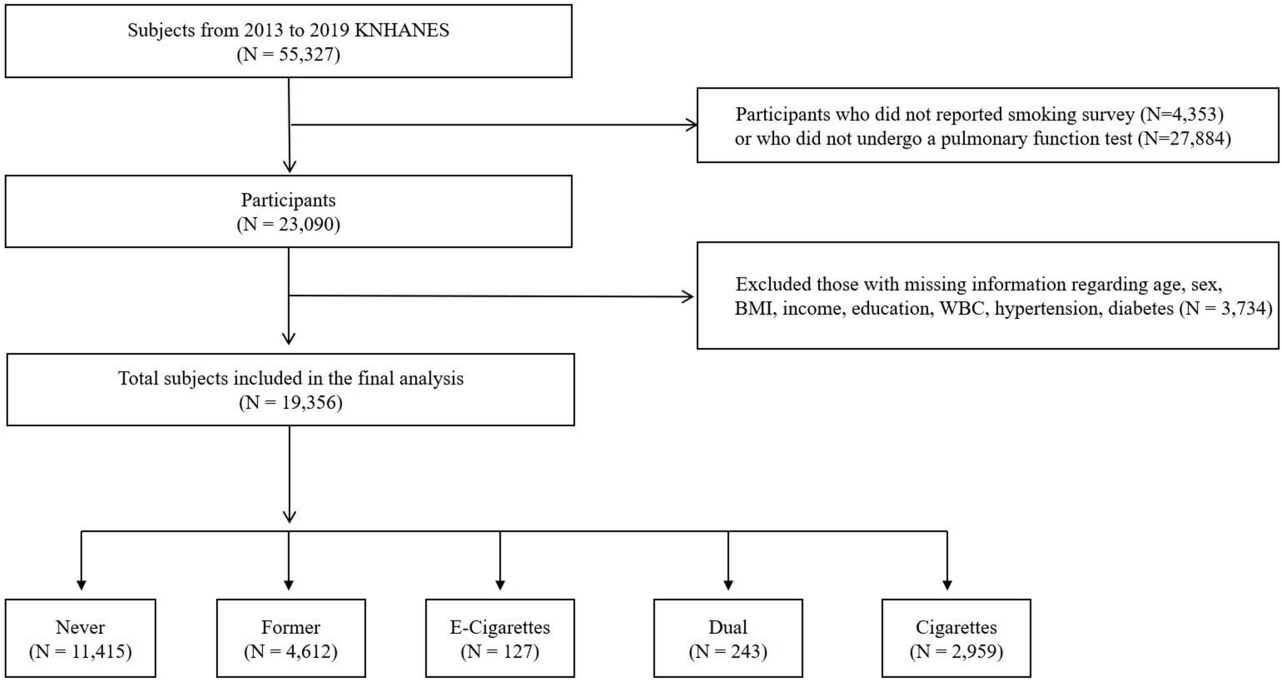

Figure 1 Flow diagram of the study participant selection process.
Abbreviations: BMI, body mass index; KNHANES, Korean National Health and Nutrition Examination Survey; WBC, white blood cell.

smoke cigarettes. Dual users were defined as individuals who had smoked > 100 cigarettes in their lifetime and had used an e-cigarette in the past month.

Statistical Analysis

All analyses were performed using R statistical software version 4.3.0 (The R Foundation for Statistical Computing, Vienna, Austria; https://www.R-project.org/). Continuous variables were compared across smoking groups using complex-sample general linear models (equivalent to ANOVA under complex sampling conditions), and categorical variables were analyzed using complex-sample chi-squared tests. Continuous variables are presented as means ± standard errors or medians with interquartile ranges, depending on their distributions. For comparisons of urinary cotinine and NNAL levels across the five smoking groups, the Kruskal–Wallis test was applied. When overall differences were statistically significant, post-hoc pairwise comparisons were performed using the Mann–Whitney *U*-test with Bonferroni correction for multiple testing. Complex-sample logistic regression analysis was conducted to examine the association between dual use and the prevalence of COPD and other smoking-related diseases. A two-tailed p-value < 0.05 was considered statistically significant.

Ethics Statement

The Institutional Review Board of Yonsei University Gangnam Severance Hospital approved this study (IRB No. 2023–0663-001) and waived the need for obtaining informed consent.

Results

Prevalence of e-Cigarette Use

Among the 50,974 participants who reported their smoking status, 6566 (12.88%) were identified as current smokers, defined as either cigarette-only smokers (n = 6250) or dual users of e-cigarettes and cigarettes (n = 316). A total of 1130 participants (2.22%) reported using e-cigarettes, comprising 814 exclusive e-cigarette users and 316 dual users. Compared with the overall study population, the analytic subgroup included in Table 1 (N = 19,356) had a significantly higher prevalence of current

Table 1 Baseline Characteristics in Korean Adults

Total (n = 19,356)	Never Smoker (n = 11,415)	Former Smoker (n = 4612)	E-cigarettes (n = 127)	Dual (n = 243)	Cigarette (n = 2959)	*P*-value
Age (years)	57.97 ± 10.83	59.5 ± 11.01	52.65 ± 10.32	50.46 ± 8.49	54.34 ± 9.85	< 0.001
Male sex	1509 (13.22)	4146 (89.9)	116 (91.34)	222 (91.36)	2554 (86.31)	< 0.001
BMI, kg/m^2	24.03 ± 3.17	24.53 ± 2.93	25.33 ± 3.4	24.73 ± 3.19	24.19 ± 3.24	< 0.001
WBC, $10^3/\mu L$	5.8 ± 1.57	6.18 ± 1.59	6.31 ± 1.51	7.32 ± 2.09	7.28 ± 1.98	< 0.001
Hypertension	3220 (28.21)	1601 (34.71)	29 (22.83)	54 (22.22)	7,88 (26.63)	< 0.001
Diabetes mellitus	1091 (9.56%)	677 (14.68%)	15 (11.81%)	27 (11.11%)	363 (12.27%)	< 0.001
FVC, % predicted	91.89 ± 11.6	88.87 ± 12.41	88.51 ± 10.67	90.07 ± 12.14	90.74 ± 12.1	< 0.001
FEV_1, % predicted	92.25 ± 12.69	88.43 ± 14.37	87.08 ± 12.46	86.24 ± 14.11	87.23 ± 13.33	< 0.001
Income						< 0.001
1st	2204 (19.31)	843 (18.28)	9 (7.09)	12 (4.94)	496 (16.76)	
2nd	2293 (20.09)	856 (18.56)	26 (20.47)	48 (19.75)	602 (20.34)	
3rd	2080 (18.22)	904 (19.6)	28 (22.05)	48 (19.75)	628 (21.22)	
4th	2215 (19.4)	938 (20.34)	36 (28.35)	66 (27.16)	644 (21.76)	
5th	2623 (22.98)	1071 (23.22)	28 (22.05)	69 (28.4)	589 (19.91)	
Education						< 0.001
1st	3279 (28.73)	897 (19.45)	6 (4.72)	17 (7)	505 (17.07)	
2nd	1546 (13.54)	687 (14.9)	14 (11.02)	26 (10.7)	405 (13.69)	
3rd	3609 (31.62)	1478 (32.05)	45 (35.43)	91 (37.45)	1163 (39.3)	
4th	2981 (26.11)	1550 (33.61)	62 (48.82)	109 (44.86)	886 (29.94)	

Notes: Data are presented as mean ± standard deviation or n (%). Income was categorized into five quintiles. Education level was classified into four groups: elementary school or lower, middle school, high school, and college or higher.
Abbreviations: FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; BMI, body mass index; WBC, white blood cell.

smokers (16.56% vs 12.88%; $p < 0.001$), as confirmed by a chi-squared test. Detailed baseline characteristics and differences among the five smoking groups are presented in Table 1.

Baseline Characteristics

In total, 19,356 participants (55.8% women) were included in this study's analysis, comprising current smokers (cigarette, e-cigarette, dual user), former smokers, and participants who never smoked. Table 1 presents the baseline characteristics of all participants in the analysis. The average age of participants was 57.7 years. Smoking history was gathered via a questionnaire and used as covariates for association analyses. Among the participants who smoked, 5.7% reported current use of e-cigarettes, including dual users. Smoking status was classified into five groups: participants who never smoked (N = 11,415, 59.0%), former smokers (N = 4612, 23.8%), current cigarette smokers (N = 2959, 15.3%), e-cigarette users (N = 127, 0.7%), and dual users (N = 243, 1.3%). The proportions of participants who never smoked, former smokers, and current smokers were 59.0%, 23.8%, and 17.2%, respectively. Compared with conventional cigarette smokers, e-cigarette users were generally younger, more often male, and more likely to be classified in the higher income quintiles and the highest education group, as shown in Table 1.

Table 2 Prevalence of and OR for COPD via Smoking Status in Korean Adults

	Prevalence (%, 95% CI)	**OR (95% CI)**	***P*-value**
Never	7.29 (6.74–7.85)	Reference	
Former	19.9 (18.4–21.39)	1.753 (1.482–2.072)	< 0.001
E-cigarettes	13.01 (6.73–19.29)	2.207 (1.214–4.011)	0.009
Dual	14.73 (9.8–19.65)	2.776 (1.809–4.259)	< 0.001
Cigarettes	20.47 (18.67–22.27)	2.876 (2.393–3.456)	< 0.001

Notes: Multivariable logistic regression adjusted for age, sex, smoking, BMI, FEV1, FVC, hypertension, diabetes mellitus, education, and income.
Abbreviations: OR, odds ratio; COPD, chronic obstructive pulmonary disease; CI, confidence interval; E-cigarettes, electronic cigarettes; Cigarettes, conventional cigarettes.

Prevalence of COPD

The prevalence and odds ratios (OR) for COPD based on smoking status in Korean adults are presented in Table 2. Compared with never smokers, the prevalence of COPD was significantly higher among cigarette smokers (20.47%), dual users (14.73%), and exclusive e-cigarette users (13.01%). In multivariable logistic regression analysis, conventional cigarette smoking demonstrated the strongest association with COPD (odds ratio [OR], 2.876; 95% confidence interval [CI], 2.393–3.456; $p < 0.001$), followed by dual use (OR, 2.776; 95% CI, 1.809–4.259; $p < 0.001$) and exclusive e-cigarette use (OR, 2.207; 95% CI, 1.214–4.011; $p = 0.009$). These findings suggest that while conventional cigarette smoking confers the highest risk for COPD, the use of e-cigarettes, either exclusively or concurrently with conventional cigarettes, is also significantly associated with an increased risk compared with never smokers.

Urine Cotinine and 4-(Methylnitrosamino)-1-(3-Pyridyl)-1-Butanol (NNAL) Levels

The comparison of urinary cotinine and NNAL levels according to smoking status is depicted in Figure 2. Cigarette and dual (cigarettes and e-cigarette) users exhibited higher urine NNAL and cotinine levels than did participants who had never smoked and former smokers. Although the interquartile ranges partially overlapped, dual users had significantly higher urinary cotinine and NNAL levels than cigarette users ($p < 0.05$), as confirmed by post hoc analysis (Supplementary Table 1).

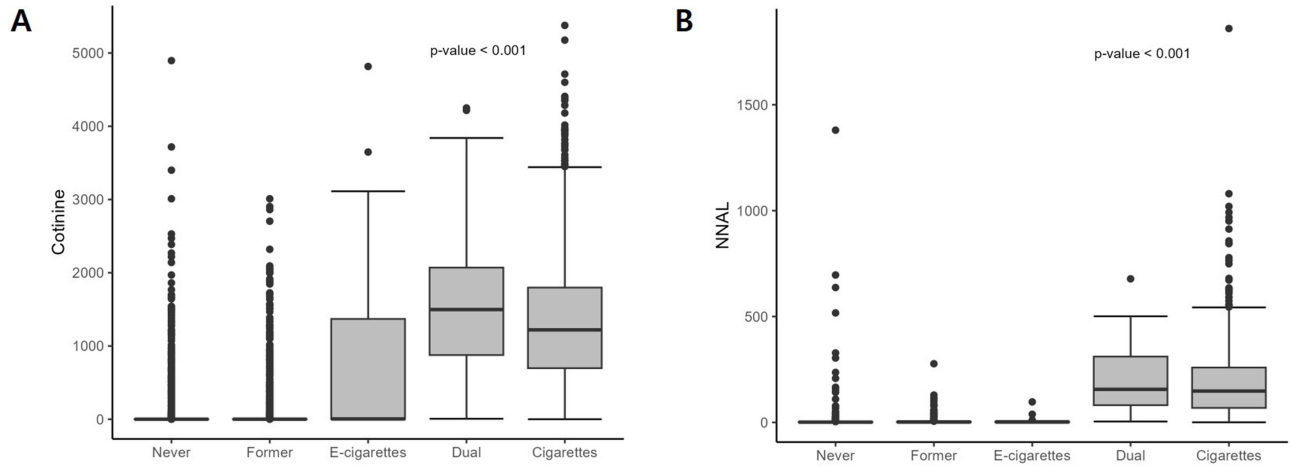

Figure 2 Comparison of urinary cotinine and 4-(methylnitrosamino)-1-(3-pyridyl)-1 butanol (NNAL) levels according to smoking status. The figures illustrate the levels of urinary cotinine and NNAL according to different smoking statuses. Participants were categorized into four groups: never smoked, former smokers, cigarette users, and dual users (cigarettes and e-cigarettes). The box plots demonstrate that both cotinine and NNAL levels are higher in cigarette users and dual users than in never smokers and former smokers. Additionally, dual users exhibit higher levels of urinary cotinine and NNAL than cigarette users. (**A**) Cotinine; (**B**) NNAL.

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Table 3 OR for Insomnia, Anxiety, and Depression by Smoking Status in Korean Adults

	Insomnia		Anxiety		Depression	
	OR (95% CI)	**p-value**	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**
Never	Reference		Reference		Reference	
Former	1.232 (1.003–1.514)	0.047	1.432 (1.257–1.63)	<0.001	1.447 (1.166–1.797)	<0.001
E-cigarettes	2.147 (1.033–4.465)	0.041	1.079 (0.701–1.659)	0.729	1.829 (1.000–3.347)	0.050
Dual	1.429 (0.783–2.61)	0.245	2.178 (1.638–2.895)	<0.001	2.676 (1.694–4.227)	<0.001
Cigarettes	1.486 (1.109–1.991)	0.008	1.604 (1.389–1.853)	<0.001	1.832 (1.451–2.314)	<0.001

Notes: Multivariable logistic regression adjusted for age, sex, smoking, BMI, FEV1, FVC, hypertension, diabetes mellitus, education, and income.
Abbreviations: OR, odds ratio; CI, confidence interval; E-cigarettes, Electronic cigarettes; Cigarettes, conventional cigarettes.

Prevalence of Anxiety and Depression

We also assessed anxiety and depression through a participant survey included in the health-related quality of life of the general Korean population using EuroQol-5 Dimension (EQ-5D), as suggested by the executive committee of the EQ-5D group. Table 3 shows the OR for insomnia, anxiety, and depression among participants who responded to the smoking and EQ-5D surveys. The multivariable logistic regression analysis demonstrated that the OR for anxiety and depression were significantly higher in dual users than in individuals who had never smoked (OR: 2.178, 95% CI 1.638–2.895; OR: 2.676, 95% CI, 1.694–4.227, respectively, $P < 0.001$).

Discussion

In this study, we evaluated the association between the use of e-cigarettes, including dual usage and cigarettes only, and estimated the presence of COPD in a nationally representative sample of Korean adults. This study underscores the significance of considering individual factors, including sex, age, education level, and smoking history, regarding using e-cigarettes. The ORs for COPD were highest among cigarette users, followed by dual users and e-cigarette-only users when classifying current smokers according to their smoking status. Furthermore, individuals who reported experiencing anxiety and depression exhibited a higher likelihood of engaging in dual use, including e-cigarette users.

Cigarette smoking is a risk factor for COPD.[21] However, the association between e-cigarettes and COPD has not been widely evaluated. Using e-cigarettes was associated with an increased risk of COPD[13,16,22] and other respiratory disorders,[22] consistent with this study's findings. However, despite numerous studies, evaluating the effects of e-cigarettes on COPD risk is challenging. This difficulty arises from the fact that many e-cigarette users simultaneously smoke tobacco, making it challenging to accurately account for the contributory effects of tobacco use. E-cigarettes are relatively new products, and long-term data on their health effects are limited.[23,24]

The use of e-cigarettes in Korea since their introduction in 2007 has increased from 2.0% in 2013[25] to 17.2% of current smokers in this study, based on data from the KNHANES. The use of e-cigarettes is increasing rapidly, and understanding the effects of e-cigarette use alone and their dual use with conventional cigarettes is crucial for public health because e-cigarettes have been marketed as a less harmful alternative to tobacco.[25] Some studies[22,26] suggest that e-cigarette use may reverse some of the harm caused by tobacco smoking in patients with COPD.

Dual users had more psychosocial and behavioral risk factors,[22,27,28] with higher proportions of perceived stress and continuous depressive mood, compared to those in tobacco cigarette-only smokers and participants who never smoked. Many individuals, especially young adults, use e-cigarettes and conventional cigarettes concurrently.[29–31] Despite dual users perceiving their health status as worse than that of participants who never smoked, they had more mental health problems and showed greater nicotine dependence and lower cessation rates than did the tobacco cigarette-only smokers.[32]

E-cigarettes have been marketed as healthier alternatives to cigarettes or as smoking cessation aids.[29,33] However, most e-cigarette users do not stop smoking and instead combine e-cigarette and cigarette use. A 1-year follow-up study showed that only 5.9% of dual smokers switched to e-cigarettes completely, and 1.4% of dual users abstained from both

products.[34] Among e-cigarette users, the most prevalent usage pattern is dual usage, showing a higher risk than that with using either product alone.[35,36] Combining cigarettes and e-cigarettes can result in a higher intake of nicotine, as each product contributes to the overall nicotine exposure. This study reveals higher levels of NNAL and nicotine in dual users than those in conventional cigarette users.

These findings underscore the importance of understanding the potential health risks associated with e-cigarette use, especially for youth and young adults. In cases of dual use, individuals can be exposed to a large quantity of nicotine. The health implications of e-cigarette use, especially for developing bodies and brains, are a major concern. Nicotine exists in varying amounts across different types of e-cigarettes and can have adverse effects on cognitive development, potentially leading to addiction and even suicidal attempts.[37,38] Educational initiatives and campaigns inform young people about the risks of e-cigarette use, focusing on health consequences and addiction. Future public health policy should raise awareness about potential complications, such as COPD and depression, and implement interventions to reduce use in at-risk populations.

The strength of this study is that it is first to compare dual smokers with cigarette smokers in developing COPD and to confirm that only e-cigarette use among current smokers was associated with a higher prevalence of COPD, anxiety, and depression with reliable representative nationwide data. We also demonstrated that e-cigarette use is associated with male sex, younger age, higher education level, and higher household income compared with those associated with cigarette use.

This study has several limitations. First, there was a substantial difference in sex distribution between smoking and non-smoking groups, with a higher proportion of males among smokers and a higher proportion of females among non-smokers. Second, a significant proportion of participants were excluded due to missing information on smoking status, pulmonary function tests, or baseline clinical characteristics. This exclusion process may have introduced selection bias by disproportionately removing individuals with poorer compliance, lower socioeconomic status, or distinct health profiles, potentially affecting the representativeness of the final analytic population. Third, smoking status was based on self-reported data, which may have led to misclassification or underreporting, particularly among female participants due to cultural factors. Finally, the cross-sectional design of the study limits the ability to establish causal relationships between smoking behaviors and health outcomes, and residual confounding by unmeasured variables cannot be completely excluded despite adjustment for major covariates.

Conclusion

In conclusion, the study findings indicate that e-cigarette use alone, and not only tobacco cigarette use and dual usage, is associated with an increased risk of developing COPD. E-cigarette use was also associated with a higher prevalence of insomnia and depression in Korean adults in a nationally representative survey. Furthermore, dual smokers had the highest risk of anxiety and depression. More active education or campaigns for smoking cessation for dual use, including e-cigarettes, should be prioritized.

Data Sharing Statement

The cohort data used in this study are publicly available.

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Disclosure

This paper has been uploaded to ResearchSquare as a preprint: https://www.researchsquare.com/article/rs-4352866/v1.

The authors report no conflicts of interest in this work.

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