

1

2 DR. SOO JIE CHUNG (Orcid ID : 0000-0002-7717-1188)

3 DR. BYUNG-KEUN KIM (Orcid ID : 0000-0001-5147-6306)

4 DR. JIHYUN OH (Orcid ID : 0000-0002-9491-0405)

5 DR. JI-SU SHIM (Orcid ID : 0000-0002-8846-0364)

6 DR. YOON-SEOK CHANG (Orcid ID : 0000-0003-3157-0447)

7 PROF. MIN-SUK YANG (Orcid ID : 0000-0002-9861-0530)

8

9

10 Article type : Original Article: Asthma and Lower Airway Disease

11

12

13 **Novel tobacco products including electronic cigarette and heated tobacco products**
14 **increase risk of allergic rhinitis and asthma in adolescents: Analysis of Korean youth**
15 **survey**

16 Soo Jie Chung^{1,2*}, Byung-Keun Kim^{3*}, Ji Hyun Oh⁴, Ji-Su Shim⁵, Yoon-Seok Chang^{1,6},
17 Sang-Heon Cho^{1,2}, and Min-Suk Yang^{1,7}

18 ¹Department of Internal Medicine, Seoul National University College of Medicine, Seoul,
19 Korea

20 ²Institute of Allergy and Clinical Immunology, Seoul National University Medical Research
21 Center, Seoul

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/ALL.14212](https://doi.org/10.1111/ALL.14212)

This article is protected by copyright. All rights reserved

³Department of Internal Medicine, Korea University Medical Center Anam Hospital, Seoul, Korea

⁴Division of Respiratory-Allergy Medicine, Department of Internal Medicine, Soonchunhyang University College of Medicine, Cheonan, Korea

⁵Department of Internal Medicine, Ewha Womans University College of Medicine, Seoul, Korea

⁶Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea

⁷Department of Internal Medicine, SMG-SNU Boramae Medical Center, Seoul, Korea

*The two authors contributed equally to this work.

Short running title: Novel tobacco products and allergic airway diseases

Correspondence

Min-Suk Yang., MD., Ph.D.

Department of Internal medicine, SMG-SNU Boramae Medical Center, Seoul, Korea

Tel: 82-2-870-2237

Fax: 82-2-831-0714

E-mail: iatrus13@hanmail.net

Author contributions

S.J.J., B.K.K., and M.S.Y. designed the study, collected and analyzed the data and wrote the manuscript. J.H.O., J.S.S., Y.S.C., and S.H.C. contributed to the design of the study, collection and interpretation of data and revision of the draft critically for important intellectual content.

Conflict of Interest statements

This article is protected by copyright. All rights reserved

48 None of the authors have any conflicts of interest to declare.

49 **Role of funding source**

50 None

51 **Ethics committee approval**

52 Done

53 **Word count excluding title page: 2,830 words**

54

55 **References: 29**

56

57 **Figures and tables: one figure and four tables**

58 **Abbreviations:**

59 AR, Allergic rhinitis

60 CC, Conventional cigarettes

61 EC, Electronic cigarettes

62 HTP, Heated tobacco products

63

64 Abstract

65 **Background:** The effect of novel tobacco products, such as electronic cigarettes (EC) and
66 heated tobacco products (HTP), on allergic rhinitis (AR) and asthma is not well known.

67 **Objective:** To evaluate the health effect of novel tobacco products on asthma and AR.

68 **Methods:** This study was conducted using large survey data on Korean middle and high
69 school students. The relationship between current asthma/AR and novel tobacco products
70 user status was evaluated. In order to compare the combined effects of conventional cigarette
71 (CC), EC, and HTP use on current allergic diseases, the participants were classified into 18
72 groups based on CC (current, former, and never), EC (current, former, and never), and HTP
73 (ever and never) status.

74 **Results:** A total of 60,040 participants representing 2,850,118 Korean adolescents were
75 analyzed. Of all participants, 6.7%, 2.7%, and 2.9% were current CC, current EC, and ever
76 HTP users, respectively. Current CC and ever HTP use was significantly associated with
77 current asthma and AR in adjusted models. Current EC showed association with current AR
78 but the association with asthma disappeared in the adjusted model. Among 18 groups, the
79 groups including current CC use showed higher risk of current AR and asthma than never
80 HTP-never EC-never CC group. The odds ratio of current asthma especially increased more
81 in those who used EC and/or HTP with CC concurrently than those in the never HTP-never
82 EC-current CC user group.

83 **Conclusion:** Using EC and/or HTP in adolescents might enhance the adverse effect of CC on
84 AR and asthma.

85 **Abstract word count: 247 words**

86 **Keywords:** Electronic Nicotine Delivery Systems; Asthma; Rhinitis, allergic

Introduction

Asthma and allergic rhinitis (AR) are the most common chronic inflammatory diseases of the upper and lower airway worldwide and can affect people of any age.^{1,2} A number of environmental and genetic risk factors may play a role in the development of asthma and AR. Tobacco smoking is known to be one of the important risk factors in asthma and is related to the development of asthma³ as well as asthma exacerbation⁴ and increased asthma severity.⁵ Although the effect of tobacco smoking on AR has not been studied as thoroughly as that on asthma, some researchers speculate that tobacco smoking will affect the symptom control of AR and the development of chronic rhinitis.⁶

Electronic cigarettes (ECs) are electronic devices that vaporize a liquid that is inhaled by the user. Liquids used in EC usually contain nicotine. Heated tobacco products (HTPs) or heat-not-burn tobacco products are electronic devices that use electric heating elements to heat tobacco producing aerosols containing nicotine and other chemicals that are inhaled by the user.⁷ Although ECs and HTPs work differently, both are considered alternatives to conventional cigarettes (CCs).

There is still no convincing evidence on the health effects of these novel tobacco products. In case of ECs, some previous studies showed that they produced equal or lower emission of several kinds of hazardous substances compared to CCs,^{8,9} and even reported that these products could help users quit smoking.^{8,10} However, some studies suggested that ECs are more harmful than CCs.^{11,12} HTPs are less studied than ECs. There is no study that demonstrates the effects of quitting CC smoking by HTP. One study found that the amount of harmful materials emitted from HTPs was less than that from CCs.¹³ Nevertheless, the health influences of ECs and HTPs are not yet clear.

Although the health effects of ECs and HTPs are controversial as mentioned above, EC use has been increasing rapidly since its introduction in 2003, especially among adolescents. The US Center for Disease Control and Prevention reported that the current EC use among high school students aged 14–18 years increased steeply from 11.7% in 2017 to 20.8% in 2018.¹⁴ In Korea, an estimated 9.1% of Korean adolescents used ECs according to the 10th Youth Health Survey.¹⁵ Although the number of users in Korea is not as high as in the US, it is likely to increase considering the growing trend of users in the other parts of the globe.^{16,17} Therefore, in this study, we evaluated the effects of ECs and HTPs on the development of asthma and AR, which is clinically important but less studied.

Methods

We used the Fourteenth Korea Youth Risk Behavior Survey (KYRBS-XIV, available from: <http://www.cdc.go.kr/yhs/>). KYRBS-XIV is a nationwide, cross-sectional survey performed in June 2018, the detailed description of which is reported elsewhere.¹⁸ KYRBS-XIV used a two-stage cluster sampling and systematic sampling method within each stratum. Middle and high school students aged 13–18 years voluntarily completed the anonymous, self-administered, web-based survey at their school. A total of 62,823 students from 400 middle and 400 high schools were enrolled in the survey with a response rate of 95.6%. Therefore, 60,040 eligible participants (30,463 males and 29,577 females) were included in the analysis. This sample was representative of all 2,850,118 Korean students.

The questions ‘In the last 12 months, have you been diagnosed with asthma by a doctor?’ and ‘In the last 12 months, have you been diagnosed with AR by a doctor?’ were used as the indicator for current asthma and AR. Prevalent asthma and AR were estimated by the following questions: ‘Have you ever been diagnosed with asthma by a doctor?’ and ‘Have you ever been diagnosed with AR by a doctor?’

The experience of CC (or EC) use was determined by the questionnaire “Have you ever used a CC (or EC)?” A current CC (or EC) user was defined when their answer to the question “How many days have you used at least one CC (or EC) in the last 30 days?” was more than one a day. If a participant replied that he or she had ever used CC (or EC) but not within the past 30 days, he or she was classified as a “former CC user” (or a “former EC user”). A participant who had never used CC (or EC) was classified as “never CC used” (or “never EC used”). The definition of smoking frequency was determined by the questionnaire “How many days have you smoked in the last 30 days?” If a current CC user used more than one CC (or EC) per day for 20 or more days in the past 30 days, he or she was defined as a “frequent CC user” (or a “frequent EC user”). A frequent CC user who smoked ten or more CC per day was classified as a “heavy CC user” and less than ten per day was “light CC user”. The use of HTPs was assessed by asking: “Have you ever used a heated tobacco product before?”

Socio-demographic and health-related factors included age, sex, body mass index (BMI), residential area, regular exercise, sedentary time, exposure to secondhand smoke, and socioeconomic status (SES). Weight status was classified using age- and sex-specific BMI

(calculated as self-reported weight in kilograms divided by the square of self-reported height in meters) percentiles based on the 2017 Korea National Growth Chart for Children and Adolescents. Age- and sex-specific BMI was divided into two categories: normal or underweight (0th-84th percentile), and overweight or obese (≥ 85 th percentile).¹⁹ The residential area was divided into urban and rural areas. Regular exercise was defined as engaging, at least two days a week, in either moderate-intensity exercise for more than 60 min a day, in vigorous exercise for more than 20 min a day, or in any muscle-strengthening exercise. Sedentary time was divided into two categories: less than ten hours per day and ten hours or more per day. Exposure to secondhand smoke was defined as exposure to the cigarette smoke from other people in the participant's home once or more in a week. SES was assessed with the self-reported SES of the participant's family. In addition, the relationship between the use of CC (or EC) and school absenteeism was analyzed using KYRBS-XIII as previous study analyzed (see **supplementary method**).²⁰

Statistical analysis

Complex sample survey data analysis was used for the statistical analysis of KYRBS-XIV data, except when the unweighted number was checked. Descriptive statistics were used to examine the distribution of variables. Continuous variables were presented as weighted mean and standard error, and categorical variables were presented as unweighted numbers and weighted percent. Descriptive statistics for each variable were presented according to the disease status.

First, the effects of each product (CC, EC, or HTP) on current asthma and AR were analyzed regardless of whether the participants used the other two products. For example, when we analyzed the effect of EC use on current asthma and AR, we divided the subjects into three groups which were 'Never EC user', 'Former EC user', and 'current EC user', regardless of whether they used CC or HTP. Univariate logistic regression analysis was used to investigate the influence of each variable on current asthma and AR. Covariate-adjusted logistic regression models were used to estimate the influence of CC, EC, and HTP using on current asthma and AR. Covariates used for the adjustment in model 1 were age and sex. In model 2, the relationship between current AR (or asthma) and CC, EC, or HTP using was analyzed adjusted for age, sex, BMI, residential area, regular exercise, sedentary time,

exposure to secondhand smoke, and SES. Besides various factors mentioned above, the presence of AR was also included as a covariate to analyze the relationship between current asthma and CC, EC, and HTP using in model 2.

Next, we assessed the combined effect of CC, EC, and HTP using status on current asthma or AR by subdividing the participants in the analysis. CC and EC users were divided into three categories, respectively: current user, former user, and never user. HTP users were divided into two categories: never or ever used. The name of each group was made by combining the using status of each device in order of HTP, EC, and CC (For example, an ever HTP-former EC-current CC group). A total of 18 smoking status groups was made as described in **table 1**. Multinomial logistic regression was used to assess the risk of current asthma and AR in the smoking status groups mentioned above. All statistical tests were two-sided and a p-value of <0.05 represented statistical significance. SPSS version 18.0 (SPSS Inc., Chicago, IL, USA) was used.

Results

General characteristics of the participants in KYRBS-XIV

Mean age of the participants was 15.2 years old. The number of male students (52.1%) was slightly higher than that of female students, and 95.3% of participants lived in an urban area. About 20% of the participants were overweight or obese. More than half of the participants (58.8%) did not exercise more than two days a week whereas about half (48.7%) of them had a sitting time of ten or more hours a day. Twenty-three percent of the participants were exposed to secondhand smoke at home (**Table 2**). Overall, 8.7% and 36.6% of the participants had prevalent asthma and AR, respectively. In addition, 2.5% and 20.8% of the participants had current asthma and AR, respectively. Among asthma patients, 70.4% had AR and 15.7% of AR patients had asthma.

Relationship between each tobacco product (CC, EC, and HTP) use and current allergic diseases

Current CC and EC users were 6.7% and 2.7%, respectively and 2.9% of the whole participants ever used HTPs (**Figure 1 and supplementary figure**). There were more frequent CC users (3.9%) than non-frequent CC users (2.8%) among the current CC users and more light CC users (2.6%) than heavy CC users (1.3%) among the frequent CC users. The percentage of current EC users were 2.7% and 2.9% of the participants had ever used HTPs. About 50% of current EC users and 60% of frequent EC users replied that they had ever used HTPs.

Current CC users had higher odds for current AR and asthma than those who never used CCs in all models. Among current CC users, frequent CC users showed significantly increased odds for current AR than non-frequent CC users. However, smoking frequency and amount were not related to current asthma. Similarly, current EC users showed a higher risk of current AR than those who never used ECs. Among current EC users, frequent EC users showed a significantly increased risk of current AR in all models. However, the relationship between current EC use and asthma disappeared after adjusting for multiple covariates in model 2. The relationship between the frequency of EC use and current asthma showed a similar result. Interestingly, those who had ever used HTP showed a significantly increased

risk of current AR and asthma than those who never HTP used regardless of CC or EC use status (**Supplementary table 1, 2**).

To further elucidate the effects of CC and EC using on acute asthma exacerbation, the relationship between CC and EC using and school absenteeism due to asthma was assessed using KYRBS-XIII. Baseline characteristics of the KYRBS-XIII were similar to those of KYRBS-XIV (**Supplementary table 3**). More than three days of absenteeism in the last 12 months was significantly correlated with current CC and EC use in all models (**Supplementary table 4**).

The combined effects of CC, EC, and HTP using on current allergic diseases

In order to compare the combined effects of CC, EC, and HTP using on current allergic diseases, the participants classified into 18 groups based on CC, EC, and HTP using status as mentioned in method. Numbers of participants in each group were presented in table 1.

‘Never HTP-never EC-current CC’, ‘Never HTP-current EC-current CC’, and ‘Ever HTP-current EC-current CC’ groups showed the tendency of higher odds for current AR than ‘Never HTP-never EC-never CC’ group (OR 1.3, 95% CI 1.1 – 1.6 in the ‘Never HTP-never EC-current CC’; OR 1.6, 95% CI 1.2 – 2.1 in the ‘Never HTP-current EC-current CC’; OR 1.6, 95% CI 1.1 – 2.2 in the ‘Ever HTP-current EC-current CC’ groups in model 2).

Interestingly, although statistically not significant, odds ratio of current AR increased more in those who used concurrently EC and/or HTP with CC (‘Never HTP-current EC-current CC’, and ‘Ever HTP-current EC-current CC’ groups) than those in the ‘Never HTP-never EC-current CC’ group (**Table 3**). In case of asthma, ‘Never HTP-never EC-current CC’, ‘Ever HTP-never EC-current CC’, and ‘Ever HTP-current EC-current CC’ groups also showed the tendency of higher odds for current asthma (OR 1.7, 95% CI 1.3 – 2.3 in the ‘Never HTP-never EC-current CC’; OR 6.4, 95% CI 3.6 – 11.6 in the ‘Ever HTP-never EC-current CC’; and OR 2.9, 95% CI 2.1 – 3.9 in the ‘Ever HTP-current EC-current CC’ groups in model 2).

Similar to the results from current AR, the ‘Ever HTP-never EC-current CC’ and ‘Ever HTP-

254 current EC-current CC' groups showed higher OR than 'Never HTP-never EC-current CC'
255 group. Particularly, 'Ever HTP-never EC-current CC' group showed significantly increased
256 odds of current asthma than 'Never HTP-never EC-current CC' group (OR 3.9, 95% CI 2.0 –
257 7.5) (**Table 4**).

Discussion

This study showed the possibility for EC and HTP to have an adverse effect on adolescents' respiratory health. Although there was no increase in the risk of current AR and asthma in groups that use EC (never HTP-current EC-never CC) or HTP (ever HTP-never EC-never CC) alone, the risk of AR and asthma seemed to increase compared to current CC only users when using EC and/or HTP with CC. These findings implied that using EC or HTP in adolescence could exacerbate the adverse effect of CC on AR and asthma.

Various environmental factors such as air pollution, tobacco smoke, and chemicals can cause upper²¹ and lower airway inflammation.²² Several previous studies have shown that EC can cause inflammation in various types of cells in airway.²³⁻²⁵ The substances in EC increased airway inflammation, especially type 2 inflammation, in a mouse model.²³ One study showed that using EC inhibited the immunity of nasal epithelial cells.²⁶ Therefore, EC usage has shown to increase the possibility of causing or exacerbating asthma through increasing airway inflammation. Even though studies on HTP and chronic airway diseases are less common than EC, several studies have reported airway toxicity associated with HTP.^{27,28} Therefore, both EC and HTP have the potential to cause and aggravate AR and asthma through airway inflammation or toxicity as shown in this study.

EC and HTP increased the risk of asthma only when combined with CC in this study. These results may suggest that certain chemical compounds in EC or HTP could act as the adjuvant that strengthens the adverse effects of CC on allergic diseases. On the other hand, the exposure time to EC and/or HTP in Korea might be too short to reveal their own adverse health effects. In other words, short-term exposure to EC and/or HTP on the airway that had been already inflamed by CC might be enough to cause additional adverse effects.

Meanwhile, HTP showed the stronger additive effect combined with CC on asthma but not on AR in this study. One explanation of this effect could be that the amount of aerosols is lower than that of CC. It is possible that aerosols from HTP arrive at the lower airways first but do not return to the upper airways. The other hypothesis is that the particle size of HTP aerosol and its distribution could be mainly in the lower airways different from CC.²⁹ These phenomena might enable aerosols produced by HTP to mainly influence the lower airways.

290 This study has several limitations. First, this study cannot fully explain the accurate
291 causality because of the limitations of a cross-sectional survey. Long term and prospective
292 studies should be conducted in the future. Second, this study did not reflect the long-term
293 effect of EC or HTP as mentioned above, such as the effect of the introduction of liquid
294 type EC in 2013 and HTP in 2017 in Korea. Third, the status of use of HTP was only
295 identified by “ever” and “never” and we could not know whether the participant used HTP
296 currently. Similarly, the definition of former users in CC and EC included everything from
297 participants who used CC or EC once in a life time to previous heavy smoker who quit
298 a month ago and the former users of CC and EC could be very heterogeneous. The
299 difference among current, former and never used of HTP and more refining definition of
300 amount in EC using should be studied. Nevertheless, this study is important since this is
301 the first study to examine the risk of asthma and AR due to EC as well as HTP in
302 adolescents.

303 In conclusion, we have demonstrated the effects of novel tobacco products on current
304 AR and asthma in adolescents. Thus, until the health effects of these products can be fully
305 assessed, adolescent exposure to these products should be strictly avoided.

References

1. Asher MI, Montefort S, Björkstén B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *The Lancet*. 2006;368(9537):733-743.
2. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet Respiratory medicine*. 2017;5(9):691-706.
3. Jaakkola JJ, Gissler M. Maternal smoking in pregnancy, fetal development, and childhood asthma. *American journal of public health*. 2004;94(1):136-140.
4. Chilmonczyk BA, Salmun LM, Megathlin KN, et al. Association between exposure to environmental tobacco smoke and exacerbations of asthma in children. *The New England journal of medicine*. 1993;328(23):1665-1669.
5. Siroux V, Pin I, Oryszczyn MP, Le Moual N, Kauffmann F. Relationships of active smoking to asthma and asthma severity in the EGEA study. Epidemiological study on the Genetics and Environment of Asthma. *The European respiratory journal*. 2000;15(3):470-477.
6. Bousquet PJ, Cropet C, Klossek JM, Allaf B, Neukirch F, Bousquet J. Effect of smoking on symptoms of allergic rhinitis. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology*. 2009;103(3):195-200.
7. Organization WH. *Heated tobacco products (HTPS): market monitoring information sheet*. World Health Organization;2018.
8. Hecht SS, Carmella SG, Kotandeniya D, et al. Evaluation of toxicant and carcinogen metabolites in the urine of e-cigarette users versus cigarette smokers. *Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco*. 2015;17(6):704-709.
9. Hartmann-Boyce J, Begh R, Aveyard PJB. Electronic cigarettes for smoking cessation. 2018;360:j5543.
10. Hartmann-Boyce J, McRobbie H, Bullen C, Begh R, Stead LF, Hajek P. Electronic cigarettes for smoking cessation. *Cochrane Database of Systematic Reviews*. 2016(9).
11. Wang JB, Olgin JE, Nah G, et al. Cigarette and e-cigarette dual use and risk of

cardiopulmonary symptoms in the Health eHeart Study. *PloS one*.

2018;13(7):e0198681.

12. Wills TA, Pagano I, Williams RJ, Tam EK. E-cigarette use and respiratory disorder in an adult sample. *Drug and alcohol dependence*. 2019;194:363-370.

13. Helen GS, Jacob III P, Nardone N, Benowitz NLJTc. IQOS: examination of Philip Morris International's claim of reduced exposure. 2018;27(Suppl 1):s30-s36.

14. Kirby T. Concerns over increased vaping in schoolchildren. *The Lancet Respiratory medicine*. 2019;7(3):211-212.

15. Ministry of Education, Ministry of Health and Welfare, Korea Centers for Disease Control and Prevention. The tenth Korea youth risk behavior web-based survey. Osong: Korea Centers for Disease Control and Prevention; 2014.

16. Farsalinos KE, Poulas K, Voudris V, Le Houezec J. Electronic cigarette use in the European Union: analysis of a representative sample of 27 460 Europeans from 28 countries. *Addiction*. 2016;111(11):2032-2040.

17. Jiang N, Chen J, Wang M-P, et al. Electronic cigarette awareness and use among adults in Hong Kong. *Addictive behaviors*. 2016;52:34-38.

18. Kim Y, Choi S, Chun C, Park S, Khang YH, Oh K. Data Resource Profile: The Korea Youth Risk Behavior Web-based Survey (KYRBS). *Int J Epidemiol*. 2016;45(4):1076-1076e.

19. Moon JS, Lee SY, Nam CM, et al. 2007 Korean National Growth Charts: review of developmental process and an outlook. *Korean J Pediatr*. 2008;51(1):1-25.

20. Cho JH, Paik SY. Association between electronic cigarette use and asthma among high school students in South Korea. *PloS one*. 2016;11(3):e0151022.

21. Hisinger-Mölkänen H, Piirilä P, Haahtela T, Sovijärvi A, Pallasaho PJWAOJ. Smoking, environmental tobacco smoke and occupational irritants increase the risk of chronic rhinitis. 2018;11(1):6.

22. Maddox L, Schwartz DAJArom. The pathophysiology of asthma. 2002;53(1):477-498.

23. Lerner CA, Sundar IK, Yao H, et al. Vapors produced by electronic cigarettes and e-juices with flavorings induce toxicity, oxidative stress, and inflammatory response in lung epithelial cells and in mouse lung. *PLoS One*. 2015;10(2):e0116732.

24. Schweitzer RJ, Wills TA, Tam E, Pagano I, Choi K. E-cigarette use and asthma in a multiethnic sample of adolescents. *Preventive medicine*. 2017;105:226-231.

25. Lerner CA, Rutagarama P, Ahmad T, Sundar IK, Elder A, Rahman I. Electronic cigarette aerosols and copper nanoparticles induce mitochondrial stress and promote DNA fragmentation in lung fibroblasts. *Biochemical and biophysical research communications*. 2016;477(4):620-625.
26. Martin EM, Clapp PW, Rebuli ME, et al. E-cigarette use results in suppression of immune and inflammatory-response genes in nasal epithelial cells similar to cigarette smoke. *American journal of physiology Lung cellular and molecular physiology*. 2016;311(1):L135-144.
27. Leigh NJ, Tran PL, O'Connor RJ, Goniewicz ML. Cytotoxic effects of heated tobacco products (HTP) on human bronchial epithelial cells. *Tobacco control*. 2018;27(Suppl 1):s26-s29.
28. Moazed F, Chun L, Matthay MA, Calfee CS, Gotts J. Assessment of industry data on pulmonary and immunosuppressive effects of IQOS. *Tobacco control*. 2018;27(Suppl 1):s20-s25.
29. Ingebrethsen BJ, Cole SK, Alderman SL. Electronic cigarette aerosol particle size distribution measurements. *Inhal Toxicol*. 2012;24(14):976-984.

389

390

Table 1. Distribution and baseline characteristics of the participants in the KYRBS-XIV according to the using status of conventional cigarettes, electronic cigarettes, and heated tobacco products

HTP	EC	CC	Total (%)*	Ever AR, % (SE)	Current AR, % (SE)	Ever asthma, % (SE)	Current asthma, % (SE)
Never	Never	Never	50,778 (83.8)	36.6 (0.3)	56.3 (0.4)	8.4 (0.1)	2.5 (0.1)
		Former	3,420 (5.8)	37.7 (0.9)	56.0 (1.4)	10.2 (0.6)	3.2 (0.3)
		Current	1,270 (2.1)	33.1 (1.4)	63.1 (2.3)	9.5 (0.8)	4.2 (0.6)
	Former	Never	475 (0.8)	33.0 (2.2)	52.4 (4.1)	12.2 (1.5)	5.3 (1.1)
		Former	1,054(1.8)	38.8 (1.5)	53.6 (2.3)	8.8 (0.9)	2.7 (0.5)
		Current	743(1.4)	37.6 (2.0)	59.4 (2.9)	9.7 (1.3)	3.3 (0.9)
	Current	Never	96 (0.2)	29.7 (4.7)	58.1 (9.6)	4.7 (2.2)	1.4 (1.2)
		Former	105 (0.2)	33.8 (4.5)	60.1 (8.1)	5.3 (2.0)	0.0 (0.0)
		Current	531 (1.0)	36.1 (2.2)	67.4 (3.2)	11.1 (1.3)	4.5 (0.9)
Ever	Never	Never	59 (0.1)	35.5 (6.8)	72.8 (10.1)	16.8 (5.6)	11.5 (3.9)
		Former	42 (0.1)	42.8 (7.0)	46.5 (11.1)	5.8 (3.4)	2.6 (1.6)
		Current	105 (0.2)	36 (4.5)	67.6 (6.7)	19.2 (3.7)	14 (3.6)
	Former	Never	48 (0.1)	31.6 (6.1)	63.3 (10.8)	7.8 (3.6)	4.9 (3.1)
		Former	155 (0.3)	34.2 (3.9)	71.3 (5.5)	12.6 (2.9)	5.4 (2.0)
		Current	435 (0.8)	41.4 (2.4)	59.6 (4.2)	9.4 (1.3)	3.5 (0.8)
	Current	Never	44 (0.1)	29.7 (6.6)	55.4 (13.6)	13.3 (4.9)	5.0 (3.4)

Former	42 (0.1)	28.0 (7.2)	66.6 (14.5)	10.6 (4.5)	4.2 (2.8)
Current	638 (1.2)	35.4 (2.0)	69.3 (3.2)	11.7 (1.2)	6.7 (1.0)

*Values are expressed in unweighted number (weighted %). Abbreviations: KYRBS-XIV, Fourteenth Korea Youth Risk Behavior Survey; CC, conventional cigarette; EC, electronic cigarette; HTP, heated tobacco product; AR, allergic rhinitis; SE, standard error

Table 2. Baseline characteristics of the study population of Korean adolescents (KYRBS-XIV)

Variables	Total (%) [*]	Ever AR, % (SE)	Current AR, % (SE)	Ever asthma, % (SE)	Current asthma, % (SE)
Numbers [*]	60,040	21,480	12,189	5,158	1,532
Age, y ^{**}	15.2 (0.02)	15.3 (0.03)	15.3 (0.03)	15.2 (0.03)	15.1 (0.05)
Sex					
Male	29,577 (52.1)	35.8 (0.4)	19.7 (0.3)	9.7 (0.2)	2.9 (0.1)
Female	30,463 (47.9)	37.6 (0.3)	21.9 (0.3)	7.5 (0.2)	2.1 (0.1)
Body-mass index					
Underweight/ Normal	46,531 (79.9)	36.8 (0.3)	20.9 (0.2)	8.3 (0.1)	2.3 (0.1)
Overweight/ Obese	11,805 (20.1)	37.0 (0.5)	20.8 (0.4)	9.5 (0.3)	3.0 (0.2)
Residence					
Urban	56,579 (95.3)	37.0 (0.3)	21.1 (0.2)	8.7 (0.1)	2.5 (0.1)
Rural	3,461 (4.7)	28.5 (1.0)	15.0 (0.9)	7.9 (0.5)	2.4 (0.2)
Regular exercise					
< 2 d/w	35,006 (58.8)	36.9 (0.3)	20.7 (0.2)	8.3 (0.2)	2.2 (0.1)
≥ 2 d/w	25,034 (41.2)	36.1 (0.4)	20.8 (0.3)	9.2 (0.2)	2.9 (0.1)
Sedentary time					
< 10 h/d	31,326 (51.3)	34.1 (0.3)	19.2 (0.2)	8.4 (0.2)	2.7 (0.1)
≥ 10 h/d	28,714 (48.7)	39.3 (0.3)	22.4 (0.3)	8.9 (0.2)	2.4 (0.1)
Secondhand smoking					
Never	45,981 (77)	36.8 (0.3)	20.5 (0.2)	8.4 (0.1)	2.4 (0.1)
Ever	14,059 (23)	36.0 (0.4)	21.7 (0.4)	9.5 (0.3)	3.1 (0.2)
Socioeconomic status					
High	24,207 (40.8)	37.8 (0.4)	22.0 (0.3)	8.8 (0.2)	2.6 (0.1)
Middle	27,808 (46)	35.6 (0.3)	19.6 (0.3)	8.2 (0.2)	2.3 (0.1)
Low	8,025 (13.2)	36.4 (0.6)	21.1 (0.5)	9.9 (0.3)	3.2 (0.2)
CC use status					
Never	51,500 (85.1)	36.6 (0.3)	20.6 (0.2)	8.4 (0.1)	2.3 (0.1)
Former	4,818 (8.2)	37.7 (0.7)	21.1 (0.6)	9.9 (0.5)	2.9 (0.3)
Current	3,722 (6.7)	35.9 (0.9)	22.9 (0.8)	10.4 (0.5)	4.4 (0.4)

CC use frequency

Non-frequent	1,589 (41.3)	37.1 (1.2)	22.3 (1.1)	10.8 (0.8)	3.9 (0.5)
Frequent	2,133 (58.7)	35.1 (1.1)	23.3 (1.0)	10.2 (0.7)	4.8 (0.5)

CC use amount

Light	1,439 (67.5)	36.4 (1.4)	23.8 (1.3)	9.9 (0.8)	4.0 (0.6)
Heavy	694 (32.5)	32.4 (1.9)	22.2 (1.7)	10.8 (1.2)	6.5 (1.0)

EC use status

Never	55,674 (92.1)	36.6 (0.3)	20.7 (0.2)	8.5 (0.1)	2.4 (0.1)
Former	2,910 (5.2)	37.6 (0.9)	21.4 (0.8)	9.8 (0.6)	3.3 (0.4)
Current	1,456 (2.7)	34.8 (1.3)	23.3 (1.1)	10.6 (0.8)	4.7 (0.6)

HTP use status

Never	58,472 (97.1)	36.6 (0.3)	20.7 (0.2)	8.6 (0.1)	2.5 (0.1)
Ever	1,568 (2.9)	34.5 (1.9)	23.6 (1.6)	11.7 (1.1)	6.1 (0.9)

*Values are expressed in unweighted number (weighted %). **Age is expressed as a mean (SE). Other values are expressed in weighted percentages (SE). Abbreviations: KYRBS-XIV, Fourteenth Korea Youth Risk Behavior Survey; AR, Allergic rhinitis; CC, conventional cigarette; EC, electronic cigarette; HTP, heated tobacco product.

Table 3. The risk of current allergic rhinitis according to conventional cigarettes, electronic cigarettes, and heated tobacco products using status in Korean adolescents

HTP	EC	CC	Unadjusted		Model 1*		Model 2**	
			OR (95% CI)	P-value	aOR (95% CI)	P-value	aOR (95% CI)	P-value
Never	Never	Never	Ref		Ref		Ref	
		Former	1.0 (0.9 – 1.1)	0.86	1.0 (0.9 – 1.2)	0.63	1.0 (0.9 – 1.1)	0.96
		Current	1.3 (1.1 – 1.6)	0.004	1.3 (1.1 – 1.6)	0.005	1.3 (1.1 – 1.6)	0.02
	Former	Never	0.9 (0.6 – 1.2)	0.34	0.9 (0.7 – 1.2)	0.49	0.8 (0.6 – 1.1)	0.21
		Former	0.9 (0.7 – 1.1)	0.24	1.0 (0.8 – 1.1)	0.64	0.9 (0.8 – 1.1)	0.43
		Current	1.1 (0.9 – 1.4)	0.30	1.2 (0.9 – 1.5)	0.14	1.2 (0.9 – 1.5)	0.24
	Current	Never	1.1 (0.5 – 2.3)	0.85	1.1 (0.5 – 2.5)	0.73	1.0 (0.4 – 2.2)	0.96
		Former	1.2 (0.6 – 2.3)	0.64	1.3 (0.7 – 2.5)	0.46	1.2 (0.6 – 2.4)	0.59
		Current	1.6 (1.2 – 2.1)	0.001	1.7 (1.2 – 2.2)	0.001	1.6 (1.2 – 2.2)	0.002
	Ever	Never	2.1 (0.8 – 5.6)	0.15	2.1 (0.8 – 5.8)	0.16	1.9 (0.7 – 5.1)	0.21
		Former	0.7 (0.3 – 1.6)	0.38	0.7 (0.3 – 1.7)	0.43	0.6 (0.3 – 1.6)	0.34
		Current	1.6 (0.9 – 3.0)	0.12	1.9 (1.0 – 3.5)	0.04	1.9 (1.0 – 3.6)	0.05
		Former	1.3 (0.5 – 3.3)	0.53	1.3 (0.5 – 3.2)	0.59	1.1 (0.4 – 2.9)	0.82
		Former	1.9 (1.1 – 3.2)	0.01	2.0 (1.2 – 3.5)	0.009	1.9 (1.1 – 3.2)	0.02
		Current	1.1 (0.8 – 1.6)	0.43	1.2 (0.9 – 1.7)	0.26	1.2 (0.9 – 1.7)	0.30
	Current	Never	1.0 (0.3 – 2.9)	0.95	1.2 (0.4 – 3.8)	0.81	1.2 (0.3 – 4.4)	0.80
		Former	1.5 (0.4 – 5.6)	0.50	1.5 (0.4 – 5.5)	0.55	1.4 (0.4 – 5.0)	0.62

Current	1.8 (1.3 – 2.4)	<0.001	1.8 (1.3 – 2.4)	<0.001	1.6 (1.1 – 2.2)	0.005
---------	------------------------	------------------	------------------------	------------------	------------------------	--------------

Abbreviations: Ref, reference; AR, allergic rhinitis; EC, electronic cigarette; CC, conventional cigarette; HTP, heated tobacco products. *P*-values are expressed in the second digit of the decimal unless it was less than 0.01. *the covariates used in model 1 were age and sex. **The covariates used in model 2 were age, sex, body-mass index, residential area, regular exercise, sedentary time, exposure to secondhand smoke, and socioeconomic status.

Table 4. The risk of current asthma according to conventional cigarettes, electronic cigarettes, and heated tobacco products using status in Korean adolescents

HTP	EC	CC	Unadjusted		Model 1*		Model 2**	
			OR (95% CI)	P-value	aOR (95% CI)	P-value	aOR (95% CI)	P-value
Never	Never	Never	Ref		Ref		Ref	
		Former	1.3 (1.1 – 1.6)	0.01	1.3 (1.0 – 1.6)	0.02	1.2 (1.0 – 1.5)	0.08
		Current	1.7 (1.3 – 2.3)	<0.001	1.6 (1.2 – 2.1)	0.004	1.6 (1.1 – 2.2)	0.005
	Former	Never	2.2 (1.5 – 3.4)	<0.001	2.1 (1.3 – 3.3)	0.001	1.8 (1.1 – 3.0)	0.02
		Former	1.1 (0.7 – 1.6)	0.61	1.0 (0.7 – 1.5)	0.88	1.0 (0.7 – 1.5)	0.95
		Current	1.4 (0.8 – 2.3)	0.28	1.3 (0.8 – 2.3)	0.31	1.3 (0.7 – 2.3)	0.35
	Current	Never	0.6 (0.1 – 3.3)	0.52	0.6 (0.1 – 3.4)	0.53	-	
		Former	-		-		-	
		Current	1.9 (1.2 – 2.9)	0.003	1.5 (1.0 – 2.4)	0.08	1.2 (0.8 – 2.0)	0.39
		Current	1.9 (1.2 – 2.9)	0.003	1.5 (1.0 – 2.4)	0.08	1.2 (0.8 – 2.0)	0.39
Ever	Never	Never	5.1 (2.4 – 11)	<0.001	5.4 (2.5 – 11.7)	<0.001	3.8 (1.5 – 9.6)	0.005
		Former	1.1 (0.3 – 3.6)	0.93	1.1 (0.3 – 3.7)	0.92	0.9 (0.2 – 3.1)	0.81
		Current	6.4 (3.6 – 11.6)	<0.001	6.2 (3.4 – 11.3)	<0.001	6.0 (3.1 – 11.5)	<0.001
	Former	Never	2.0 (0.5 – 7.7)	0.29	1.1 (0.2 – 6.7)	0.92	1.2 (0.2 – 7.6)	0.88
		Former	2.3 (1.1 – 4.8)	0.03	2.0 (0.9 – 4.4)	0.09	2.2 (1.0 – 5.1)	0.06
		Current	1.5 (0.9 – 2.4)	0.13	1.4 (0.9 – 2.3)	0.14	1.2 (0.7 – 2.0)	0.52
	Current	Never	2.1 (0.5 – 8.6)	0.30	2.4 (0.6 – 10.2)	0.22	1.1 (0.2 – 7.4)	0.92
		Former	1.8 (0.4 – 6.9)	0.42	0.8 (0.1 – 5.3)	0.83	0.9 (0.1 – 6.4)	0.92

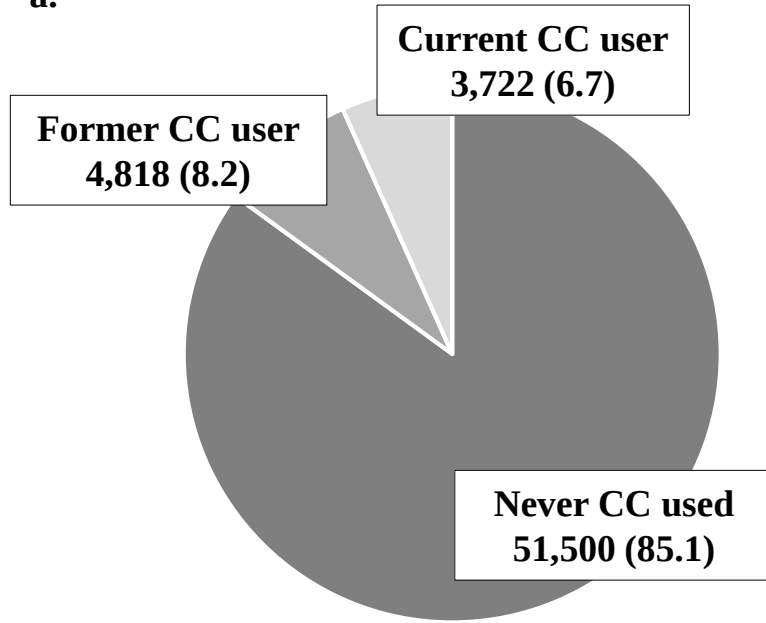
Current	2.9 (2.1 – 3.9)	<0.001	2.3 (1.6 – 3.3)	<0.001	1.7 (1.1 – 2.7)	0.01
---------	------------------------	------------------	------------------------	------------------	------------------------	-------------

Abbreviations: Ref, reference; AR, allergic rhinitis; EC, electronic cigarette; CC, conventional cigarette; HTP, heated tobacco products. *P*-values are expressed in the second digit of the decimal unless it was less than 0.01. *the covariates used in model 1 were age and sex. **the covariates used in model 2 were age, sex, body-mass index, residential area, regular exercise, sedentary time, exposure to secondhand smoke, socioeconomic status, and the presence of AR – This cell was too small to measure the statistical significance.

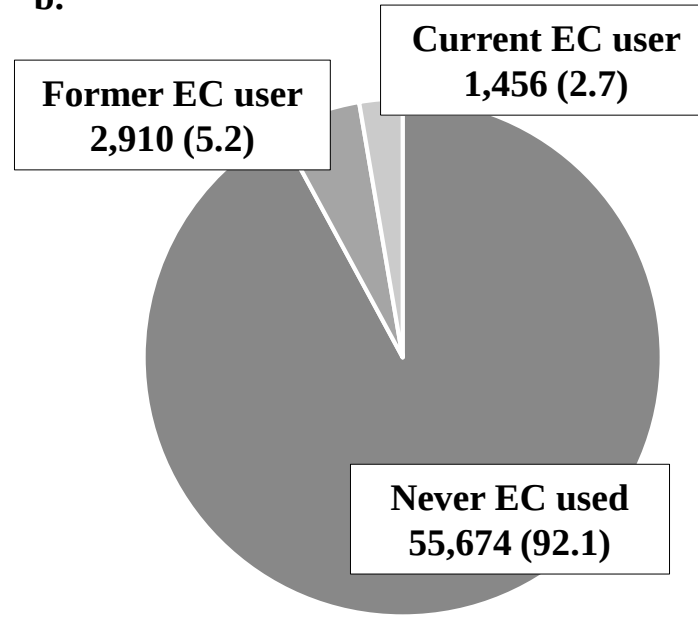
Figure Legend

Figure 1. The detailed CC, EC, and HTP using status of the participants. Detailed (a) conventional cigarette (CC), (b) electronic cigarette (EC), and (c) heated tobacco product (HTP) using status of the participants are expressed in unweighted numbers and weighted %.

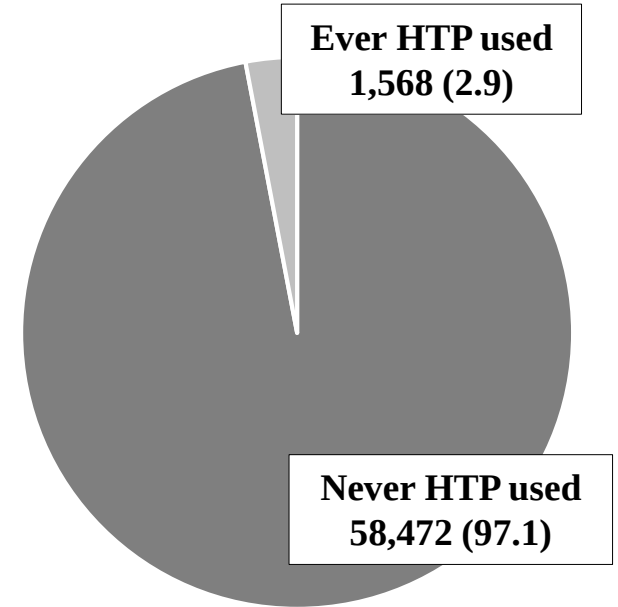
a.



b.



c.



Supplementary table 1. The association between current allergic rhinitis and conventional and electronic cigarette use in Korean adolescents

	Unadjusted		Model 1*		Model 2**	
	OR (95% CI)	P-value	aOR (95% CI)	P-value	aOR (95% CI)	P-value
CC use status						
Never	Ref					
Former	1.0 (0.9 – 1.1)	0.81	1.0 (0.9 – 1.1)	0.51	1.0 (0.9 – 1.1)	0.92
Current	1.4 (1.2 – 1.5)	<0.001	1.4 (1.2 – 1.6)	<0.001	1.3 (1.2 – 1.5)	<0.001
CC use frequency[†]						
Non-frequent	Ref					
Frequent	1.3 (1.0 – 1.7)	0.03	1.4 (1.1 – 1.8)	0.007	1.4 (1.1 – 1.8)	0.006
CC use amount[†]						
Light	Ref					
Heavy	1.2 (0.8 – 1.7)	0.43	1.1 (0.8 – 1.6)	0.55	1.1 (0.8 – 1.6)	0.56
EC use status						
Never	Ref					
Former	1.0 (0.9 – 1.2)	0.75	1.1 (0.9 – 1.2)	0.29	1.0 (0.9 – 1.2)	0.63
Current	1.6 (1.3 – 1.9)	<0.001	1.6 (1.3 – 1.9)	<0.001	1.5 (1.2 – 1.8)	<0.001
EC use frequency[‡]						
Non-frequent	Ref					
Frequent	1.8 (1.1 – 2.9)	0.02	1.9 (1.1 – 3.1)	0.02	1.9 (1.1 – 3.2)	0.02
HTP use status						
Never	Ref					
Ever	1.7 (1.3 – 2.2)	0.001	1.7 (1.2 – 2.2)	0.001	1.5 (1.1 – 2.0)	0.009

Abbreviations: OR, odds ratio; CI, confidential interval; aOR, adjusted odds ratio; Ref, reference; CC, conventional cigarette; EC, electronic cigarette; HTP, heated tobacco product. *P*-values are expressed in the second digit of the decimal unless it was less than 0.01. * the covariates used in model 1 were age and sex. ** the covariates used in model 2 were age, sex, body-mass index, residential area, regular exercise, sedentary time, exposure to secondhand smoke, and socioeconomic status. [†]Analyses on the CC use frequency and amount were conducted only in CC users. [‡]Analysis on the EC use frequency was conducted only in EC users.

Supplementary table 2. The association between current asthma and conventional and electronic cigarette use in Korean adolescents

	Unadjusted		Model 1*		Model 2**	
	OR (95% CI)	P-value	aOR (95% CI)	P-value	aOR (95% CI)	P-value
CC use status						
Never	Ref					
Former	1.3 (1.0 – 1.5)	0.03	1.2 (1.0 – 1.5)	0.10	1.1 (0.9 – 1.4)	0.21
Current	1.9 (1.6 – 2.3)	<0.001	1.7 (1.4 – 2.1)	<0.001	1.5 (1.2 – 1.9)	<0.001
CC use frequency[†]						
Non-frequent	Ref					
Frequent	1.2 (0.9 – 1.7)	0.21	1.3 (0.9 – 1.9)	0.14	1.4 (0.9 – 2.0)	0.19
CC use amount[†]						
Light	Ref					
Heavy	1.6 (1.0 – 2.6)	0.04	1.4 (0.9 – 2.3)	0.16	1.2 (0.7 – 2.1)	0.53
EC use status						
Never	Ref					
Former	1.4 (1.1 – 1.8)	0.004	1.3 (1.0 – 1.7)	0.03	1.2 (1.0 – 1.5)	0.13
Current	2.0 (1.5 – 2.6)	<0.001	1.6 (1.2 – 2.1)	0.003	1.2 (0.8 – 1.6)	0.35
EC use frequency[‡]						
Non-frequent	Ref					
Frequent	2.6 (1.5–4.4)	0.001	2.0 (1.1 – 3.8)	0.02	1.8 (0.9 – 3.5)	0.21
HTP use status						
Never	Ref					
Ever	2.5 (1.9 – 3.5)	<0.001	2.0 (1.4 – 2.9)	<0.001	1.5 (1.0 – 2.3)	0.05

Abbreviations: OR, odds ratio; CI, confidential interval; aOR, adjusted odds ratio; Ref, reference; CC, conventional cigarette; EC, electronic cigarette; HTP, heated tobacco product. *P*-values are expressed as the second digit of the decimal unless it was less than 0.01. *the covariates used in model 1 were age and sex. **the covariates used in model 2 were age, sex, body-mass index, residential area, regular exercise, sedentary time, exposure to secondhand smoke, socioeconomic status, and the presence of AR. [†]Analyses on the CC use frequency and amount were conducted only in CC users. [‡]Analysis on the EC use frequency was conducted only in EC users.

Supplement Table 3. Baseline characteristics of the study population of Korean adolescents (KYRBS-XIII)

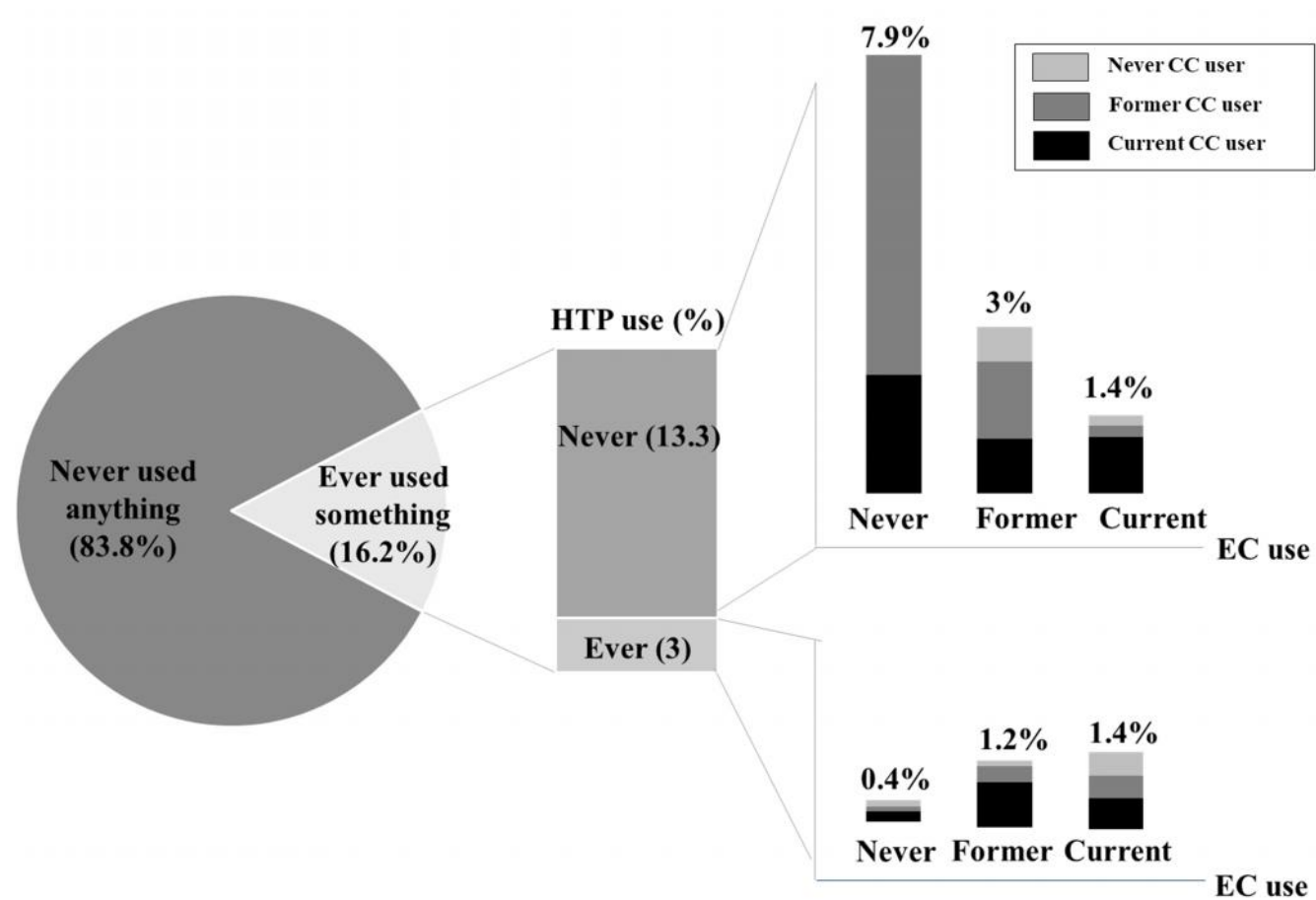
Variables	Total (%) [*]	Ever asthma, % (SE)	Current asthma, % (SE)
Numbers[*]	62,276	5,422	1,493
Age, y^{**}	15.1 (0.02)	15.1 (0.03)	14.9 (0.05)
Sex			
Male	31,624 (52.1)	9.8 (0.2)	2.7 (0.1)
Female	30,652 (47.9)	7.7 (0.2)	2.0 (0.1)
Body-mass index			
Underweight/ Normal	50,209 (80.7)	8.5 (0.1)	2.2 (0.1)
Overweight/ Obese	11,651 (18.6)	9.8 (0.3)	2.5 (0.1)
Residence			
Urban	57,437 (93.9)	8.9 (0.1)	2.4 (0.1)
Rural	4,839 (6.1)	7.6 (0.5)	2.1 (0.3)
Regular exercise			
< 2 d/w	41,089 (66.6)	8.6 (0.2)	2.2 (0.1)
≥ 2 d/w	21,187 (33.4)	9.3 (0.2)	2.8 (0.1)
Sedentary time			
< 10 h/d	31,178 (51.2)	8.5 (0.2)	2.4 (0.1)
≥ 10 h/d	28,456 (48.8)	9.1 (0.2)	2.2 (0.1)
Secondhand smoking			
Never	44,511 (72.1)	8.6 (0.1)	2.2 (0.1)
Ever	17,765 (27.9)	9.2 (0.2)	2.9 (0.1)
Socioeconomic status			
High	24,802 (40.4)	9.1 (0.2)	2.6 (0.1)
Middle	28,582 (45.6)	8.2 (0.2)	2.1 (0.1)
Low	8,892 (14.1)	9.7 (0.3)	2.7 (0.2)
CC use status			
Never	54,126 (86.3)	8.6 (0.1)	2.2 (0.1)
Former	4,381 (7.4)	9.5 (0.5)	2.1 (0.2)
Current	3,769 (6.4)	11.1 (0.5)	4.7 (0.3)
CC use frequency			
Non-frequent	1,643 (43.4)	10.9 (0.8)	3.5 (0.4)
Frequent	2,126 (56.6)	11.2 (0.8)	5.6 (0.5)
CC use amount			
Light	2,927 (78.0)	10.3 (0.6)	3.6 (0.4)
Heavy	842 (22.0)	14.0 (1.1)	8.3 (0.9)
EC use status			
Never	57,974 (92.6)	8.6 (0.1)	2.2 (0.1)
Former	1,244 (2.2)	9.9 (0.5)	3.1 (0.3)
Current	3,058 (5.2)	13.1 (0.1)	6.5 (0.7)

*Values are expressed in unweighted number (weighted %). **Age is expressed as a mean (SE). Other values are expressed in weighted percentages (SE). Abbreviations: KYRBS-XIV, Fourteenth Korea Youth Risk Behavior Survey; AR, Allergic rhinitis; CC, conventional cigarette; EC, electronic cigarette; HTP, heated tobacco product.

Supplement Table 4. The association between school absenteeism due to asthma and conventional and electronic cigarette use in Korean adolescents (KYRBWS-XIII)

	Unadjusted		Model 1 [*]		Model 2 ^{**}	
	OR (95% CI)	<i>P</i> -value	aOR (95% CI)	<i>P</i> -value	aOR (95% CI)	<i>P</i> -value
CC use status						
Never	Ref					
Former	0.9 (0.5 – 1.7)	0.84	1.0 (0.5 – 2.0)	0.90	1.0 (0.5 – 2.0)	0.97
Current	4.3 (3.1 – 6.1)	<0.001	3.1 (2.0 – 4.8)	<0.001	2.7 (1.8 – 4.3)	<0.001
CC use frequency						
Non-frequent	Ref					
Frequent	1.2 (0.7 – 2.5)	0.46	0.6 (0.3 – 1.4)	0.24	0.5 (0.2 – 1.3)	0.15
CC use amount						
Light	Ref					
Heavy	3.3 (1.8 – 6.2)	<0.001	2.2 (1.0 – 4.6)	0.04	1.5 (0.7 – 3.5)	0.32
EC use status						
Never	Ref					
Former	1.3 (0.7 – 2.3)	0.37	1.3 (0.7 – 2.4)	0.44	1.1 (0.6 – 2.2)	0.70
Current	7.7 (5.0 – 11.7)	<0.001	6.5 (3.8 – 11.2)	<0.001	4.5(2.6 – 8.0)	<0.001
EC use frequency						
Non-frequent	Ref					
Frequent	4.9 (2.0 – 11.9)	<0.001	3.4 (1.1 – 10.2)	0.03	2.1 (0.6 – 7.2)	0.26

School absenteeism was defined when the participant was absent from school more than three days in the last 12 months. ^{*}the covariates used in model 1 were age and sex. ^{**}the covariates used in model 2 were age, sex, body-mass index, residential area, regular exercise, sedentary time, exposure to secondhand smoke, socioeconomic status, and the presence of AR. Abbreviations: OR, odds ratio; CI, confidential interval; aOR, adjusted odds ratio; Ref, reference; CC, conventional cigarette; EC, electronic cigarette; HTP, heated tobacco product.



Supplement figure 1. The stratified using status of the participants according to CC, EC and HTP using. Firstly, they were classified according to HTP use, secondly, according to EC use, and finally, according to CC use.

Supplementary methods

To further evaluate the influence of these products on daily activity limitation among asthmatics, the relationship between the use of CC (or EC) and school absenteeism was analyzed using KYRBS-XIII. School absence was defined by the question: “How many days were you absent from school in the last 12 months due to asthma?” Responses were classified into two categories; three days or less, and above three days. Univariate logistic regression analysis was used to investigate the influence of each variable on school absenteeism. Covariate-adjusted logistic regression models were used to estimate the influence of CC, EC, and HTP using on school absenteeism. Covariates used for the adjustment in model 1 were age and sex. In model 2, the relationship between current AR (or asthma) and CC, EC, or HTP using was analyzed adjusted for age, sex, BMI, residential area, regular exercise, sedentary time, exposure to secondhand smoke, and SES.

