

Directions and Challenges in Smoking Cessation Treatment

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Raising the tax on tobacco-related products is the most effective and sustainable intervention for smoking cessation. The 2015 tobacco-tax increase resulted in a decreased smoking rate among Korean adult men. However, participation in the government-sponsored smoking-cessation programs developed after the 2015 tobacco tax increase has declined sharply since 2018. The popularity of electronic cigarettes (e-cigarettes) seems to be an important factor in this decline. Indeed, the market share of e-cigarettes has increased steadily since 2007, when the e-cigarette was introduced in Korea as a vaporizer. The introduction of the tobacco-heating device IQOS in 2017 resulted in the skyrocketing popularity of e-cigarettes, especially among the young generation of Koreans. The U.S. Food and Drug Administration (FDA) authorized marketing of IQOS as a “reduced exposure” tobacco product on July 7, 2020, further complicating smoking-cessation efforts. The agency announced that IQOS produces fewer or lower levels of some toxins than combustible cigarettes. However, FDA authorization does not mean that these products are safe. There is no evidence that reducing the harmful chemical components leads to health benefits. Clinicians need to maintain the position that those who smoke, regardless of tobacco-product type, should be counseled for smoking cessation and prescribed appropriate proven pharmacologic agents.

Keywords: Smoking Cessation; E-Cigarette; Closed System Vaporizer; Heated Tobacco Product

Smoking Rate among Korean Adults after the Tobacco Tax Increase in 2015

The price of a pack of cigarettes in Korea increased by 80% from KRW 2,500 to 4,500 in 2015. This was the sharpest hike in both relative and absolute terms in Korean history. The proportion of current smokers among Korean adults decreased from 19.2% in 2014 to 17.7% in 2015. Those who planned to

quit smoking within six months increased from 38.6% in 2014 to 41.6% in 2015¹. More remarkably, the smoking rate among adult men decreased to below 40% for the first time in Korea (Figure 1). Although the smoking rate among adult men rebounded to above 40% in the next year, it decreased to below 40% again in 2017 and stayed at that level thereafter.

Smoking Cessation Promotion Programs

A month after the tobacco tax increase on January 1, 2015, the Korean National Health Insurance implemented multiple programs to support smoking cessation. As one of these programs, smoking cessation counseling and pharmacologic treatment provides 12 weeks of counseling sessions and covers the costs of pharmacologic agents, either varenicline or bupropion, for smoking cessation. At first, it was provided only once a year, and then it was extended to three times a year beginning in 2017. If participants stayed in the program for ≥ 8 weeks or make clinic visits ≥ 3 times during the 12-week period, all the expenses for the counseling and pharmacologic treatment were fully refunded. Even health care products (e.g., electronic sphygmomanometers, electronic scales, and elec-

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Received: Nov. 28, 2020

Revised: Dec. 1, 2020

Accepted: Dec. 2, 2020

Published online: Dec. 2, 2020

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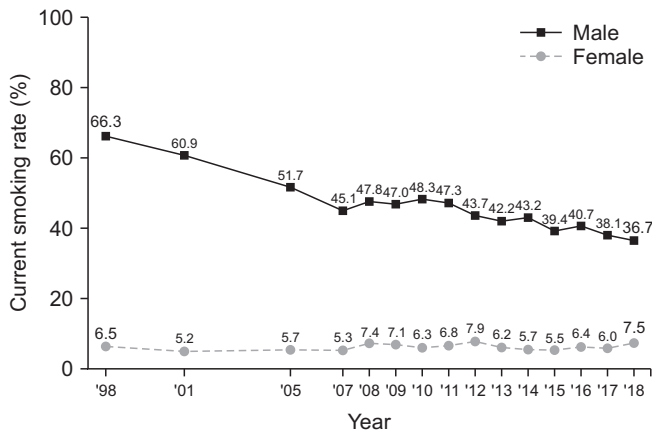


Figure 1. Smoking rate among Korean adult men and women from 1998 to 2018. The price of tobacco increased from KRW 2,500 (approx. USD 2.2) to KRW 4,500 (approx. USD 4) in 2015. Data adapted from the Korea Centers for Disease Control and Prevention, September 1, 2020².

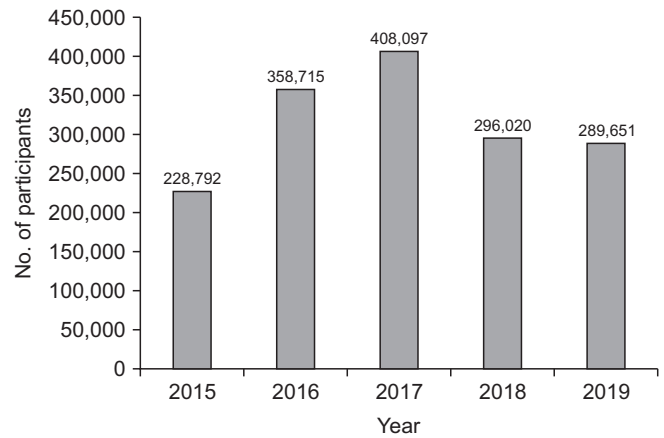


Figure 2. Number of smokers participating in the smoking-cessation counseling and pharmacologic treatment program provided by the Korean National Health Insurance.

tronic toothbrushes) were provided as incentives. However, this special treatment was terminated on January 1, 2019³. In the first year of introduction, this program registered more than 200,000 smokers; the number of participants increased to more than 400,000 in 2017. However, the number of participating smokers has sharply decreased since 2018 (Figure 2)⁴. Not only smoking cessation counseling and pharmacologic treatment by medical doctors but also other services for quitting smoking, such as smoking cessation clinics at public health centers, phone consultation for smoking cessation, on-line services for smoking cessation, and visiting services for smoking cessation have experienced rapid decline in participation since 2018⁵. Increased tolerance to the raised prices of cigarettes and the popularity of electronic cigarettes (e-cigarettes) are seen as important factors for the loss of interest in these programs. In the face of the increased prices of cigarettes, smokers are seeking ways to continue smoking, such as switching to cheaper products or reducing other expenses⁶. This explains the dramatic rise in sales of e-cigarettes in Korea since 2015. E-cigarettes were relatively more economical compared with combustible cigarettes because they were excluded from the tax increase. In addition, companies that produced e-cigarettes actively marketed their products by describing them as less harmful to people's health.

Electronic Cigarettes

1. History

An e-cigarette is a battery-powered electronic device that vaporizes a nicotine-containing solution⁷. Instead of burning tobacco, the user inhales aerosolized substances—vapor:

This type of e-cigarette is called a closed system vaporizer (CSV), and the use of a CSV is popularly known as “vaping.” Although tobacco companies have been developing nicotine aerosol-generation devices since as early as 1963, the modern e-cigarette was invented in 2003 by the Chinese pharmacist Hon Lik⁸. Hon's father died in 2004 from lung cancer. Hon himself was a heavy smoker, smoking one to two packs per day. His father's death was the main influence for him to develop e-cigarettes. In 2003, he formulated the idea of using a high-frequency piezoelectric ultrasound-emitting element to vaporize a nicotine-containing solution. This vapor, similar to cigarettes, would then be inhaled to deliver nicotine to consumers. He filed his first patent in China in 2003, and then in the United States and the European Union. The first e-cigarette was manufactured using ultrasound technology a year later in Beijing, China. The first e-cigarette model, named “Ruyan,” consisted of three parts: a battery, a plastic cartridge containing a nicotine solution, and a heating element composed of an ultrasonic atomizer.

2. Closed system vaporizers vs. heated tobacco products

The use of CSVs has increased sharply worldwide, including Korea. According to the 11th Korea Youth Risk Behavior Web-based Survey conducted in 2015, 9.8% of teenagers used CSV-type e-cigarettes⁹. However, the entrance of heated tobacco products (HTPs) changed the picture of the global e-cigarette market. HTPs heat, rather than combust, processed tobacco in a controlled fashion. HTPs are rapidly gaining market share in some countries, such as Japan and South Korea, and have been introduced in more than 50 countries as of May 2020¹⁰. IQOS was introduced to Korea as the first type of HTP in 2017. According to a study that evaluated more than 6,000 subjects aged ≥19 years who participated in the Korea National Health and Nutrition Examination Survey (KNHANES), those who

used an HTP within the past 30-days comprised 4.4% (7.8% for men and 0.9% for women) of South Korean adults in 2018¹¹.

3. Market share of HTPs and closed system vaporizers in Korea

In Korea, the market share of e-cigarettes has increased steadily after the tobacco tax increase in 2015 (Figure 3). In recent data, from the first half of 2020, 182,000,000 packs of e-cigarettes have been sold (180,000,000 packs of HTPs+2,000,000 packs of CSVs), accounting for 10.5% of the total sales of tobacco products (1,740,000,000 packs). The share of e-cigarettes was 11.1% in the same period last year (decrease of 0.57%). The sales of HTPs decreased by 6.6% and that of CSVs plummeted by 80.3%³. The plunge in sales of CSVs may have been affected by the warning against the use of CSVs announced by the Korean government in October 2019, which came after the report of vaping-associated acute lung injury in the United States.

4. E-cigarette or vaping product-use associated lung injury

In July 2019, the Wisconsin Department of Health Services and Illinois Department of Public Health received reports regarding rapid increase in visits to the emergency department owing to lung injury that was possibly associated with the use of e-cigarettes. In a preliminary report, they analyzed 53 cases, most of whom were young (median age, 19 years; range, 16–53 years), male (44/53, 83%), and white (82%). Many of them (83%) had a history of vaping cartridges containing

cannabis products, either alone or in combination with other products. Meanwhile, 17% used products containing nicotine only. More than two-thirds of the cases showed hypoxia at presentation, which indicated extensive pulmonary infiltration. Of the patients, 83% had an abnormal chest radiograph at presentation, usually in the form of bilateral, ground-glass opacity. In the initial reports, the mortality rate was 2% (1/53). The final report noted 98 cases and two deaths¹². The number of cases peaked in September 2019, and as of February 18, 2020, 2,807 e-cigarette or vaping product-use associated lung injury (EVALI) cases had been reported, with 68 deaths¹³. The exact cause of EVALI has not been determined, although the vitamin E acetate and tetrahydrocannabinol in the products are highly suspected to be the culprits. Upon learning of reports of EVALI cases in the United States, the Korean government issued a strong warning against the use of CSVs in October 2019, which remains in effect. CSV products sold in the Korean market have been analyzed, and no product has been found to contain cannabis components. Vitamin E acetate was detected in three of 112 products, but only at a minimal concentration (0.03–0.12 ppm). An animal study showed that the concentration of vitamin E acetate would need to be ≥ 3.12 mg/kg to provoke significant pulmonary toxicity¹⁴. At present, Korea does not have a confirmed case of EVALI.

5. U.S. Food and Drug Administration announcement of IQOS as “reduced harmful tobacco product”

The U.S. Food and Drug Administration (FDA) authorized the marketing of Philip Morris Products S.A.’s “IQOS Tobacco Heating System” as a modified risk tobacco product (MRTP) as of July 7, 2020. The products authorized for sale include the IQOS device, Marlboro Heatsticks, Marlboro Smooth Menthol Heatsticks, and Marlboro Fresh Menthol Heatsticks. This announcement permits the marketing of MRTPs as containing a reduced level of or presenting a reduced exposure to a substance, to benefit the health of the population. Although the U.S. FDA has stressed that this action does not imply that IQOS is safe nor “FDA approved,” this decision has a huge impact on the behavior of current or potential consumers of HTPs. The issue of the relative safety of HTPs would be hotly debated in the future.

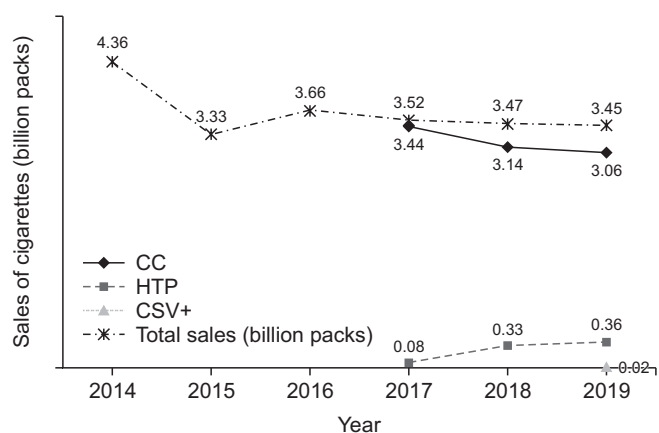


Figure 3. Trend of annual sales of tobacco products in Korea from 2014 to 2019. The price of a pack of cigarette increased from KRW 2,500 to KRW 4,500 in 2015. CC: combustible cigarettes; HTP: heated-tobacco products; CSV+: closed-system vaporizer and others. Data from the Ministry of Economy and Finance published on July 31, 2020¹⁵.

Smoking Cessation Counseling and Pharmacologic Treatment

1. Impact of smoking on respiratory diseases in South Korean patients

By smoking cigarettes, a person inhales an estimated 7,000 compounds, including numerous toxic components, such as benzene, formaldehyde, benzopyrene, carbon monoxide, ac-

rolein, and even metals. These materials cause injury through inflammation, irritation, asphyxiation, carcinogenesis, and other mechanisms, with the respiratory tract being the first system to be hit. Undoubtedly, smoking causes and aggravates various respiratory diseases, including chronic obstructive pulmonary disease (COPD), lung cancer, bronchitis, and asthma¹⁶.

In South Korea, pneumonia ranked tenth among all causes of death in 2004; its rank climbed to the third position, after malignancies and cardiovascular diseases in 2019¹⁷. Smoking is the second most important risk factor after congestive heart failure in patients hospitalized with community-acquired pneumonia in South Korea¹⁸. Given this context, Korean hospitals provide counseling and pharmacologic treatment to smokers who are hospitalized for pneumonia. The percentage of community-acquired pneumonia patients with a history of smoking within a 1-year period who are offered smoking cessation counseling is reported to be as high as 92.2%¹⁹. In the case of COPD, smoking cessation is one of the most important interventions for disease management. It is also the only way of slowing the decline rate of forced expiratory volume in 1 second and improving survival²⁰. Regarding lung cancer, smoking is an important factor for its development and outcomes. Cigarette smoking status is reported as an independent predictor of mortality in patients with lung cancer²¹. Smoking increases the risk of all-cause mortality in a dose-response manner²². Pharmacotherapy and nicotine replacement reliably increase the long-term smoking abstinence rates.

2. Pharmacologic treatment of smoking cessation

The smoking cessation promotion program developed after the 2015 tobacco tax increase in South Korea covers the cost of pharmacologic agents. Physicians can choose between varenicline and bupropion. Varenicline has shown a superior smoking cessation effect compared with a nicotine substitute or sustained-release bupropion in many prospective controlled studies²³⁻²⁵. In the initial period of introduction of varenicline, cardiovascular adverse effects, and neuropsychiatric symptoms, such as abnormal dreams, have been raised as safety issues. However, a subsequent study found no risk of serious cardiovascular adverse events during or after varenicline treatment²⁶. Varenicline, bupropion, and nicotine patch are well tolerated and effective in adults with psychotic, anxiety, and mood disorders²⁷. Thus, varenicline can be used as the most effective anti-smoking drug by most smokers, including those with psychiatric disorders, cardiovascular diseases, and COPD.

Conclusion

The tobacco tax increase in 2015 was helpful for the decrease of the smoking rate below 40% among adult males for the first time in Korean history. Financial resources secured by tobacco tax increase were diverted to multiple programs to promote smoking cessation. However, the loss of enthusiasm for smoking cessation was evident since 2018. The skyrocketing popularity of new type of cigarettes, HTPs and CSVs especially among young generation was also an important factor for the loss of interest in these programs. However, the ultimate health benefits of e-cigarettes and their role as intermediary agents before final quitting of smoking have not been established scientifically yet. As clinicians, we need to adhere to proven ways of the counseling and pharmacologic treatment for smoking cessation.

Conflicts of Interest

Jae Yeol Kim serves as editor-in-chief of the *Tuberculosis of Respiratory Diseases*, but has no role in the decision to publish this article.

Funding

No funding to declare.

References

1. Jung JW, Kim JY. Characteristics of a “rebound” in smoking after a tobacco price increase. *Int J Tuberc Lung Dis* 2020;24:390-5.
2. Korea Centers for Disease Control and Prevention. The 7th Korea National Health and Nutrition Examination Survey (KNHANES VII). Cheongju: Korea Centers for Disease Control and Prevention; 2019.
3. Lee CM. The impact of heated tobacco products on smoking cessation, tobacco use, and tobacco sales in South Korea. *Korean J Fam Med* 2020;41:273-81.
4. Oh SW. The current status and challenges of national smoking cessation support program in Korea. *Korean J Fam Med* 2019;40:351-2.
5. Ajzen I, Brown TC, Carvajal F. Explaining the discrepancy between intentions and actions: the case of hypothetical bias in contingent valuation. *Pers Soc Psychol Bull* 2004;30:1108-21.
6. Kuipers MA, Partos T, McNeill A, Beard E, Gilmore AB, West R, et al. Smokers' strategies across social grades to minimise the cost of smoking in a period with annual tax increases: evidence from a national survey in England. *BMJ Open* 2019;9:e026320.

7. Brown CJ, Cheng JM. Electronic cigarettes: product characterisation and design considerations. *Tob Control* 2014;23 Suppl 2:ii4-10.
8. Janssen BP, Boykan R. Electronic cigarettes and youth in the United States: a call to action (at the local, national and global Levels). *Children (Basel)* 2019;6:30.
9. Korea Centers for Disease Control and Prevention. The 11th Korea Youth Risk Behavior Web-based Survey. Cheongju: Korea Centers for Disease Control and Prevention; 2015.
10. Hori A, Tabuchi T, Kunugita N. Rapid increase in heated tobacco product (HTP) use from 2015 to 2019: from the Japan 'Society and New Tobacco' Internet Survey (JASTIS). *Tob Control* 2020 Jun 5 [Epub]. <https://doi.org/10.1136/tobaccocontrol-2020-055652>.
11. Kim SH, Cho HJ. Prevalence and correlates of current use of heated tobacco products among a nationally representative sample of Korean adults: Results from a cross-sectional study. *Tob Induc Dis* 2020;18:66.
12. Layden JE, Ghinai I, Pray I, Kimball A, Layer M, Tenforde MW, et al. Pulmonary illness related to E-cigarette use in Illinois and Wisconsin: final report. *N Engl J Med* 2020;382:903-16.
13. The Lancet Respiratory Medicine. The EVALI outbreak and vaping in the COVID-19 era. *Lancet Respir Med* 2020;8:831.
14. Department of Health Promotion, Ministry of Health and Welfare. The report for the analysis of suspectful, harmful components contained in domestically marketed closed system vaporizers. Sejong: Ministry of Health and Welfare, 2019.
15. Ministry of Economy and Finance. MOEF public report 132241438196990879. Sejong: Ministry of Economy and Finance; 2020.
16. Willemse BW, Postma DS, Timens W, ten Hacken NH. The impact of smoking cessation on respiratory symptoms, lung function, airway hyperresponsiveness and inflammation. *Eur Respir J* 2004;23:464-76.
17. Statistics Korea. Statistics on the causes of death of Koreans in 2019. Daejeon: Statistics Korea; 2020.
18. Restrepo MI, Sibila O, Anzueto A. Pneumonia in patients with chronic obstructive pulmonary disease. *Tuberc Respir Dis* 2018;81:187-97.
19. Hong JY, Kang YA. Evaluation of the quality of care among hospitalized adult patients with community-acquired pneumonia in Korea. *Tuberc Respir Dis* 2018;81:175-86.
20. Kanner RE, Connett JE, Williams DE, Buist AS. Effects of randomized assignment to a smoking cessation intervention and changes in smoking habits on respiratory symptoms in smokers with early chronic obstructive pulmonary disease: the Lung Health Study. *Am J Med* 1999;106:410-6.
21. Thun MJ, Carter BD, Feskanich D, Freedman ND, Prentice R, Lopez AD, et al. 50-Year trends in smoking-related mortality in the United States. *N Engl J Med* 2013;368:351-64.
22. Cao Y, Kenfield S, Song Y, Rosner B, Qiu W, Sesso HD, et al. Cigarette smoking cessation and total and cause-specific mortality: a 22-year follow-up study among US male physicians. *Arch Intern Med* 2011;171:1956-9.
23. Cinciripini PM, Robinson JD, Karam-Hage M, Minnix JA, Lam C, Versace F, et al. Effects of varenicline and bupropion sustained-release use plus intensive smoking cessation counseling on prolonged abstinence from smoking and on depression, negative affect, and other symptoms of nicotine withdrawal. *JAMA Psychiatry* 2013;70:522-33.
24. Chang PY, Shiu MN, Yuan YT, Chang HC, Su PY, Lan TH. Comparative effectiveness of varenicline and nicotine replacement therapy for smoking cessation in older and younger smokers: a prospective cohort in Taiwan. *Nicotine Tob Res* 2019;21:149-55.
25. Taylor GM, Taylor AE, Thomas KH, Jones T, Martin RM, Munafò MR, et al. The effectiveness of varenicline versus nicotine replacement therapy on long-term smoking cessation in primary care: a prospective cohort study of electronic medical records. *Int J Epidemiol* 2017;46:1948-57.
26. Benowitz NL, Pipe A, West R, Hays JT, Tonstad S, McRae T, et al. Cardiovascular safety of varenicline, bupropion, and nicotine patch in smokers: a randomized clinical trial. *JAMA Intern Med* 2018;178:622-31.
27. Evins AE, Benowitz NL, West R, Russ C, McRae T, Lawrence D, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with psychotic, anxiety, and mood disorders in the EAGLES trial. *J Clin Psychopharmacol* 2019;39:108-16.