



# Smoking Cessation Strategies Targeting Specific Populations

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Quitting smoking helps smokers maintain their health and extend their lifespan by 10 or more years. Treatment strategies for smoking cessation should be tailored to individual smokers with special needs based on their specific circumstances. It is recommended that pregnant women adopt smoking cessation through counseling and behavioral interventions because the safety of medications has yet to be established. Counseling is the main strategy for smoking cessation in adolescents and nicotine replacement therapy can be used with caution in individuals with serious nicotine dependence. It is important for smokers with psychiatric diseases to quit smoking following accurate assessment of their depression status. Nicotine replacement therapy, varenicline, and bupropion can be used for smoking cessation in smokers with psychiatric disorders. The incidence of cardiovascular disease decreased according to the smoking status and the duration of smoking cessation. In smokers with chronic obstructive pulmonary disease (COPD) who used a combination of counseling and pharmacotherapy the quitting rate was more than twice as high as subjects who used behavioral interventions alone. Varenicline can be used as the most effective anti-smoking drug by most smokers including those with psychiatric disorders, cardiovascular disease, and COPD.

**Keywords:** Smoking Cessation; Population; Pharmacotherapy

## Introduction

Quitting smoking not only helps smokers maintain their health, but also extends their lifespan by 10 or more years, avoiding the risk of premature death. In particular, smokers between 35 and 44 years old who have smoked for more than

20 years benefit most by quitting smoking, which prevents smoking-related diseases and premature deaths<sup>1</sup>.

In America, after the correlation between smoking and lung cancer was established in the 1960s, the government banned smoking advertising at the policy level and has continuously increased cigarette taxes. The result was a drastic reduction in smoking rates. The anti-smoking policies of increasing cigarette taxes, restricting tobacco advertising in the media, and adding messages or pictorial warnings about the harmful effects of smoking to tobacco labeling are known to be effective in preventing smoking and/or encouraging smoking cessation.

When smokers attempt to quit on their own will without using smoking cessation medication, the quit rate is as low as 2%–4%. However, when combined with pharmacotherapy, the quitting rate increases up to 20%–40%<sup>2</sup>. Nonetheless, 92.9% of smokers in Korea reported that they had tried quitting smoking through willpower alone, without using medication therapy. For effective smoking cessation, four or more consultations should take place, along with pharmacotherapy.

Regarding the duration of smoking cessation consultations, 20 minutes or more of intensive consultations has been found to be effective. However, sessions as short as 3 minutes have

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also been shown to be effective (1.7 times higher quit rates). Moreover, the effect of smoking cessation is proportional to the duration of the consultations<sup>3</sup>. The smoking rate in Korea is gradually decreasing. Nonetheless, despite increased cigarette prices and the provision of financial support for smoking cessation therapies, the smoking rate among males in Korea remains high, at 39.3%<sup>4</sup>.

The methods of smoking cessation treatment should be tailored to smokers with special needs, such as adolescents, pregnant, and breastfeeding women, and those with underlying diseases, according to their specific circumstances.

## Smoking Cessation Treatment for Specific Populations

### 1. Smoking cessation treatment for pregnant and breastfeeding women

Women are more vulnerable to smoking than men and show more intense nicotine dependence than their male counterparts. Smoking negatively affects ovarian function; when female smokers quit smoking, menstrual pain and other gynecological problems such as secondary amenorrhea, premature menopause, and infertility improve. Moreover, smoking has negative cosmetic effects, as it decreases skin elasticity, increases wrinkles, and causes hair loss and teeth discoloration. It has been reported that female smokers who are on oral contraceptives have a 12 or more times greater risk of developing cardiovascular diseases, including myocardial infarction, than their non-smoking counterparts<sup>5</sup>.

Smoking is an important trigger associated with pregnancy-related complications (e.g., preterm birth, miscarriage, low birth weight, sudden infant death, and childhood cancer). It also causes important long-term problems in women and newborns. Approximately 20%–30% of pregnant smokers attempt to quit smoking during pregnancy. However, 70% or more of them resume smoking during pregnancy or after delivery. As many pregnant women do not candidly disclose their smoking status to healthcare professionals, it is important for medical staff to determine whether pregnant women smoke by conducting appropriate consultations.

Clinical studies involving the administration of anti-smoking medications during pregnancy are difficult to conduct, and for this reason, the safety of these medications has not yet been clearly proven. Therefore, it is recommended to induce smoking cessation through smoking cessation consultations with psychosocial support (behavioral interventions) before attempting pharmacotherapy<sup>6</sup>. Only very limited evidence suggests that nicotine replacement therapy (NRT) is effective for smoking cessation in pregnant women; for this reason, NRT should be considered with caution only when the benefits of NRT outweigh the harm of continued smoking.

To date, no studies have been conducted on varenicline and e-cigarettes in pregnant or breastfeeding women. A previous study reported that the quit rates of women who used NRT in late pregnancy increased by 40% (relative risk [RR], 1.41; 95% confidence interval [CI], 1.03–1.93; eight studies on 2,199 subjects). However, that report may have been subject to bias, because the group using NRT in a randomized controlled trial (RCT) without a placebo group showed higher effectiveness than the group using NRT in trials with a placebo group. When the RCT without a placebo group was excluded, pregnant women using NRT did not show significantly higher smoking cessation rates than their counterparts who were administered a placebo<sup>7</sup>.

If NRT is needed for smoking cessation, pregnant or breastfeeding women can use NRT intermittently. If a nicotine patch is used, it needs to be removed during sleep, to avoid transmission of nicotine to the fetus. Varenicline and bupropion (an antidepressant) have rarely been clinically studied in pregnant women. Thus, the use of these drugs is not recommended due to safety issues. When pregnant women receive smoking cessation consultations, their quit rate increases by about 44% compared to other common smoking control methods (RR, 1.44; 95% CI, 1.19–1.73). Smoking cessation consultation alone without pharmacotherapy reduces smoking rates in late pregnancy by 35%, the incidence of low birth weight by 17%, and the admission of newborns to the intensive care unit by 22%<sup>8</sup>.

### 2. Smoking cessation treatment for adolescents

Smoking in adolescence has a tremendous influence on one's health throughout life. Healthcare professionals should accurately assess adolescents' smoking status and strongly recommend various cessation methods. Adolescents suffer more seriously than adults from the harmful effects exerted by the chemicals contained in cigarettes. Most smokers start smoking in adolescence, and more than 80% of smokers become addicted to nicotine as adolescents. Adolescence is a crucial phase in life, in which one's experimentation out of curiosity about smoking may develop into nicotine dependence. The focus of smoking cessation programs for adolescents is to prevent smoking, rather than smoking cessation.

The primary strategy of smoking cessation for adolescents is consultation. In cases of serious nicotine dependence requiring pharmacotherapy, NRT can be used with limitations and caution. However, the evidence of its effectiveness for smoking cessation is insufficient. In an RCT, among those adolescents who received behavioral therapy for smoking cessation, 18% did not initiate smoking, compared to their counterparts who did not receive such an intervention (RR, 0.82). Moreover, the subjects who received behavioral therapy showed 34% higher quit rates than those who did not (RR, 1.34)<sup>9</sup>.

In adolescents, NRT did not demonstrate a statistically sig-

nificant effect. Administration of bupropion alone or a combination of NRT and bupropion likewise did not show a statistically significant difference in quit rates<sup>10</sup>. If a nicotine patch is used for smoking cessation, short-term (1–2 weeks) use and additional consultation to encourage quitting is advised, instead of the generally recommended period of 12 weeks. The first-line oral smoking cessation agents, varenicline and bupropion, have not been clinically studied in individuals younger than 18 years old, similarly to pregnant women, and therefore these medications are not recommended as anti-smoking agents for this population.

### 3. Smoking cessation treatment for smokers with psychiatric disorder

The smoking rates of individuals with neuropsychiatric diseases are remarkably higher (80%–90%) than those of individuals without such conditions (20%–30%). Moreover, smokers with nicotine dependence are more likely to suffer from depression (26.7%) than those who are not nicotine-dependent (12%)<sup>11</sup>. Moreover, smokers with depression who have failed to quit smoking have higher nicotine dependence than those with depression who succeeded in smoking cessation. Furthermore, individuals whose preexisting depression worsens during smoking cessation treatment are more likely to resume smoking. Therefore, it is important to facilitate quitting through an accurate assessment of an individual's depression status while undergoing smoking cessation treatment<sup>12</sup>.

Smokers who are addicted to alcohol have more serious nicotine dependence, and thus need an approach that incorporates treatment for alcohol addiction. Those who have psychiatric diseases need aggressive smoking cessation consultations and follow-up observations after quitting smoking. During pharmacotherapy for smoking cessation, if the smoker is taking medications that may interact with psychotropic agents, regular examinations with a psychiatrist are also helpful as a component of smoking cessation treatment.

NRT, varenicline, and bupropion can be used for smoking cessation treatment. However, bupropion is not recommended for smokers who are receiving treatment for neuropsychiatric problems such as seizures, anorexia, or bulimia, or on other types of antidepressants<sup>13,14</sup>.

In a meta-analysis, smokers with psychiatric diseases who received bupropion showed a significantly higher quit rate than the placebo group (RR, 3.03; 95% CI, 1.69–5.42). Patients receiving varenicline likewise showed a significantly higher quit rate than the placebo group (RR, 4.74; 95% CI, 1.34–16.71). In that study, there were no significant differences between the treatment and placebo groups in terms of the aggravation of preexisting psychiatric conditions<sup>15</sup>. In the past, some reports have suggested that varenicline increased the frequency of depression or suicide attempts, concluding that the use of varenicline was not to be advised. However, a large-scale RCT

conducted on 8,144 subjects known as the Evaluating Adverse Events in a Global Smoking Cessation Study (EAGLES), published in 2016 in *The Lancet*, showed that smokers with neuropsychiatric diseases exhibited no significant differences between varenicline, bupropion, NRT, and placebo groups in terms of the aggravation of mental conditions or serious neuropsychiatric side effects, including suicide attempts.

The control group of patients with no mental disorders showed no differences from other groups in the frequency of serious neuropsychiatric side effects, which were observed in 13 of the 99 subjects in the varenicline group (1.3%), 22 of the 989 subjects in the bupropion group (2.2%), 25 of the 1,006 subjects in the nicotine patch group (2.5%), and 24 of the 999 subjects in the placebo group (2.4%). The risk differences between the varenicline and placebo groups and between the bupropion and placebo groups were  $-1.28$  (95% CI,  $-2.40$  to  $-0.15$ ) and  $-0.08$  (95% CI,  $-1.37$  to  $1.21$ ), respectively<sup>16</sup>.

The results of that study established the safety of clinical administration of varenicline, the first-line anti-smoking agent for smoking cessation treatment, based on the finding that there was no causal relation between the medication and neuropsychiatric adverse effects. This prompted the U.S. Food and Drug Administration to approve the removal of the warning label from the varenicline packaging (December 16, 2016). Also, in a clinical study of smokers with cardiovascular disease, subjects who quit smoking using varenicline showed a lower frequency of cerebrovascular and cardiovascular diseases than those who continued smoking.

Based on the above research, varenicline can be considered the most effective anti-smoking agent developed to date in terms of inducing smoking cessation with the fewest side effects. It is also recommended for most smokers, excluding pregnant women and those under 18 years old, as a safe first-line smoking cessation treatment agent.

### 4. Smoking cessation treatment for smokers with chronic obstructive pulmonary disease

Quitting smoking is an essential way both to prevent the aggravation of chronic obstructive pulmonary disease (COPD) and COPD-related mortality and to treat COPD in smokers. In smokers with COPD, groups of subjects who used a combination of smoking cessation consultations and pharmacotherapy showed quit rates more than twice as high as those observed among subjects who used behavioral interventions alone (RR, 2.53; 95% CI, 1.83–3.50). In a meta-analysis of 16 studies ( $n=13,123$ ), in the groups of patients who used NRT, varenicline, and bupropion, subjects with COPD showed significant results compared to the placebo group (RR, 2.60; 95% CI, 1.29–5.24 in the NRT group; RR, 3.34; 95% CI, 1.88–5.92 in the varenicline group; and RR, 2.03; 95% CI, 1.26–3.28 in the bupropion group)<sup>17</sup>.

In a study of 14,350 smokers with COPD, varenicline re-

duced the risk of heart failure and depression by 44% (hazard ratio [HR], 0.56; 95% CI, 0.34–0.92) and 27% (HR, 0.73; 95% CI, 0.61–0.86), respectively<sup>18</sup>.

A study that followed up 3233 smokers with COPD from 2008 to 2012 found that compared those aged 70 years or older, subjects between 50 and 69 years old and between 30 and 49 showed lower quit rates (HR, 0.84; 95% CI, 0.71–0.99 and HR, 0.53; 95% CI, 0.37–0.76, respectively). Moreover, low socioeconomic status (HR, 0.79; 95% CI, 0.67–0.94), living alone (HR, 0.75; 95% CI, 0.64–0.88), being jobless, and being in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) D group compared to the GOLD A group (HR, 0.70; 95% CI, 0.54–0.90) were associated with low smoking cessation rates.

In smokers with COPD, those who are young and had low socioeconomic status had particular difficulty quitting smoking<sup>19</sup>. Therefore, when providing smoking cessation treatment for smokers with COPD, it is necessary to focus on the characteristics of each subgroup and to offer customized options.

### 5. Smoking cessation treatment for smokers with cardiovascular diseases

Smoking is a major risk factor that contributes to the development and exacerbation of cardiovascular disease. Moreover, smoking cessation can prevent mortality caused by cardiovascular disease. In a study that followed 3,251 subjects for 25 years, in which 631 cases of cardiovascular disease occurred, among participants without diabetes, the incidence rates of cardiovascular disease were 5.9% for smokers (95% CI, 4.9–7.1); 3.2% for people who had quit smoking just recently (95% CI, 2.1–4.5); 3.1% for people who had quit smoking a long time previously (95% CI, 2.6–3.7); and 2.4% for non-smokers (95% CI, 2.0–3.0). These findings demonstrate that the incidence of cardiovascular diseases continuously decreased according to smoking status (lower in non-smokers than in smokers) and the duration of smoking cessation.

After adjusting for the risk factors of cardiovascular disease, compared to current smokers, those who had quit smoking just recently and those who had quit smoking a long time previously showed decreased risk, with HRs of 0.47 (95% CI, 0.23–0.94) and 0.46 (95% CI, 0.34–0.63), respectively<sup>20</sup>. In a meta-analysis, in smokers with cardiovascular disease, varenicline and bupropion significantly increased abstinence from smoking (RR, 2.64; 95% CI, 1.34–5.21 and RR, 1.42; 95% CI, 1.01–2.01, respectively) compared to the placebo group. However, NRT did not clearly show significant effects (RR, 1.22; 95% CI, 0.72–2.06)<sup>21</sup>.

## Conclusion

The methods of smoking cessation treatment should be

tailored to smokers according to special populations such as adolescents, pregnant and breastfeeding women, and those with combined diseases. The main strategy of smoking cessation for adolescents and pregnant women is counselling except a few cases of NRT trial. NRT, varenicline, and bupropion can be used safely as first line medications for smoking cessation in most of smokers as well as special populations such as smokers with psychiatric disorder, cardiovascular disease, and COPD excluding pregnant women and those under 18 years old.

## Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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