

# Bupropion for smoking cessation in adolescents

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## Abstract

**Question** An adolescent who smokes regularly came to my clinic for help quitting. While I am aware that bupropion is a first-line medication for smoking cessation among adults, is it effective and safe for adolescents?

**Answer** Most adolescent smokers in Canada would like to quit, but more than 90% of the attempts are unsuccessful. Bupropion appears to be more effective than other pharmacologic options in improving abstinence among adolescents who smoke in the short term; however, it is not approved by Health Canada for those younger than 18 years. Bupropion has not been associated with an increase in adverse events in smoking cessation trials. More research is needed on the long-term effectiveness and safety of bupropion in this population.

Preventing tobacco product use among adolescents is essential, as nearly 90% of smokers tried their first cigarette before 18 years of age.<sup>1</sup> Smoking increases the risk of premature death by an average of 10 years, but those who quit before 34 years of age may regain this loss of life expectancy.<sup>2</sup> While prevalence of smoking has steadily decreased in Canada over the past 20 years, 2017 data from the Canadian Tobacco Use Monitoring Survey and the Canadian Student Tobacco, Alcohol and Drugs Survey reported that close to 8% of Canadians aged 15 to 19 years are smokers.<sup>3</sup> This may be an underestimation when considering the validity of adolescent self-reporting<sup>4</sup> and the survey's exclusion of territory residents and those without telephones.<sup>3</sup> Furthermore, it is unclear how the legalization of recreational cannabis in Canada may impact cigarette use among youth. In a United States study with more than 1 million adolescent participants, cigarette use decreased in grade 8 students but increased in grade 12 students after medical marijuana law enactment (odds ratio [OR]=0.74, 95% CI 0.66 to 0.82,  $P \leq .0001$ ; and OR=1.17, 95% CI 1.06 to 1.29,  $P = .0026$ ; for grade 8 and grade 12 students, respectively).<sup>5</sup>

More than 60% of current Canadian smokers aged 15 to 19 years report having attempted to quit at some point, but only 8% of attempts were successful.<sup>3</sup> The use of electronic cigarettes is becoming increasingly popular among adolescents and potentially serves as a gateway to other tobacco products,<sup>6</sup> further highlighting the growing need for effective smoking cessation interventions for young people.

According to the Canadian Action Network for the Advancement, Dissemination and Adoption of Practice-informed Tobacco Treatment guidelines, little empirical evidence is available regarding pharmacotherapy for adolescent smoking cessation, such as nicotine replacement therapy, varenicline, or bupropion.<sup>7</sup> Similarly, a recent statement by the US Preventive Services Task Force concluded that there is insufficient evidence to recommend behavioural counseling interventions or pharmacotherapy for adolescent smoking cessation.<sup>8</sup>

## Bupropion efficacy for smoking cessation

Originally developed as an atypical antidepressant, bupropion's anti-smoking effect is hypothesized to work through the inhibition of dopamine and noradrenaline reuptake and the blockade of nicotinic acetylcholine receptors, although the exact mechanism of action is largely unknown.<sup>9</sup> A Cochrane review of 267 studies suggests that bupropion is a first-line option for smoking cessation in adults, reporting bupropion and nicotine replacement therapy to be similarly superior to placebo in improving abstinence (OR=1.82, 95% CI 1.60 to 2.06; and OR=1.84, 95% CI 1.71 to 1.99; for bupropion and nicotine replacement therapy, respectively).<sup>10</sup>

Among the first to explore bupropion's anti-smoking effects in adolescents was an Austrian group more than 15 years ago. Twenty-two adolescents 16 to 19 years of age received bupropion (150 mg/day) or placebo for 90 days, and 55% (6 of 11) of those in the bupropion group self-reported abstinence (confirmed by breath carbon monoxide testing) at treatment conclusion compared with 18% (2 of 11) in the placebo group ( $P = .0014$ ). Mean cumulative abstinence durations were 78.4 and 30.2 days, respectively ( $P = .0042$ ), for this small sample.<sup>11</sup>

A larger study sought to investigate the role of bupropion in augmenting behavioural therapy for adolescents quitting smoking.<sup>12</sup> Among 312 adolescent smokers receiving bupropion (150 mg/day or 300 mg/day) or placebo with weekly brief individual counseling for 6 weeks, those receiving 300 mg of bupropion (but not 150 mg) reported superior 7-day point prevalence abstinence rates compared with placebo at the end of week 6 of treatment (14.5% vs 5.6%,  $P = .03$ ).<sup>12</sup> However, the significant effect was lost at 26 weeks' follow-up (13.9% vs 10.3%,  $P = .28$ ).<sup>12</sup> The 7-day point prevalence abstinence was self-reported, then biochemically confirmed by either urinary cotinine level at treatment conclusion or by exhaled carbon monoxide level at 26 weeks' follow-up.<sup>12</sup> While bupropion with brief individual counseling was efficacious during treatment, relapse was documented soon after discontinuation.<sup>12</sup> The 6-week treatment regimen was a limitation compared with the

typically longer treatment duration for up to 12 weeks as recommended for adults.<sup>10</sup>

In a Cochrane review with more than 13 000 participants younger than 20 years, no pharmacologic interventions were reported to be efficacious in increasing smoking abstinence rates at 6 months' follow-up (nicotine replacement therapy, risk ratio=1.11, 95% CI 0.48 to 2.58; bupropion, risk ratio=1.49, 95% CI 0.55 to 4.02).<sup>13</sup> Notably, this review only included trials with at least 6 months' follow-up, excluding 2 bupropion trials with shorter study durations.<sup>13</sup> A more recent meta-analysis included all 4 available bupropion trials among the 9 total studies, reporting that only bupropion was associated with an increased abstinence rate at the longest follow-up period in each study validated by biochemical markers (relative risk=2.03, 95% CI 1.09 to 3.77).<sup>14</sup> In the pooled analysis of all pharmacotherapies (nicotine patch, nicotine gum, bupropion, nicotine nasal spray), increased abstinence rates were maintained only for 4 weeks' follow-up (relative risk=1.87, 95% CI 1.22 to 2.87), whereas no effect was demonstrated for longer follow-up periods at 8, 12, 24, and 52 weeks.<sup>14</sup> These findings suggest that bupropion may be the only effective pharmacotherapy for adolescents to quit smoking, but no option has yet to demonstrate long-term increased abstinence.<sup>14</sup>

### Challenges with bupropion therapy

While most adolescent smokers say they would like to quit,<sup>3,15</sup> a multitude of factors including cultural background, gender, peer and family support, mental health conditions, and personal needs and preferences result in a low rate of quitting in this population.<sup>16</sup>


A particular challenge with bupropion therapy is its lack of evidence for long-term effectiveness in adolescents.<sup>14</sup> Among the available trials, clinically significant increased abstinence rates have been short term and limited to the treatment period.<sup>11,12,17,18</sup> Further investigation is warranted into bupropion's long-term efficacy in adolescent smokers.

The importance of medication adherence was demonstrated by a study of 95 adolescent smokers receiving 300 mg of bupropion daily for 6 weeks. Among those who took at least 80% of the prescribed medication, the cotinine-confirmed abstinence rates were significantly higher (12 of 58, 20.7%) compared with those with low adherence (0 of 37). These findings reinforce the value of addressing obstacles to adherence when assessing treatment effectiveness.<sup>19</sup>

Finally, Health Canada has not approved any antidepressants for use in children younger than 18 years,<sup>20</sup> raising safety concerns for bupropion therapy in this population. Common adverse events including headache, irritability, insomnia, or dream disturbances affected 64% of those taking bupropion in a trial of 134 adolescents,<sup>18</sup> but a pooled analysis of all adolescent

bupropion studies found no significant difference compared with those in the control groups,<sup>14</sup> perhaps reflecting the general symptoms of nicotine withdrawal. Two serious adverse events (1 involving recreational jimson weed (*Datura stramonium*), 1 an intentional overdose) were reported among 312 adolescents in 1 of the trials.<sup>12</sup>

### Conclusion

Early smoking cessation is essential to prevent use in adulthood and premature death. Bupropion is the most effective pharmacologic option in improving abstinence rates among adolescent smokers. However, this clinical benefit has been limited to the treatment period and its long-term efficacy remains inconclusive. Further research is warranted on bupropion in this population, recognizing challenges to therapy, including individual differences, adherence, safety, and the evolving methods of tobacco use. 

#### Competing interests

None declared

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