Nicotine Patch Therapy in 101 Adolescent Smokers
Efficacy, Withdrawal Symptom Relief, and Carbon Monoxide and Plasma Cotinine Levels
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Objectives: To determine the efficacy of nicotine patch therapy in adolescents who want to stop smoking and to assess biochemical markers of smoking and nicotine intake.

Design: Nonrandomized, open-label trial using a 15 mg/16 h patch.

Setting: Two midwestern cities.

Subjects: One hundred one adolescents aged 13 through 17 years smoking at least 10 cigarettes per day (cpd).

Intervention: Six weeks of nicotine patch therapy and follow-up visits at 12 weeks and 6 months.

Main Outcome Measures: Self-reported smoking abstinence verified by expired-air carbon monoxide (CO) level of no more than 8 ppm, nicotine withdrawal symptoms, and plasma cotinine level.

Results: Forty-one participants were female (mean ± SD age, 16.5 ± 1.1 years). Median baseline smoking rate was 20.0 cpd (range, 10-40 cpd). Biochemically confirmed point prevalence smoking abstinence was 10.9% (11/101) at 6 weeks and 5.0% (5/101) at 6 months. The mean ± SD plasma cotinine level at baseline was 1510.9 ± 732.7 nmol/L; for nonsmoking subjects at weeks 3 and 6, 607.8 ± 386.2 and 710.0 ± 772.5 nmol/L, respectively. Plasma cotinine levels were correlated with CO levels at baseline (r = 0.27; P = .006), week 3 (r = 0.34; P = .004), and week 6 (r = 0.26; P = .03) and with mean cigarettes smoked per day during weeks 3 (r = 0.24; P = .04) and 6 (r = 0.30; P = .02). Mean smoking rates decreased significantly during the study, an effect that lessened at 12 weeks and 6 months.

Conclusions: Nicotine patch therapy plus minimal behavioral intervention does not appear to be effective for treatment of adolescent smokers. Plasma cotinine and CO levels appear to be valid measures of smoking rates during the cessation process, but not at baseline. Smoking rates were reduced throughout the study. Additional pharmacological and behavioral treatments should be considered in adolescent smokers.


Editor’s Note: Just think. If this had worked, the ad folks could have packaged the intervention as nico-teen patches. Too bad—for everyone.

Catherine D. DeAngelis, MD

SMOKING PREVALENCE among adolescents has increased recently.1 The percentage of 8th and 10th graders reporting having smoked during the past 30 days increased almost 50% from 1991 through 1995 and for high school students reached 36.4% in 1997.2,3 Furthermore, in 1991, 28% of US high school seniors had smoked cigarettes in the past 30 days, but by 1998 this had increased to 35.1%.4,5 The persistence of smoking among adolescents will increase the public health burden of smoking,2 thus underscoring the need for intensifying intervention efforts among adolescent smokers.

The natural history of smoking cessation among adolescents has shown abstinence rates of 0% to 11%.6-8 Nicotine dependence develops among adolescent smokers, and they exhibit withdrawal symptoms similar to those of adults when they try to stop smoking.6-8 In adolescent smokers, scores for the Fagerstrom Tolerance Questionnaire and the Fagerstrom Test for Nicotine Dependence have been in the range seen among adult smokers with comparable smoking rates.9,10,11 Moreover, 3 of 4 adolescent smokers have tried unsuccessfully to stop
SUBJECTS AND METHODS

This study was approved by the Mayo Institutional Review Board, Rochester, Minn, and performed in Rochester and La Crosse, Wis. Subjects were recruited by fliers in schools, press releases, and television and radio announcements. A telephone interview determined the initial eligibility. Adolescents aged 13 through 17 years in general good health who smoked at least 10 cpd for at least the past year and were motivated to stop smoking were eligible for inclusion. Pregnancy, lactation, current use (within the past 30 days) of major psychoactive drugs (eg, major tranquilizers, neuroleptics, or antidepressants), use of nicotine replacement therapy or other tobacco products, and current enrollment in a smoking cessation program were exclusion criteria.

Adolescents who qualified through the telephone screen were invited, along with a parent or guardian, to an informational meeting where an overview of the study and a discussion of its requirements were presented. Signed informed consent was obtained from all adolescents and a parent or legal guardian. Questionnaires for smoking (including the Fagerstro¨m Test for Nicotine Dependence18) and drinking behavior (Self-Administered Alcoholism Screening Test19) were completed, expired-air carbon monoxide (CO) testing was performed, and blood was drawn for measurement of a baseline (while the subjects were smoking their usual number of cigarettes) plasma cotinine level. Female adolescents of childbearing potential were required to have a negative result of a pregnancy test before study entry. Adolescents were given a daily diary to record the number of cigarettes smoked and the nicotine withdrawal symptoms experienced between the informational meeting and their first clinic visit before their target quit date. Nicotine withdrawal symptoms included desire to smoke; anger, irritability, or frustration; anxiety or nervousness; difficulty concentrating; impatience or restlessness; hunger; awakening at night; and depression.20 Each symptom was scored as none (0), slight (1), mild (2), moderate (3), or severe (4). At the first clinic visit, a physician collected medical history information (including the adolescent’s self-report of medical and psychiatric problems), performed a brief physical examination, and delivered a strong, personalized message about smoking cessation to each subject according to the guidelines of the National Cancer Institute.41 Subjects were instructed in the use of the nicotine patch (Nicotrol; 15 mg/16 h) and were given self-help material from the package insert used in the over-the-counter product. Brief individual counseling (10-15 minutes) was provided by a trained study assistant at the subject’s request. No additional materials or behavioral instructions were provided. All subjects returned for weekly visits during the 6 weeks of nicotine patch therapy. At each visit, the daily diaries were collected, vital signs were measured, and CO testing of expired air was performed. Used and unused patches were collected, and a new supply was dispensed. Adverse events and concomitant medication information was recorded. At weeks 3 and 6, plasma cotinine levels were recorded, and a pregnancy test was performed for female participants. Subjects returned at 12 and 26 weeks for assessment of self-reported smoking status and expired-air CO testing. During the week 26 visit, adolescent subjects were interviewed to ascertain their expectations regarding their study participation, to assess aspects of the study that were perceived as helpful or nonhelpful, and to determine their future smoking cessation efforts among adolescents. Study participants received $100 in remuneration on study completion.

The target sample size for this study was 100 adolescents. We overrecruited and ended with 101 adolescents. The sample size of 100 was based on providing a 95% confidence interval (CI) width ranging from 10% to 20% for an end-of-treatment abstinence rate ranging from 5% to 30%. The sample consisted of the first 101 subjects who met all eligibility criteria. Other than being motivated to stop smoking, there was no selection bias based on level of motivation.

For weekly point-prevalence abstinence rates, subjects were considered abstinent from smoking if they self-reported not smoking during the 7 days before a visit and had an expired-air CO level of no more than 8 ppm at that visit. In all cases, an intent-to-treat analysis was performed. Subjects missing visits for any reason were considered to be smoking.

Self-reported smoking rates as reported in the daily diary were summarized as mean cigarettes per day and change from baseline. The data were summarized with weekly means for each of the 6 weeks of the medication phase and at the 12-week and 6-month follow-up visits. The mean change in cigarettes per day was compared with 0 using the 1-sample t test.

The mean change in plasma cotinine level from baseline was calculated at weeks 3 and 6 and compared with 0 using the 1-sample t test. We also assessed the relationship between plasma cotinine level, expired-air CO measurement, and reported smoking rate in cigarettes per day for baseline and at each visit using linear correlation.

For each subject, withdrawal symptoms were assessed daily with a composite withdrawl score computed as the mean score of the 8 items from the daily diary. A baseline withdrawal score was calculated for each subject using data from all diaries completed before their target quit date. The data were summarized daily for the first week following the target quit date and with weekly means for each week of treatment. The mean change in withdrawal score from baseline was compared with zero using the 1-sample t test. In all cases, 2-tailed P values of no greater than .05 were considered as evidence of findings not attributable to chance. Unless otherwise indicated, data are given as mean ± SD.

smoking at least once.6 Adolescents who become regular smokers indicate that important reasons for continuing to smoke are addiction or habit, pleasure, reduction of negative affect, and being around other smokers.15-16 Thus, adolescents who are regular smokers have many characteristics similar to those of adult smokers.

Despite the realization that nicotine dependence begins in the teenage years, very little work has been done to provide intervention for adolescent smokers. In a pilot nicotine patch study of 22 adolescent smokers, withdrawal symptom relief and a significant reduction in the number of cigarettes smoked per day (cpd) were observed, but only 1 adolescent maintained abstinence at 1 year.10 In a recent review of the behavioral treatment of smoking among adolescents, end-of-treatment abstinence rates averaged 21% (range, 0%-36%), whereas abstinence rates at 3 to 6 months fell to an average of 13%.17 Most studies reported rates of smoke-
ing reduction but not cessation and were subject to a number of methodological limitations.

We undertook this trial to determine if there was evidence of efficacy of nicotine patch therapy in adolescent smokers and to assess biochemical markers of smoking and nicotine intake as they relate to self-reported smoking rates in adolescent smokers.

## RESULTS

The 101 adolescents were recruited within a 3-month period from March 1 through May 30, 1997, and we had more potential volunteers than were needed for the study. Their baseline characteristics are presented in Table 1. In addition, 95.0% were white. A history of major depression was reported by 23.8% of the subjects; a history of alcohol abuse or dependence by 23.8%; a history of other drug abuse or dependence by 19.8%; and a history of attention deficit or attention-deficit/hyperactivity disorder by 15.8%.

There were 71 adolescents who completed the entire 6 weeks of patch therapy. Of the 30 who did not complete patch therapy, 24 subjects (80%) withdrew consent, 5 subjects (17%) discontinued study participation because of an adverse event, and 1 subject (3%) was unavailable for follow-up. Ten (33%) of these 30 subjects failed to return for any visits following baseline. For the 91 subjects who returned for visits during the 6 weeks, the average number of days' participation was 38 ± 8 days (median, 42 days; range, 10-42 days). Patch use was reported in the daily diaries of patch therapy, the average number of days' participation was 38 ± 8 days (median, 42 days; range, 10-42 days). Patch use was reported in the daily diaries for 85% ± 20% (median, 95%; range, 4%-100%) of the days during that duration. Fifty-eight adolescents returned for the 6-month visit. Eighty-seven subjects reported experiencing at least 1 adverse event during the 6 weeks of patch treatment. The most commonly reported adverse events were upper respiratory tract infections (44 subjects [44%]), headache (43 [43%]), nausea and/or vomiting (13 [13%]), skin reaction at the patch site (12 [12%]), and sleep disturbance (10 [10%]). There was no difference in the frequency of adverse events in those adolescents who completed the patch therapy compared with those who did not.

The biochemically confirmed 7-day point-prevalence smoking abstinence rates and 95% CIs are presented in the following tabulation:

<table>
<thead>
<tr>
<th>Time</th>
<th>% (95% CI) of Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1</td>
<td>7.9 (3.5-15.0)</td>
</tr>
<tr>
<td>Week 2</td>
<td>9.9 (4.9-17.5)</td>
</tr>
<tr>
<td>Week 3</td>
<td>14.9 (8.6-23.3)</td>
</tr>
<tr>
<td>Week 4</td>
<td>12.0 (7.0-21.0)</td>
</tr>
<tr>
<td>Week 5</td>
<td>14.9 (8.6-23.3)</td>
</tr>
<tr>
<td>Week 6</td>
<td>10.9 (5.6-18.7)</td>
</tr>
<tr>
<td>12-Week Follow-up</td>
<td>5.0 (1.6-11.2)</td>
</tr>
<tr>
<td>6-Month follow-up</td>
<td>5.0 (1.6-11.2)</td>
</tr>
</tbody>
</table>

All 101 subjects who entered the trial were included in this analysis (intent to treat). Only those who had biochemically confirmed smoking abstinence are included in the numerator. At the end of patch therapy, 11 (10.9%; 95% CI, 5.6%-18.7%) of the 101 subjects were abstinent. By the 6-month visit, only 5 (5.0%; 95% CI, 1.6% to 11.2%) subjects were abstinent from smoking. The end-of-treatment abstinence rate for the 76 adolescents with Fagerström Test for Nicotine Dependence scores of no greater than 6 was not significantly different compared with that of the 25 adolescents with Fagerström scores of greater than 6 (11.8% vs 8.0%, respectively). There was no statistically significant effect of the presence of other smokers in the household on the adolescent smoking abstinence rates at either time point.

Self-reported smoking rates and CO levels of expired air for all adolescents and for only those smoking at each time point are presented in Table 2. Overall, and for the smokers only, the adolescents had reduced their smoking significantly from baseline throughout the study. Some of the adolescents classified as smokers at a clinic visit had reported smoking no cigarettes in their daily diaries, but reported on interview smoking within the past 7 days or had expired-air CO levels of greater than 8 ppm.
The mean plasma cotinine levels are presented in Table 3. The mean cotinine level for the adolescents was significantly lower than baseline at weeks 3 (P < .001) and 6 (P < .001). The mean cotinine level for the adolescents who were not smoking at week 3 was also significantly lower than baseline (P = .009), but at week 6 it was not. Adolescents who were smoking at weeks 3 and 6 had a mean cotinine level of 1175.8 ± 681.6 and 1005.4 ± 573.7 nmol/L, respectively. Both were significantly lower than at baseline (P < .001).

Using Pearson correlation analysis, the mean plasma cotinine levels were found to be significantly correlated with CO levels at baseline (r = 0.27; P = .006) and at weeks 3 (r = 0.34; P = .004) and 6 (r = 0.26; P = .03) and with mean cpd during weeks 3 (r = 0.24; P = .04) and 6 (r = 0.30; P = .02). The CO levels were significantly correlated with mean cpd, with correlation coefficients ranging from 0.39 to 0.44 during weeks 1, 2, 3, and 5 (P < .001 for each week), and at weeks 4 and 6 (r = 0.25; [P = .03] vs r = 0.24; [P = .05], respectively). Baseline cotinine and CO levels were not significantly correlated with baseline cpd. After adjusting for the time since last cigarette before each weekly visit, the only significant association among cotinine level, CO level, and mean cpd was at baseline for the mean cpd during weeks 3 (P = .04) and 6 (P < .001 for each week). The only significant association among cotinine level, mean cpd during weeks 3 (P = .04) and 6 (P = .03; [P = .05], respectively). Baseline cotinine and CO levels were not significantly correlated with baseline cpd. After adjusting for the time since last cigarette before each weekly visit, the only significant association among cotinine level, CO level, and mean cpd was at baseline for the mean cotinine and CO level correlation. Time since last cigarette was found to be highly associated with CO level, having significant correlations at baseline and at weeks 1, 2, 4, 5, and 6. Correlations ranged from −0.32 to −0.56.

The mean (± 1 SD) nicotine withdrawal scores are shown in the Figure. On day 1 of the first week, the adolescents had a slight increase in nicotine withdrawal scores compared with baseline (mean change, 0.2 ± 0.7; P = .04). By the second week, mean withdrawal scores had significantly reduced from baseline and remained that way through week 6 (P < .05 for each week).

At the 6-month follow-up visit, 53 of the 58 adolescents who returned were interviewed by one of us (C.A.P.) and Nicotine Research Center staff using a structured interview. The primary reasons cited for enrollment in a study to stop smoking were health concerns (21 subjects [40%]), financial incentives of the study (15 [28%]), and peer or parental advice to stop smoking (8 [15%]). When asked how much the study was going to help them, 34 (64%) of the adolescents were unsure, 13 (25%) said that they thought it would help them reduce their smoking, and 6 (11%) reported that they thought the patches would help them stop smoking. When asked what they liked about the study, 21 subjects (40%) indicated that they liked the opportunity to quit smoking or reduce the number of cigarettes they smoked, 15 (28%) liked the free patches, 14 (26%) liked the money for participation, and 7 (13%) liked follow-up visits. When asked what they did not like about the study, 10 subjects (30%) said there was nothing they disliked, 12 (23%) disliked completing the daily diaries or returning used patches, 10 (19%) did not like the commute or weekly visits, and 6 (11%) did not like wearing the patches. Adolescents were also asked to indicate the most and least helpful parts of the study in terms of their effort to stop smoking. The patches (24 subjects [45%]) and weekly visits (13 [25%]) were reported as the most helpful aspects. Most adolescents (38 [72%]) said there was nothing unhelpful or were unsure. Least helpful things included the diaries and forms (7 subjects [13%]) and the patches (6 [11%]).

Adolescents were also asked to describe helpful and nonhelpful behaviors of household members during their efforts to stop smoking. Helpful behaviors included talking to the adolescent about the program and quitting smoking, not smoking near the adolescent, restricting smoking or access to cigarettes in the household, encouragement, praise, reinforcement, reminders, and driving with the adolescent to appointments. Nonhelpful behaviors included smoking near the adolescent, access to cigarettes in the household, not talking to the adolescent about the study or his or her progress at cessation, and nagging or bothering the adolescent to stop smoking.

Finally, the adolescents were asked how someone should go about encouraging them to stop smoking. Responses indicated that 36% (19 subjects) would be helped by support or encouragement, 23% (12 subjects) said by keeping cigarettes away from them or not smoking near them, and 13% (7 subjects) by providing more information on how

Table 2. Adolescent Smoking Rates and Carbon Monoxide Levels*

<table>
<thead>
<tr>
<th>Time</th>
<th>Overall</th>
<th>Smokers Only†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cigarettes per Day</td>
<td>CO, ppm</td>
</tr>
<tr>
<td></td>
<td>No. of Subjects</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Baseline‡</td>
<td>101</td>
<td>18.2 ± 6.2</td>
</tr>
<tr>
<td>Week 1</td>
<td>90</td>
<td>1.8 ± 2.2</td>
</tr>
<tr>
<td>Week 2</td>
<td>86</td>
<td>1.8 ± 2.6</td>
</tr>
<tr>
<td>Week 3</td>
<td>82</td>
<td>1.9 ± 2.7</td>
</tr>
<tr>
<td>Week 4</td>
<td>75</td>
<td>2.2 ± 3.1</td>
</tr>
<tr>
<td>Week 5</td>
<td>73</td>
<td>2.1 ± 2.9</td>
</tr>
<tr>
<td>Week 6</td>
<td>70</td>
<td>2.5 ± 3.5</td>
</tr>
<tr>
<td>3 Months</td>
<td>35</td>
<td>9.1 ± 6.8</td>
</tr>
<tr>
<td>6 Months</td>
<td>49</td>
<td>9.4 ± 6.5</td>
</tr>
</tbody>
</table>

*CO indicates carbon monoxide.
†Indicated by smoking status at each specified time. Some smokers had recorded 0 cigarettes per day in the daily diaries, but were classified as smoking with a CO level of greater than 8 ppm or had reported smoking within the past 7 days at the visit.
‡All adolescents were smokers at baseline.
to stop. When asked how they would advise a friend to stop smoking, 21 subjects (40%) were unsure, 10 (19%) would advise using the patches, and 7 (13%) would recommend having some type of substitute for smoking.

**COMMENT**

Our results indicate that nicotine patch therapy plus minimal behavioral intervention is not effective for smoking cessation in adolescent smokers. Our 6-month abstinence rate of 5% appears lower than some of the estimates of the natural history of smoking cessation in adolescents that range from 0% to 11%.6-8 These findings are similar to those of a pilot study of patch therapy in adolescents using a 22 mg/24 h patch and a group-based behavioral intervention.10 A limitation of our study is that it was an open-label rather than a placebo-controlled design. However, as in the previous trial, the stop rates with active treatment were very low, whereas in adults, the abstinence rates have been consistently much more robust.22 We were encouraged by the large number of adolescent smokers who responded to this study and by the interest among adolescent smokers to try to stop smoking, which is markedly different from the findings of the adolescent study in 1993-1994.10 However, the adolescents in our study were motivated to stop smoking and had to have parental or guardian permission to enroll; therefore, they may not be representative of all teenage smokers. However, some individuals may have enrolled seeking the money rather than being seriously motivated to stop smoking. Despite our negative results, research on other pharmacological treatments and/or more intensive behavioral counseling interventions tailored to adolescents are clearly needed to learn how to assist young smokers effectively in stopping.

Our study adds to the knowledge of plasma cotinine and expired-air CO levels in adolescent smokers, which may be useful in developing alternative pharmacological interventions for adolescent smokers. The cotinine levels in the abstinent adolescents appear to be evidence of their compliance in using this pharmacotherapy. Despite lower mean smoking rates (18.2 ± 6.2 vs 23.3 ± 5.0 cpd; P<.001), the baseline cotinine levels of the adolescent smokers in our study were higher than those observed in the previous, smaller study (1510.9 ± 732.7 vs 829.3 ± 477.1 nmol/L; P<.001).10 The baseline cotinine levels in our study seem to be comparable with those in adults and do not support the notion that there may be metabolic differences in adolescents, which was speculated as a reason for the difference observed in the earlier trial. The week 3 vs week 4 cotinine levels were comparable, at 1073.5 ± 670.2 vs 1119.0 ± 522.5 nmol/L (present vs previous study, respectively). After adjusting for concomitant smoking, there were no significant differences in cotinine levels at weeks 3 and 6 for the adolescents in our study compared with the week 4 plasma cotinine levels of the 22 adolescents from the previous patch study.

When we restricted the analysis to the 14 abstinent adolescents from our study, the week 3 mean cotinine level was only 607.8 ± 386.2 nmol/L, compared with the mean baseline level of 1510.9 nmol/L. Plasma cotinine levels were significantly correlated with reported cigarettes smoked per day at weeks 3 and 6, but not at baseline. Not observing a significant correlation between baseline smoking rate and plasma cotinine is different from previous observations made in light, moderate, and heavy adult smokers.23 We believe this may be caused by rounding to the nearest 5 or 10 cigarettes the adolescent smokers reported when asked their smoking rate at baseline, or it could be the result of individual variation in smoking behavior. We also observed a significant correlation between expired-air CO level and smoking rate at most time points throughout the study. The reliability of the adolescents’ self-report is supported by the correlation of expired-air CO levels.
level with smoking rate and also with plasma cotinine levels. We also were encouraged by the compliance of the adolescent smokers in reporting through their daily diaries and their compliance in the use of the nicotine patch. However, more information is needed on these biochemical measures in adolescent smokers and their relationship to the adolescent’s smoking rate.

In addition, we observed a reduction in nicotine withdrawal symptoms from baseline, but not to the degree observed in the earlier patch study. Just as in adults, this raises concern of adequacy of nicotine replacement in adolescents. Additional pharmacological alternatives should be considered in adolescent smokers, including other nicotine replacement products and/or bupropion hydrochloride, none of which has been tested in adolescents.

As with pharmacological therapy, little is known about the efficacy of behavioral treatment for adolescent smokers. Most cessation programs to date have been school-based and include some type of cognitive behavioral intervention such as instruction in coping skills. Our study provided no behavioral intervention aside from the self-help material packaged with the over-the-counter medication and the brief counseling provided when requested at the weekly visits. Intervention concepts that seem to be endorsed by participants in our study include receiving advice about smoking cessation from people they know or who care about them or from a smoker who has stopped successfully; emphasis on the positive benefits of smoking cessation; and a desire to be involved in their own treatment decisions and to set their own progress and treatment goals.

Presence of other smokers in the household is a predictor of poorer smoking cessation outcome in adult smokers, but this may not be invariably the case in adolescent smoking adoption or maintenance. Our data indicate that there was no significant effect on adolescent abstinence rates by the presence of other smokers in the household, despite the higher percentage of other smokers in the household compared with adult smokers. Little information is available to help parents or other household members (smokers or nonsmokers) to be supportive of adolescents attempting to stop smoking. The adolescents we interviewed were quite specific about behaviors by others in the household that would be helpful and behaviors perceived not to be helpful. Although these findings are limited by the number of adolescents who were interviewed, they suggest several program components that could be included in the design of future interventions. As with the previous trial, we observed a substantial reduction in smoking rates throughout the treatment period as well as during the 6-month follow-up. Studies in adult smokers suggest that reduction in smoking is not a valid end point in clinical trials and that any smoking during the initial 2 weeks of patch therapy predicts poorer long-term cessation. However, the long-term effect of smoking reduction in adolescents is not known, and fewer cigarettes smoked per day could mean that fewer behavioral changes will be needed during the next attempt to stop. Perhaps a behavioral intervention should be developed to capitalize on the smoking reduction that occurs after nicotine patch therapy in adolescent smokers that would provide the necessary boost to complete the cessation process.

Consistent with other studies, many of our subjects reported a history of comorbid psychiatric diagnoses, such as major depression, alcohol abuse or dependence, or other drug use. Thus, a high score in adolescents likely indicates a problem. In adults, a history of alcohol or other drug use has been associated with more difficulty in stopping smoking. Moreover, adult smokers with a history of major depression may have a lower cessation rate than those without such a history, although there is disagreement from the various studies. To our knowledge, the effect of a history of comorbid psychiatric factors on smoking cessation treatment outcomes has not been studied in adolescents, an obvious deficit given the frequency of these conditions in adolescent smokers.

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