

# Major Depression Following Smoking Cessation

Lirio S. Covey, Ph.D., Alexander H. Glassman, M.D., and Fay Stetner, M.A., M.P.A.

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**Objective:** The authors examined the incidence and predictors of major depression following successful smoking cessation treatment, with special attention to the influence of past major depression. **Method:** Three-month follow-up data were obtained from 126 subjects who successfully completed a 10-week smoking cessation program. **Results:** The 3-month incidence of new major depression following treatment for nicotine dependence was 2%, 17%, and 30% among subjects with histories of no major depression, single major depression, and recurrent major depression, respectively. A history of major depression and persistent withdrawal symptoms independently predicted posttreatment major depression. **Conclusions:** Continued patient care beyond the 2–4-week period associated with the nicotine withdrawal syndrome is indicated when abstinence is attempted by smokers with prior major depression.

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Widespread recognition of the enormous health risks associated with cigarette smoking and the health benefits of quitting smoking has prompted the majority of smokers to attempt cessation (1). However, the demonstrated link between cigarette smoking and certain psychiatric disorders, particularly major depression (2), and the possibility that tobacco use may provide psychological relief for certain individuals (3) raise questions about the emotional aftermath of smoking cessation. Several studies have described the emergence of depressed mood during the nicotine withdrawal period (4–6); two of these studies, one based on a clinical sample (4), the other based on an epidemiological sample of young adults (5), found that postcessation depressed mood occurred more frequently among smokers with a history of major depression. The onset of emotional states resembling full-blown major depression during the nicotine withdrawal period has also been reported (2, 7, 8). Whether the period of vulnerability to a new episode of major depression extends beyond the usual 2–4-week duration of the nicotine

withdrawal syndrome, however, is not known. This study examined the frequency of new major depression during the 3-month period immediately following successful completion of a 10-week smoking cessation treatment and the effect of a pretreatment history of major depression on those events.

## METHOD

Data are based on 3-month follow-up information from 126 subjects successfully treated in a trial of clonidine for smoking cessation, which was described elsewhere (8). This group represents a 96% follow-up completion rate, based on 131 successfully treated subjects (27% of 486 participants) who had maintained abstinence (serum cotinine level of 15 ng/ml or less) through the end of a 10-week treatment period. All subjects were heavy smokers (20 or more cigarettes daily) who had failed in previous attempts to quit, had no current diagnosis of major depression or substance abuse or dependence, had not used psychotropic medication in the past 6 weeks, and had no lifetime diagnosis of a psychotic illness. Written informed consent for the follow-up phase was obtained from all study participants during their initial visit.

The group's mean age was 45.6 years (SD=11.2); 50% were women, 89% were white, 89% were college-educated, 46% were married, 54% had received clonidine, and 20% had a history of alcohol abuse or dependence. These distributions did not differ markedly from those of subjects who were treatment failures (N=355). However, the distribution by history of major depression among subjects who were successfully treated (N=131) (no history=72% [N=94], single episode of major depression=20% [N=26], recurrent major depression=8% [N=11]) differed significantly from that observed among subjects who did not maintain abstinence (N=355) (no history=64% [N=227], single major depression=16% [N=57], recurrent major depression=20% [N=71]; Pearson  $\chi^2=10.71$ ,  $df=2$ ,  $p<0.005$ ).

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Received March 18, 1996; revisions received June 19 and Aug. 13, 1996; accepted Aug. 21, 1996. From the Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, and the New York State Psychiatric Institute. Address reprint requests to Dr. Covey, Unit 116, New York State Psychiatric Institute, 722 West 168th St., New York, NY 10032.

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TABLE 1. Predictors of Major Depression Within 3 Months of Successful Participation in a 10-Week Smoking Cessation Program (N=126)

Predictor	Odds Ratio	Wald $\chi^2$ (df=1)	p
<b>Unadjusted logistic regression</b>			
Single episode of major depression (1=positive)	3.66	3.31	0.07
Recurrent major depression (1=positive)	7.86	6.52	0.01
Gender (1=female)	3.81	2.64	0.10
Beck Depression Inventory score at end of treatment (1=10 or more)	5.35	4.62	0.03
Withdrawal symptoms at end of treatment (1=9 or more)	11.92	5.29	0.02
Medication (1=clonidine)	0.73	0.20	n.s.
Age (years)	0.97	0.64	n.s.
Marital status (1=married)	0.53	0.77	n.s.
Nicotine dependence (1=high) <sup>a</sup>	1.23	0.09	n.s.
Past alcohol abuse or dependence (1=positive)	0.48	0.44	n.s.
Beck Depression Inventory score at baseline (1=10 or more)	1.00	0.00	n.s.
<b>Multiple logistic regression<sup>b</sup></b>			
Single episode of major depression	6.22	3.93	0.05
Recurrent major depression	15.50	6.94	0.008
Withdrawal symptoms at end of treatment	8.99	3.94	0.05

<sup>a</sup>On Fagerstrom Tolerance Questionnaire, high=7 or more.

<sup>b</sup>Full model:  $\chi^2=28.28$ ,  $df=11$ ,  $p<0.003$ ; final model:  $\chi^2=17.30$ ,  $df=3$ ,  $p<0.006$ .

We defined posttreatment major depression as the occurrence of symptoms that met five or more DSM-III-R criteria and lasted 2 weeks or more. Two individuals, both with past major depression, who met six criteria for major depression for less than 2 weeks but had reinitiated antidepressant medication within days of symptom onset because they felt their illness was returning, were also given a diagnosis of major depression.

The main predictor variable was a history of major depression obtained at screening through use of the Structured Clinical Interview for DSM-III-R (9). Selected variables were included as covariates because of their possible relationship with major depression relapse (10), i.e., age, gender, marital status, minor depression (defined as a Beck Depression Inventory [11] score of 10 or more at baseline or at end of treatment), and comorbid nonaffective psychiatric disorder (i.e., predominantly past alcohol dependence in our group), or because of their relationship with the cessation process, i.e., clonidine or placebo treatment, baseline nicotine dependence, and withdrawal symptoms at end of treatment. The Fagerstrom Tolerance Questionnaire (12) measured nicotine dependence level. Seven symptoms made up a nicotine withdrawal symptom inventory (craving, irritability, anxiety, restlessness, concentration difficulty, depressed mood, and increased appetite; alpha coefficient=0.86).

Logistic regression was employed to examine the association between posttreatment major depression and hypothesized predictors; stepwise (backward) multiple logistic regression was performed to test the independence of variables ( $p<0.10$ ). Design variables were created for testing the effect of two levels (single and recurrent) of past major depression. Statistical significance was set at the  $\alpha=0.05$  level (two-tailed test).

## RESULTS

Within 3 months of ending treatment, nine of 126 subjects had experienced a new episode of major depression. The incidence of posttreatment major depres-

sion was significantly different by major depression history: two (2%) of 91 subjects with no history, four (17%) of 24 subjects with past single major depression, and three (30%) of 10 subjects with past recurrent major depression (Pearson  $\chi^2=14.19$ ,  $df=2$ ,  $p<0.001$ ).

Table 1 shows that in addition to history of major depression, female gender, minor depression (Beck Depression Inventory score of 10 or more) at end of treatment, and high level of withdrawal symptoms at end of treatment were apparent risk factors for posttreatment major depression. Nonsignificant factors were clonidine versus placebo treatment, age, marital status, history of alcoholism, and minor depression at baseline. Multivariate analysis to adjust for confounding among the potential predictors, however, yielded significant associations only for single episode of major depression, recurrent major depression, and elevated withdrawal symptoms at the end of treatment.

## DISCUSSION

We observed a 3-month incidence of new major depression following smoking cessation treatment that was higher in the presence of past major depression, particularly the recurrent type, than with a nondepressed group. This effect occurred independently of other potential predictors of a new depressive episode. However, since follow-up information was not available for subjects who did not maintain abstinence, we are unable to conclude that nicotine abstinence provoked an incidence of posttreatment major depression among the group of successful abstainers that was greater than the rate among their counterparts who continued to smoke. Nevertheless, the 3-month major depression incidence rates of 17% and 30% observed among subjects with a single episode of major depression and recurrent major depression, respectively, in this study, are markedly higher than the rates commonly observed (13).

Persistent withdrawal discomfort also emerged as an independent predictor of posttreatment major depression. Among subjects who did not experience major depression following smoking cessation, withdrawal symptoms had abated by the end of treatment, about 10 weeks after the day they quit; in contrast, withdrawal symptoms had remained at moderate to severe levels among those who did experience a new episode of major depression.

Our study findings indicate the importance of obtaining information about history of depression and, when such a history is present, remaining alert to the possible onset of depression even weeks after smoking cessation treatment has ended. We have pilot data suggesting that fluoxetine and sertraline may be a useful cessation aid for smokers with prior major depression, and recent findings by S.M. Hall (unpublished paper, 1996) suggest that smokers with prior major depression benefit from mood-management counseling and nortriptyline as cessation aids. Whether those treatments will also prevent the onset of postcessation depression remains

to be examined. It also remains to be known whether effective management of withdrawal symptoms will prevent postcessation depression.

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