

Helping patients quit smoking: Lessons from the EAGLES trial

Samantha A. Gnanasegaram, MD, Cornel N. Stanciu, MD, MRO, and Saeed Ahmed, MD

Dr. Gnanasegaram is a psychiatrist, New Hampshire Hospital, Concord, New Hampshire, and a clinical instructor, Department of Psychiatric Medicine, Geisel School of Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire. Dr. Stanciu is a PGY-5 addiction psychiatry fellow, Department of Psychiatric Medicine, Geisel School of Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire. Dr. Ahmed is a PGY-3 general psychiatry resident, Department of Psychiatry, Nassau University Medical Center, East Meadow, New York.

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Psychiatrists often fail to adequately address their patients' smoking, and often underestimate the impact of ongoing tobacco use. Evidence suggests that heavy smoking is a risk factor for major depressive disorder; it also is associated with increased suicidal ideations and attempts.^{1,2} Tobacco use also has a mood-altering impact that can change the trajectory of mental illness, and alters the metabolism of most psychotropics.

Previously, psychiatrists may have been reluctant to prescribe the most effective interventions for smoking cessation—varenicline and bupropion—because these medications carried an FDA “black-box” warning of neuropsychiatric adverse effects, including increased aggression and suicidality. However, a large study called the EAGLES trial³ found that the neuropsychiatric risks associated with these medications were lower than previously thought. Consequently, in December 2016, the FDA removed the black-box warning related to serious mental health adverse effects from the labeling of varenicline and bupropion.⁴

The EAGLES trial was a large, multi-site global trial that included patients with and without mental illness. Its primary objective was to assess the risk of “clinically significant” adverse effects for individuals receiving varenicline, bupropion, nicotine replacement therapy (NRT), or placebo, and whether having a history of psychiatric conditions increased the risk of developing adverse effects when taking these therapies. Overall, 2% of smokers without mental illness experienced adverse effects, compared with 5% to 7% in the psychiatric cohort, regardless of treatment arm. The

rate of neuropsychiatric events and scores on suicide severity scales were similar across treatment arms in both cohorts.³

We should take lessons from the EAGLES trial. We propose that clinicians ask themselves the following 6 questions when forming a treatment plan to address their patients' tobacco use:

1. Does the patient meet DSM-5 criteria for nicotine use disorder and, if yes, what is the severity of his or her nicotine dependence? The Fagerstrom Test for Nicotine Dependence (FTND)⁵ is a 6-question instrument for evaluating the quantity of cigarette consumption, compulsion to use, and dependence. It provides clinicians with guidelines on preventing withdrawal by implementing NRTs, such as lozenges, an inhaler, patches, and/or gum. A score of 1 to 2 (low dependence) indicates that no NRT is needed; a score of 3 to 4 (low to moderate dependence) requires 1 NRT; and scores of 5 to 7 (moderate dependence) and ≥ 8 (high dependence) require a combination of NRTs.

In the EAGLES trial, all participants smoked at least 10 cigarettes per day, and



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had moderate dependence, with an average FTND score of 5 to 6.

2. What stage of change is the patient in, and how many times has he or she attempted to quit? Based on the answers, motivational interviewing may be appropriate.

In the EAGLES trial, the participants were motivated individuals who had on average 3 past quit attempts. Research suggests that even patients who have a serious mental illness can be motivated to quit (Box).⁶⁻⁹

3. What is the patient's mental health status? What is the patient's psychiatric diagnosis and how clinically stable is he or she? What is his or her suicide risk? Consider using the Columbia Suicide Severity Rating Scale (C-SSRS).¹⁰

In the EAGLES trial, the psychiatric cohort included only patients who had been clinically stable for the past 6 months and had received the same medication regimen for at least the past 3 months, with no expected changes for 12 weeks. Patients with certain diagnoses were excluded (eg, delusional disorder, schizophreniform disorder, impulse control disorders), and only 1% had a personality disorder, which increases mood lability and likelihood of suicidality behavior.

4. Does the patient have another comorbid substance use disorder? In the EAGLES trial, those who had active substance use in the past year or were receiving methadone or buprenorphine/naloxone were excluded.

5. Does the patient have any medical conditions? Does he or she have a history of seizures or eating disorders? It is important to determine if a patient has a seizure disorder or another medical condition that is a contraindication for using varenicline or bupropion.

In the EAGLES trial, most adverse effects related to the medications administered involved sleep (insomnia) or the gastrointestinal system (nausea). The psy-

Box

Mental illness and motivation to quit smoking

In the past, clinicians may have believed that many individuals with mental illness typically weren't motivated to quit smoking. We now know this is not the case and that such patients' motivation is similar to that of the general population, and the reasons driving their desire are the same—health concerns and social influences.⁶ Even individuals with serious mental illness such as schizophrenia who have a long history of tobacco use are highly motivated and persistent in their attempts to quit.^{7,8} The prevalence of future “readiness to quit” among individuals diagnosed with schizophrenia and depression ranges from 21% to 49%, which is similar to that among the general population (26% to 41%). Evidence also suggests that motivation translates into successful quitting, with quit rates of up to 22% for people with mental illness who use a combination of psychosocial and pharmacological interventions.⁹

Research suggests that even patients who have a serious mental illness can be motivated to quit smoking

chiatric cohort reported some anxiety with bupropion.

6. Have you discussed smoking cessation and a treatment plan with the patient at every visit? In the EAGLES trial, participants received 10-minute cessation counseling at every outpatient visit.

When it comes time to select a medication regimen, for bupropion, consider starting the patient with 150 mg/d, and increasing the dose to 150 mg twice a day 4 days later. The target quit date should be 7 days after starting the medication. Monitor the patient for symptoms of anxiety and insomnia.

For varenicline, start the patient at 0.5 mg/d, and increase the dose to 0.5 mg twice a day 4 days later. After another 4 days, increase the dose to 1 mg twice a day. Set a target quit date for 7 days after starting medication. Monitor the patient for nausea, insomnia, and abnormal dreams.

References

1. Khaled SM, Bulloch AG, Williams JV, et al. Persistent heavy smoking as risk factor for major depression (MD) incidence—evidence from a longitudinal Canadian cohort of the National Population Health Survey. *J Psychiatr Res.* 2012;46(4):436-443.

2. Han B, Compton WM, Blanco C. Tobacco use and 12-month suicidality among adults in the United States. *Nicotine Tob Res.* 2017;19(1):39-48.
3. Anthenelli RM, Benowitz NL, West R, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. *Lancet.* 2016; 387(10037):2507-2520.
4. FDA Drug Safety Communication: FDA revises description of mental health side effects of the stop-smoking medicines Chantix (varenicline) and Zyban (bupropion) to reflect clinical trial findings. <https://www.fda.gov/Drugs/DrugSafety/ucm532221.htm>. Accessed April 16, 2018.
5. Heatherton TF, Kozlowski LT, Frecker RC, et al. The Fagerström Test for nicotine dependence: a revision of the Fagerström Tolerance Questionnaire. *Br J Addict.* 1991; 86(9):1119-1127.
6. Moeller-Saxone K. Cigarette smoking and interest in quitting among consumers at a psychiatric disability rehabilitation and support service in Victoria. *Aust N Z J Public Health.* 2008;32(5):479-481.
7. Evins AE, Cather C, Rigotti NA, et al. Two-year follow-up of a smoking cessation trial in patients with schizophrenia: increased rates of smoking cessation and reduction. *J Clin Psychiatry.* 2004;65(3):307-311; quiz 452-453.
8. Weiner E, Ahmed S. Smoking cessation in schizophrenia. *Cur Psychiatry Rev.* 2013;9(2):164-172.
9. Banham L, Gilbody S. Smoking cessation in severe mental illness: what works? *Addiction.* 2010;105(7): 1176-1189.
10. Posner K, Brent D, Lucas C, et al. Columbia-Suicide Severity Rating Scale (C-SSRS). The Research Foundation for Mental Hygiene, Inc. http://cssrs.columbia.edu/wp-content/uploads/C-SSRS_Pediatric-SLC_11.14.16.pdf. Updated June 23, 2010. Accessed April 26, 2018.