CLINICAL PRACTICE

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Tobacco Addiction

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This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.*

A 58-year-old woman with chronic obstructive pulmonary disease, type 2 diabetes, hypertension, and a history of major depression that is currently in remission presents with a 45-pack-year history of smoking. She smokes 25 cigarettes per day, with her first cigarette smoked within 5 minutes after waking. She has been unable to quit smoking with the regular use of nicotine gum for 4 weeks. Her current medications include fluticasone–salmeterol, ramipril, metformin, empagliflozin, venlafaxine, and, as needed, albuterol. How should her tobacco addiction be treated?

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THE CLINICAL PROBLEM

Tobacco addiction is a treatable chronic relapsing disorder that is characterized by cravings and compulsive use. An estimated 47.1 million U.S. adults (19.0% of the population) currently use tobacco, mostly in the form of cigarettes (12.5% of the population).[1] More than 480,000 adults in the United States die annually from the effects of cigarette smoking, and approximately 16 million have a smoking-related illness.[2] The prevalence of smoking is highest among adults 25 to 64 years of age, and smoking is more common in the following groups than among their various counterparts: persons of color; those with low incomes or low levels of education; those who are divorced, separated, or widowed; those who are non-cisgender or nonheterosexual; those who receive Medicaid, disability benefits, or are uninsured; and those who have anxiety or depression.[1] In the United States, the incidence of smoking among persons with any mental illness is two to four times as high as that of the general population.[3]

Nicotine is the primary addictive compound in tobacco. Inhaling cigarette smoke delivers an arterial bolus of nicotine to the brain in 7 to 30 seconds at an average of 1 mg of nicotine per cigarette,[4] which activates the nicotinic receptors that mediate the release of dopamine in the reward pathways of the brain.[5] This rapid delivery of a high concentration of nicotine makes smoking the most addictive form of nicotine delivery. Beta carbolines that are present in tobacco smoke act as potent monoamine oxidase inhibitors, which increase levels of dopamine, norepinephrine, and serotonin in the brain.[6] The polycyclic aromatic hydrocarbons in smoke induce cytochrome P450 enzymes (CYP1A1, CYP1A2, and possibly CYP2E1), leading to clinically significant drug interactions[7] (Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). Cigarette smoke also contains approximately 7000 chemicals, including 60 to 70 known human carcinogens. Although nicotine primarily drives the addiction to cigarettes, the byproducts of combustion drive tobacco-related disease and death.

An audio version of this article is available at NEJM.org

KEY CLINICAL POINTS

TOBACCO ADDICTION

- Tobacco addiction is a chronic relapsing disorder that accounts for more than 480,000 deaths annually in the United States and is characterized by frequent attempts to quit and subsequent relapses.
- Medications including varenicline, long- and short-acting nicotine-replacement therapies, and sustained-release bupropion are recommended in guidelines for use in smoking-cessation therapy for patients who are daily cigarette smokers.
- Varenicline and the combination of nicotine patches with a short-acting nicotine-replacement formulation are currently considered the most effective medications.
- The number needed to treat for one person to attain and maintain long-term abstinence from tobacco with the use of these treatments ranges from 8 to 20.
- Counseling by itself or in addition to medication improves outcomes; counseling may be provided in person or by means of telephone, text messaging, or the Internet.

The risk factors for the onset of smoking and subsequent tobacco addiction are both genetic and environmental. The age that a person starts smoking, the number of cigarettes smoked per day, and cessation have been associated with 566 genetic variants in 406 loci.[8] Parental smoking, peer influence, and personality traits related to impulsivity and risk-taking and sensation-seeking behaviors are associated with the initiation of and experimentation with smoking. Furthermore, adverse childhood experiences are associated with twice the risk of a person becoming an adult smoker.[9] Policy-level interventions also affect trends in smoking. Recent population-based data indicate a decrease in smoking among adolescents but an increase in the proportion of smokers who initiated smoking and transitioned to daily smoking in early adulthood; this trend has been attributed to smoking-prevention efforts having been focused largely on middle school and high school students.[10]

Tobacco-related chronic diseases typically develop in smokers after a few decades of smoking. The risk of lung cancer is 25 times as high and the risk of coronary heart disease or stroke is 2 to 4 times as high among smokers as among nonsmokers.[2] Quitting smoking before 40 years of age reduces the risk of death from a tobacco-related disease by approximately 90%,[11] but quitting permanently is difficult. A person who smokes may make 30 or more attempts to quit before having permanent remission.[12] Only 3 to 5% of smokers will be abstinent 6 to 12 months after a given quit attempt, with most relapses occurring within the first 8 days after quitting,[13] owing to acute withdrawal symptoms (e.g., difficulty in concentrating and increased anxiety, sadness, anger, frustration, irritability, insomnia, and hunger) and subsequent urges to smoke (i.e., cravings).[14] Withdrawal symptoms peak within 2 days after a person quits smoking and are greatly diminished within a week after the quit date, but cravings often persist and lead to relapse. The incidence of relapse is as high as 10% in the year after 1 year of abstinence,[15] decreasing to 2 to 4% after 2 years.[16] Late relapses may occur, often caused by a stressful life event, and smoking even a single cigarette can lead to a full relapse. However, with evidence-based treatments, 10 to 30% of smokers have long-term abstinence.[17]

STRATEGIES AND EVIDENCE

TREATMENT

Although criteria are available to formally diagnose tobacco-use disorder (i.e., criteria in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* [DSM-5]), the number of cigarettes smoked per day and the time from waking to smoking the first cigarette can be used to accurately determine the severity of the addiction.[18] In assessing patients who have coexisting conditions and continue to smoke, the provider may find that asking additional questions is helpful in tailoring treatment (Table S2).

Clinical systems for screening and interventions that are systematic and congruent with guidelines for the treatment of tobacco addiction can increase quit rates.[17] These include five evidence-based steps that are effective both individually and collectively: screening, clear advice to quit, medication or behavioral support (or both) matched to the readiness of the patient to make a quit attempt, appropriate referral to additional support, and follow-up. The ultimate

goal is complete remission from smoking.[16] Opt-out models such as offering every smoker, regardless of readiness, very brief advice, a prescription for medication, and a referral to counseling are also effective (Table 1).[19]

Counseling and Behavioral Approaches

Effective behavioral interventions for smoking cessation are shown in Table 2. Brief behavioral interventions, such as encouraging a smoker to set a quit date within 30 days, increase cessation rates.[24] In addition, there is a clear dose–response relationship between the intensity of the intervention and its effectiveness in sustaining abstinence from smoking,[17,20] especially in persons who are not using cessation medications. There is high-certainty evidence that individual counseling spread over several sessions increases quit rates as compared with usual care and brief advice, and high-intensity counseling (i.e., greater length and number of treatment sessions) increases sustained abstinence as compared with low-intensity counseling.[25] Depending on the available resources, counseling may be provided by trained counselors in person or by means of state or national telephone quitlines.[26] Telephone counseling can increase the likelihood of successful cessation, irrespective of the smoker's degree of motivation to quit.

As compared with minimal support or as an addition to other forms of support, text-messaging programs also have been shown, with moderate-certainty evidence, to improve quit rates.[27] Financial incentives to stop smoking also increase the odds of quitting as compared with minimal intervention.[27] Adjunctive approaches include advice to make the home and work environments smoke-free spaces; the use of self-help booklets, Web sites, and smartphone applications (apps); and the enlistment of social support during the quitting process.[26]

Many smokers are ambivalent about quitting smoking. Motivational interviewing (a patient-centered counseling technique that is used to enhance the smoker's readiness to change) is commonly recommended, although a meta-analysis of randomized trials did not show that motivational interviewing provided a significant benefit for smoking cessation; however, the findings were based on low-quality evidence (Table 2).[28] In a pragmatic approach regarding patients who want to quit, busy clinicians may provide very brief advice, prescribe and encourage adherence to medications, or refer the patients to a smoking-cessation program or quitline (or all these strategies). For other patients, clinicians can use the therapeutic alliance that they have with a patient to enhance the patient's readiness to make a quit attempt by regularly expressing concern, recommending cessation, and offering medication to quit and a referral to counseling.

Table 1. Guideline-based Recommendations for the Management of Tobacco Addiction.[17,20]

Screen all patients starting at 9 years of age for their use of tobacco products, and counsel children not to smoke or vape.[20]
All persons who smoke should be advised to stop as soon as possible and should be treated with medications and provided counseling if they smoke five or more cigarettes per day. Prescribers should offer all evidence-based, approved medications to help the patient make an informed choice.[20]
Refer the patient to counseling when counseling is unavailable within the clinical setting. Pregnant women should be offered counseling, support, and judicious use of medication on an individual basis to help them stop smoking.[21]
Prescribe varenicline or combination nicotine patch plus a short-acting nicotine-replacement formulation as the first choice to smokers regardless of their willingness to set a quit date.[22] Patients should be advised that the combination of varenicline plus nicotine patches will increase quit rates but might cause more side effects.[22]
Consider extending treatment with varenicline for up to 26 weeks or treatment with bupropion for up to 52 weeks in patients who are at high risk for relapse at the end of 12 weeks.[22]
Vaping products are not approved by the Food and Drug Administration for use in smoking cessation.

Medications

The Food and Drug Administration has approved several medications for smoking cessation (i.e., nicotine-replacement therapies, varenicline, and sustained-release bupropion). Each of these medications treats acute withdrawal, limits cravings, and reduces the risk of relapse more than any intensity of counseling (Table 3).[34] Both varenicline and a combination of nicotine patches with short-acting nicotine-replacement therapy are considered the most effective and safe first-line treatments for smoking cessation.[20]

Nicotine-replacement therapy is usually started on the patient's target quit date (the date that the patient commits to abstaining from smoking

Table 2. Effective Counseling and Behavioral Interventions for Smoking Cessation.[27]*

Intervention	Description	Duration	Findings in Studies of Effectiveness Lasting >24 Wk†	Mode of Delivery	Considerations
Brief advice	Brief, simple advice from provider to quit smoking	<1 min	More effective than no advice or usual care (17 studies; RR, 1.66; 95% CI, 1.42–1.94)[23]	At each encounter with patients who smoke	Simple and effective intervention for all patients who smoke
Counseling (individual or group)	Advice and practical strategies on coping with challenges of quitting (e.g., withdrawal, cravings, mood swings, and treatment adherence) May involve cognitive therapy (cognitive behavioral therapy or acceptance and commitment therapy) that challenges and overcomes maladaptive thinking and feelings that lead to smoking	Variable: single session of <20 min to several longer sessions over many weeks	High-quality evidence showed that individual behavioral counseling was more effective than brief advice or self-help with no medication offered (27 studies, 11,100 participants; RR, 1.57; 95% CI, 1.40–1.77). More-intensive counseling was more effective than less-intensive counseling (11 studies, 2920 participants; RR, 1.29; 95% CI, 1.09–1.53).[25] Meta-analyses showed group counseling was more effective than no intervention (RR, 2.60; 95% CI, 1.80–3.76), than self-help (RR, 1.88; 95% CI, 1.52–2.33), or than brief support (RR, 1.25; 95% CI, 1.07–1.46).[30] There was no difference between group and individual counseling.[27,30] Meta-analysis showed cognitive therapies were more effective than NRT alone (8 studies; RR, 1.53; 95% CI, 1.06–2.19).[29]	Counseling facilitated in-person or by telephone or computer; usually combined with pharmacotherapy	Commonly delivered by trained health professional; can also be patient-directed Web-based and smartphone application–based formats are emerging as options.
Contingency management	Use of incentives (usually guaranteed financial rewards) to motivate smokers to quit and to maintain abstinence	Variable, but longer duration is more effective	Network meta-analysis calculated a pooled OR for financial incentives of 1.46 (95% CI, 1.15–1.85; 19 studies) for quitting at 6 mo as compared with minimal intervention.[27]	No counseling or therapy involved; easily implemented and not human resource intensive	Relapse rates are high when the incentive is removed Continued provision of incentives can be costly.
Text messaging	Automated text message–based cessation intervention	Variable	Automated text messaging alone was more effective than minimal smoking-cessation support (13 studies; RR, 1.54; 95% CI, 1.19–2.00). Adding text messaging to other cessation intervention improved effectiveness (4 studies; RR, 1.59; 95% CI, 1.09–2.33).[27,31]	Push messaging to patient's mobile telephone phone	Can be cost-effective, with large reach A meta-analysis of current smartphone applications did not show effectiveness (5 studies; RR, 1.00; 95% CI, 0.66–1.52).[27]

* CI denotes confidence interval, NRT nicotine-replacement therapy, and OR odds ratio.
† Relative risk (RR) indicates the relative chance of sustained abstinence at 6 months.

for at least 24 hours), whereas non-nicotine oral medications are started at least 1 week before. The duration of therapy is usually 8 to 12 weeks; even though most smokers who have a response to nicotine-replacement therapy will quit smoking within 4 weeks after starting treatment,[35] completion of the treatment regimen is associated with a higher incidence of long-term remission. The addition of counseling to pharmacotherapy increases the likelihood of cessation.[27]

Meta-analyses of randomized trials have shown that varenicline, a partial nicotine receptor agonist, more than doubles the likelihood of sustained quitting in the general population of smokers when administered at standard or reduced doses.[36] There is mixed evidence with regard to the benefit of extending treatment for an additional 12 weeks.[37]

Systematic reviews of randomized, controlled trials have shown that all forms of nicotine-replacement therapy that deliver nicotine without the products of combustion (i.e., nicotine patches, gums, lozenges, inhalers, and nasal spray) increase the likelihood of sustained quitting by 50 to 60%.[32] The maximum-strength patch (which contains 21 mg of nicotine) provides steady-state plasma nicotine concentrations that are only approximately 50% of the concentration reached from smoking 20 cigarettes per day,[38] which often results in inadequate suppression of withdrawal symptoms and therefore continued smoking. The addition of short-acting nicotine-replacement therapy (e.g., gum, lozenges, mist, or inhaler) to the patch increases the likelihood of quitting.[39] Doubling the number of patches per day may be more effective in patients who smoke a large number of cigarettes per day, but the results to date have been inconsistent.[39,40]

Sustained-release bupropion (at a dose of 150 mg administered orally twice daily), through an unproven mechanism of action, increases the likelihood of quitting by 52 to 71% independent of its effect on clinical depression.[26] The sustained-release dose may also be reduced to once daily (i.e., 150 mg administered once daily) in the morning with a minimal loss of effectiveness.[34]

A multicenter, triple-dummy, double-blind trial involving 8144 smokers (half of whom had a psychiatric illness) assessed standard treatment as compared with varenicline, bupropion, or a nicotine patch. The percentages of participants who had continuous abstinence (i.e., the last 4 weeks of treatment plus 12 weeks post-treatment) were 21.8% with varenicline, 16.2% with bupropion, 15.7% with a nicotine patch, and 9.4% with placebo.[41] All the medications were superior to placebo, and varenicline was superior to the other medications. Among smokers with a psychiatric illness, a similar pattern emerged, although the percentages of participants who quit were lower (18.3% with varenicline, 13.7% with bupropion, 13.0% with a nicotine patch, and 8.3% with placebo). There were no material differences among the groups in the incidence of adverse events, including major cardiovascular or neuropsychiatric events. Network meta-analyses indicate that among smokers who use a single smoking-cessation agent, varenicline is the best option, followed by the nicotine patch,[34,36] but that a nicotine patch plus a short-acting nicotine-replacement formulation results in cessation success similar to that with varenicline alone and superior by up to 50% to cessation success with any single formulation of nicotine-replacement therapy (Table 3). More recent analyses suggest that quit success might be higher with varenicline plus a nicotine patch at a strength of 14 mg per day or with a combination of varenicline and bupropion (Table S3).[34,42]

Guideline-based second-line agents include nortriptyline and clonidine[33,43]; however, these agents are not approved for treating smoking addiction and have less favorable safety profiles than first-line medications. Cytisine, a naturally occurring plant alkaloid, is a short-acting, orally bioavailable nicotine receptor partial agonist with demonstrated efficacy as compared with placebo in three trials.[36] It is not currently approved in the United States, although it is available in many other countries (Table S3).

AREAS OF UNCERTAINTY

Data are lacking to show the benefits and risks of smoking-cessation medications among adolescents, nondaily smokers, pregnant women, and persons who use other forms of tobacco (e.g., smokeless tobacco and electronic cigarettes [e-cigarettes]). More research is needed to determine the appropriate use of current treatments. For example, limited data support higher cessation rates with initiation of nicotine-replacement therapy before the quit day as compared with on

Table 3. Evidence-based Medications for Sustained Abstinence at 6 Months after Quit Date.*

Drug	Dose	Mechanism of Action	Pooled RR (95% CI) [Sample Size]†	No. Needed to Treat†	Contraindications and Cautions	Adverse Events	Comments
Varenicline‡		Partial agonist at the α4β2 nicotinic acetylcholine receptor					
Standard dose[55]	0.5 mg administered orally once daily for 3 days, then twice daily for 4 days, then 1 mg administered orally twice daily for 12 wk		2.24 (2.06–2.43) [27 trials, 12,625 participants]	11	Contraindications include previous adverse events and suicidal ideation Use with caution in patients with seizures, type 2 diabetes, or alcohol use	Nausea, insomnia, abnormal dreams, headache,[55] allergic reaction	Medication should be initiated 7–35 days before quit date and taken on a full stomach to reduce nausea; variable dosing might facilitate increased adherence No drug–drug interactions; considered safe in patients with stable psychiatric diseases May be stopped abruptly
Reduced or variable dose[55]	0.5 mg administered orally twice daily for 12 wk Variable at patient or physician discretion (0.5–1 mg administered once daily or twice daily)		2.08 (1.56–2.78) [4 trials, 1266 participants]	10 with low dose; 8 with variable dose			
Extended treatment[55]	24–52 wk of standard treatment		1.24 (1.08–1.42) [2 trials, 1295 participants]	11			
NRT[32]							
Patch	If patient smokes ≥10 cigarettes per day, 21 mg per day for 6 wk, then 14 mg per day for 2 wk, then 7 mg per day for 2 wk If patient smokes <10 cigarettes per day, 14 mg per day for 6 wk, then 7 mg per day for 2 wk	Full agonist at the α4β2 nicotinic acetylcholine receptor; transdermal absorption	1.64 (1.53–1.75) [51 trials, 25,754 participants]	15	Allergy to adhesives, skin disorders	Skin sensitivity and irritation; sleep disturbances	May be removed at night if associated with nightmares May be started 2 wk before quit date; concurrent smoking is safe with nicotine-replacement therapy May be used by persons with post–acute coronary syndrome
Gum	If patient smokes first cigarette ≤30 min after waking, 4 mg If patient smokes first cigarette >30 min after waking, 2 mg As needed, to a maximum of 24 doses per day	Absorbed through buccal mucosa	1.49 (1.40–1.60) [56 trials, 22,581 participants]	14	Dentures, difficulty chewing	Hiccups, gastrointestinal disturbances (due to swallowing nicotine), jaw pain, and orodental problems[55]	May be used to reduce smoking before abruptly quitting

Lozenge	If patient smokes first cigarette ≤30 min after waking, 4 mg If patient smokes first cigarette >30 min after waking, 2 mg As needed, to a maximum of 20 doses per day	Absorbed through buccal mucosa	1.52 (1.32–1.74) [8 trials, 4439 participants]	13		Hiccups, burning sensation in mouth, sore throat, coughing, dry lips and mouth, and oral lesions[55]	
Inhaler‡	One 10-mg cartridge (delivering 4 mg nicotine) over a period of 20 min every 1–2 hr Puff; do not inhale	Absorbed through buccal mucosa and upper airway	1.90 (1.36–2.67) [4 trials, 976 participants]	13	Use with caution in patients with asthma or COPD, owing to triggering cough.	Hiccups, burning sensation in mouth, sore throat, coughing, dry lips and mouth, and oral lesions[55]	
Spray‡	0.5 mg of nicotine as needed to maximum of 5 doses per hr	Absorbed through nasal mucosa and bypasses blood–brain barrier	2.02 (1.49–2.73) [4 trials, 887 participants]	8		Nasal irritation	
Oral mist	1–2 sprays every 30 to 60 min 1–2 sprays every 15 min to a maximum of 64 sprays per day		2.48 (1.24–4.94) [1 trial, 479 participants]	20	None	Altered sense of taste, headache, hiccups, nausea and vomiting, dyspepsia, oral soft-tissue pain, stomatitis, salivary hypersecretion, burning lips, dry mouth	
Sustained-release bupropion[33]‡	150 mg administered orally in the morning for 3 days, then 150 mg administered orally twice a day, with doses at least 8 hr apart, not to exceed 300 mg per day Treatment period of 7–12 wk may be extended for up to 1 yr	Norepinephrine and dopamine reuptake inhibitor; nicotinic receptor antagonist	1.64 (1.52–1.77) [45 trials, 17,866 participants]	12	Known hypersensitivity to bupropion or its excipients Seizure disorders Bulimia Anorexia nervosa and use of MAO inhibitors Should be prescribed with caution in persons taking other medications that lower the seizure threshold	Insomnia, dry mouth, nausea, tremor, allergic reactions (pruritus, hives, angioedema, dyspnea), arthralgia, myalgia, fever, symptoms related to delayed hypersensitivity, seizures, suicidal ideation and behavior	Start 7–14 days before quit date May be extended up to 52 wk in some patients Reduce intake of other stimulants, such as caffeine

* COPD denotes chronic obstructive pulmonary disease, and MAO monoamine oxidase.
† Relative risks (i.e., the relative chances of sustained abstinence at 6 months), 95% confidence intervals, and numbers needed to treat for one person to attain and maintain long-term abstinence were calculated with the use of risk-reduction estimates from Cochrane reviews.
‡ This device or medication requires a prescription.

the quit day,[39] adjustment of nicotine-patch dose to the response, and extension of the duration of treatment beyond 12 weeks to increase abstinence rates.[37]

The application of personalized medicine to tobacco addiction has been proposed, but more data are needed to determine its clinical usefulness. In one large, multicenter, placebo-controlled trial, participants who metabolized nicotine at a normal rate (as measured by the ratio of cotinine to 3OH-cotinine in plasma, urine, or saliva) had a better response to varenicline than to the nicotine patch; no difference was noted in the response to medication in participants who metabolized nicotine at a slower rate.[44]

The health benefits of reducing the number of cigarettes smoked are not well defined.[45] Still, reducing smoking as a step toward an eventual goal of quitting may be an effective strategy for patients who are not ready to stop abruptly with the use of medication or behavioral interventions.[46]

A recent meta-analysis of mindfulness-based interventions such as mindfulness training and acceptance and commitment therapy showed no evidence of the effectiveness of these interventions as compared with no intervention[35] but involved few studies and small sample sizes. Adequately powered randomized trials of these strategies are needed.

Limited data have suggested that the use of electronic nicotine delivery devices, or e-cigarettes, may be an effective replacement for tobacco smoking; however, most trials have involved e-cigarettes that are no longer on the market, and study of newer e-cigarette types (e.g., nicotine salt-pod devices) is warranted. There is moderate-certainty evidence that nicotine e-cigarettes are more effective than nicotine-replacement therapy.[34,47] There has been minimal research on efficacious interventions for persons who are exclusively addicted to vaping nicotine.

Analyses of short-term randomized trials support the benefit of noninvasive brain-stimulation techniques in reducing smoking behavior, cue-induced cravings, urges to smoke, and symptoms of nicotine dependence (pooled relative risk, 2.39 [95% confidence interval, 1.26 to 4.55] for smoking abstinence at 3 or 6 months as compared with sham stimulation).[48] Although a specific brain-stimulation device has received approval from the FDA for use in smoking-cessation interventions, the real-world effectiveness of this treatment in clinical settings has not been determined. Further study is needed, including comparisons of the safety and effectiveness of brain stimulation to first-line combination nicotine-replacement therapy or varenicline.

Psychedelic agents have also been suggested for the treatment of tobacco addiction. An open-label trial of two doses of psilocybin combined with cognitive behavioral therapy in 15 otherwise-healthy smokers showed an overall result of abstinence in 80% of the participants at 6 months[49] and 67% at 12 months post-treatment[50]; data from placebo-controlled trials are lacking.

GUIDELINES

Our recommendations are concordant with the guidelines for smoking-cessation therapies in the general population published by the U.S. Preventive Services Task Force[22] and the American Thoracic Society.[51] Guidelines are also available for special populations,[52] hospitalized patients,[53] and pregnant women.[20] Although not a guideline itself, the Surgeon General's 2020 report on smoking cessation[54] provides a comprehensive review of smoking-cessation interventions.

CONCLUSIONS AND RECOMMENDATIONS

The patient described in the vignette smokes heavily, has tobacco-related coexisting conditions, and has not had a response to over-the-counter nicotine gum, probably owing to inadequate dosing and lack of counseling. She should be educated about the risks of continued smoking (e.g., exacerbations and worsening of chronic obstructive pulmonary disease, microvascular and macrovascular complications from diabetes and hypertension, and smoking-related cancers) and the benefits of smoking cessation. We would recommend either varenicline or combination nicotine-replacement therapy as a first-line treatment, given their similar efficacy and good safety profiles in patients with stable mental health status; the choice should be guided by patient preference and past response had by the patient to either medication.

If varenicline is prescribed, we would recom-

mend setting a quit date 7 to 14 days after the patient begins treatment, whereas for combination nicotine-replacement therapy, we would recommend the quit date be the day that she begins treatment. We would closely monitor her for withdrawal symptoms, especially mood changes. After 4 weeks, if the patient had not quit smoking completely, and we had confirmed medication adherence, we would consider switching to the other first-line option or combining varenicline with a nicotine patch or with bupropion. If bupropion is prescribed, the patient's venlafaxine dose might need to be reduced to prevent a drug interaction. We would recommend against the use of e-cigarettes for smoking cessation given insufficient evidence to support their use. We would refer the patient for in-person or telephone counseling, ideally for a period of 8 to 24 weeks. We would monitor her for relapse as part of her ongoing follow-up. Should she have a relapse after quitting, the same medications may be prescribed again.

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