

CLINICAL PRACTICE

Treating Smokers in the Health Care Setting

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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 45-year-old overweight woman with a history of depression sees her physician with a recurrence of acute bronchitis. She began smoking at 15 years of age and now smokes 10 to 15 cigarettes per day. She smokes her first cigarette immediately on awakening. She has made multiple attempts to quit, once briefly using a nicotine patch, but she had a relapse because of strong urges to smoke and weight gain. She is bothered by the cost of cigarettes and is worried about the effects of smoking on her health and that of her children. However, she is reluctant to attempt to quit now, in part because she fears she will not succeed. What would you advise?

THE CLINICAL PROBLEM

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The prevalence of smoking has declined dramatically in the United States over the past half century, decreasing from about 42% in the 1960s to about 20% today.¹ However, this decline has stalled recently, and higher prevalence rates are concentrated in populations with low incomes, low educational levels, and psychiatric conditions. Fortunately, evidence suggests that persons in these populations benefit from the same treatments that are effective in other smokers.²

Smokers today tend to smoke fewer cigarettes than they did in the past.³ However, this does not necessarily translate into reduced harms; biochemical indexes of smoking intensity have not shown commensurate declines.⁴ Among heavy smokers who reduce their smoking significantly (e.g., by 50% from 15 cigarettes per day or more⁴), the rates of myocardial infarction and chronic obstructive pulmonary disease (COPD) are still closer to those among persistently heavy smokers than to the rates among persons who have quit smoking. More than 30% of deaths from cancer, 90% of cases of COPD, and 30% of cases of cardiovascular disease in the United States are attributed to tobacco use,^{5,6} and tobacco use exacts other health costs (e.g., delayed wound healing) as well.

Tobacco use remains the chief avoidable cause of death in the United States, and it is directly responsible for about one fifth of all deaths. Furthermore, smoking results in approximately \$100 billion in health care costs and another \$97 billion in lost productivity⁷ in the United States each year, with smokers incurring, on average, \$1,600 more in annual health care costs than nonsmokers.⁸

Nicotine is carried by tar particles to the lung alveoli and then to the brain — a process that takes approximately 10 seconds for each inhalation.⁹ Nicotine binds to nicotinic cholinergic receptors in the brain, leading to neurotransmitter release,¹⁰ which makes smoking and smoking cues (e.g., the sight of cigarettes) more attractive and powerfully reinforcing.¹⁰ In addition, tolerance occurs with chronic smoking, resulting in the proliferation of nicotinic receptors and permitting higher levels of self-administration of nicotine. A lack of binding to these

receptors due to decreased smoking results in withdrawal symptoms such as craving, negative moods, and restlessness; these symptoms spur a return to smoking.¹¹ About half of phenotypic variance in tobacco dependence is attributable to genetic influence.¹²

There are multiple challenges to the clinical treatment of tobacco dependence. Many clinicians do not consistently offer smoking-cessation treatments to their patients who smoke,¹³ and only about 20% of smokers are ready to attempt to quit at any given time.¹⁴ Moreover, smokers too often do not use evidence-based treatments; about 95% of unaided attempts to quit end in failure.¹⁵ Finally, nonadherence to medications and counseling is common and reduces the chances that smoking cessation will be successful.^{16,17} Patients typically receive only about 50% of recommended doses of medication,¹⁶ and they often complete less than half of scheduled counseling sessions.¹⁷

STRATEGIES AND EVIDENCE

IDENTIFYING SMOKERS IN THE HEALTH CARE SETTING

Approximately 70% of smokers in the United States see a primary care physician each year¹⁸; thus, there is a good opportunity to deliver effective interventions for smoking cessation. The inclusion of tobacco use as one of the vital signs identifies 80% or more of smokers visiting clinics.¹⁹

MOTIVATING THE UNWILLING PATIENT

Many smokers lack the motivation to attempt to quit, but various interventions can increase the number of smokers who make an attempt and the likelihood of success. One such intervention is motivational interviewing, in which the clinician uses nonconfrontational counseling to resolve the patient's ambivalence about quitting by encouraging choices that are consistent with the patient's long-term goals^{20,21} (Table 1). A meta-analysis of 14 randomized trials²¹ showed that, as compared with brief advice or usual care, motivational interviewing increased 6-month cessation rates by about 30%. Cessation rates in the two studies involving physician counselors (who typically received ≥ 2 hours of training) were about 8% with motivational interviewing versus 2% with brief advice or usual care.²¹ Cessation rates were higher if smokers received two or

more sessions rather than one session and if the sessions lasted more than 20 minutes.

The 2008 U.S. Public Health Service guideline² used components of motivational interviewing to develop an abbreviated intervention that can be used when time or training needs do not permit motivational interviewing. This "five R's" counseling focuses on personally relevant reasons to quit, risks associated with continued smoking, rewards for quitting, and roadblocks to successful quitting, with repetition of the counseling at subsequent clinic visits. Such counseling (combined with a later offer of nicotine-replacement therapy) was shown in one randomized trial²² to increase 6-month quit rates (24%, vs. 4% in the control group).

Another approach is to encourage and instruct unwilling smokers to substantially and persistently reduce their daily smoking ("as much as possible"²³), while they are receiving nicotine-replacement therapy (Table 2).²³⁻²⁵ A meta-analysis of seven randomized, controlled trials involving 2767 smokers who were initially unwilling to quit showed that the abstinence rate 6 months after the initiation of treatment²⁵ was significantly higher among smokers who were randomly assigned to nicotine-replacement therapy (nicotine gum, inhaler, or patch) for 6 months or more while trying to reduce their smoking than among those in the control group (9% vs. 5%). Another study,²⁶ involving 1154 smokers who were initially unwilling to quit, showed a benefit associated with the use of nicotine gum or patches for only 2 months (abstinence rate at 6-month follow-up, 17%, vs. 10% in the control group). Several studies showed that about one fifth of smokers who did not quit reduced their smoking by 50% or more with such treatments.^{23,25} A reassuring finding of the meta-analysis was the absence of any increase in serious adverse events with this combination; the only adverse event considerably more common in the nicotine-replacement-therapy group than in the placebo group was nausea (8.7% vs. 5.3%).²⁵

Research has also shown that making treatment easily available and reducing barriers to treatment increase treatment acceptance. For instance, when treatment is delayed and occurs at a separate location, only 10% or fewer of smokers initiate it,²⁷ whereas as many as a third of patients enter treatment that is readily accessible.²⁸ Accep-

Table 1. Treatment Recommendations for Counseling Smokers.***Smokers who are willing to attempt to quit now**

Provide support.

Provide an empathic environment.

Encourage the patient: "My office staff and I are here to help you quit." "I'm recommending treatments that can help you succeed."

Provide brief counseling on smoking cessation.

Ask the patient to: set a quit date, ideally within 2–3 wk; tell others and ask for support (e.g., ask other smokers not to smoke around the patient); and anticipate and plan for challenges and temptations.

Discuss how the patient can overcome future challenges (including stress, alcohol use, exposure to other smokers, and weight gain).

Ask when these challenges will occur and what they will be, and discuss how the patient can avoid them or cope. Emphasize healthy eating and an active lifestyle.

Encourage the patient to remove tobacco from his or her home, car, and work environment.

Urge total abstinence starting on the quit date, and emphasize adherence to treatment, even if a brief return to smoking occurs.

Provide counseling about medication.

Note the effectiveness of seven FDA-approved medications for smoking cessation.

Discuss the patient's concerns.

Recommend medication with consideration of its effectiveness, cost, and contraindications as well as the patient's preferences.

Encourage the use of varenicline or combination nicotine-replacement therapy.

Consider optional use of nicotine patch for 2–3 wk before the patient attempts to quit.

Encourage adherence to medication.

Address myths about the addictiveness and harm of medications.

Provide supplemental materials and information.

Cessation counseling by telephone (e.g., 1-800-QUIT-NOW [1-800-784-8669]).

Online cessation support (e.g., www.smokefree.gov and www.women.smokefree.gov).

Booklets on relapse prevention (e.g., Forever Free, available at www.smokefree.gov/resources.aspx).

Smokers who are unwilling to attempt to quit now

Use motivational interviewing techniques.

Express empathy.

Respond so that the patient feels heard and understood and knows that you care about his or her views and wishes.

Ask open-ended questions: "What might happen if you quit?"

Use reflective listening to communicate understanding: "I hear that you are worried about weight gain and about not being successful in quitting."

Normalize the patient's feelings and concerns: "Most smokers, like you, have tried several times before they quit successfully."

Support the patient's autonomy: "I hear that you are not ready to quit. Just let me know when you would like to try and I will help."

Encourage the patient to recognize the discrepancy between his or her continued smoking and the importance of quitting.

Accept the patient's ambivalence about quitting, but support his or her strongly held values and goals that are inconsistent with smoking.

Highlight how the patient's current behavior is discrepant with important values and goals: "So, you are strongly committed to your kids, and you worry that your smoking is not the best thing for them."

Support the patient's "change talk": "Yes, I think you are right that it helps to plan ahead for an attempt to quit."

Strengthen the patient's values that conflict with smoking: "I am impressed with your strong desire not to feel like an addict — to be free from smoking."

Accept the patient's resistance to change related to quitting.

Be open to the patient's ambivalence and reasons not to attempt to quit.

Back off if the patient expresses resistance: "You are tired of people trying to get you to quit — I can understand that."

Tell the patient that you hear and respect his or her misgivings: "Because medication did not help you before, you think a different medication will not help you now."

Ask permission to help: "May I tell you what I think will help you quit?"

Support the patient's self-efficacy with respect to quitting and the patient's belief that she or he can quit.

Build on past successes: "You were able to stop smoking for a couple of weeks the last time you tried — that means that you really have the skills to fight urges and resist temptation."

Give the patient choices and control over how to proceed: "Which of these treatments sounds good to you?"

Encourage smoking reduction plus nicotine-replacement therapy.

Consider the use of nicotine-replacement therapy for 2–6 mo.

Help the patient formulate a smoking-reduction plan, including a reduction in daily smoking as much as possible and elimination of smoking entirely in key environments and activities (e.g., in the car and while watching television).

* Adapted from Fiore et al.² FDA denotes Food and Drug Administration.

tance of treatment may also be increased by offers to help that are repeated over time, since smokers' interest in quitting can change quickly.²⁹

EVIDENCE-BASED TREATMENTS FOR THE WILLING PATIENT

Extensive research^{2,30-32} provides support for the effectiveness of counseling and pharmacologic interventions, alone or in combination, in increasing smoking-cessation rates among patients who are willing to attempt to quit.

Counseling

There is a consistent relationship between more intensive counseling (with respect to both the duration and number of counseling sessions) and abstinence from smoking. According to a meta-analysis of 35 randomized trials,² 6-month abstinence rates increased significantly with minutes of total counseling contact: about 14% for 1 to 3 minutes of counseling, 19% for 4 to 30 minutes of counseling, and 27% for 31 to 90 minutes of counseling, versus 11% for no counseling. (Some studies included pharmacotherapy across all counseling conditions, so medication contributed to these success rates.²) Successful counseling boosts the motivation to quit by personalizing the costs and risks of the patient's tobacco use (e.g., tying it to the patient's health, economic status, and family situation). Counseling also provides an opportunity to warn the patient about obstacles or hurdles to quitting and encourages the patient to plan to use coping strategies for avoiding and resisting temptations or urges to smoke (Table 1). The clinician should assess and counsel the patient regarding factors that pose especially great challenges to quitting,² such as living with a smoker, excessive alcohol use, and fear of gaining weight (Table 1). Counseling should be empathic and supportive, not confrontational.² Counseling remains underused, and a key goal is to increase its use in clinical practice — either in person or through referral to a telephone quitline such as 1-800-QUIT-NOW (1-800-784-8669).

Medications

Seven medications are approved by the Food and Drug Administration (FDA) for smoking cessation (Table 3). A meta-analysis² of 83 randomized trials examining the effectiveness of various medications with respect to the rate of abstinence 6 months after treatment showed that

Table 2. Optional Medications before Smoking Cessation.

Medication	Dose	Comments	Outcomes
For the patient who is unwilling to attempt to quit now, but willing to reduce smoking and use nicotine-replacement therapy			
Nicotine patch	7–21 mg/day, daily for up to 6 mo	Pair medication with counseling to reduce the number of cigarettes smoked/day as much as possible; see patient every 4 wk to assess interest in quitting and to provide “five R’s” counseling or conduct motivational intervention*	May result in increased attempts to quit and increased likelihood of cessation at 3–6 mo
Nicotine gum	2–4 mg, up to 10 times/day, daily for up to 6 mo	Same as above	Same as above
Nicotine inhaler	4 mg, up to 10 times/day, daily for up to 6 mo	Same as above	Same as above
For the patient who is willing to attempt to quit now			
Nicotine patch	7–21 mg/day, daily for 2–3 wk before target quit date	Patients may or may not reduce smoking while receiving nicotine-replacement therapy before target quit date	May result in increased likelihood of cessation

* “Five R’s” counseling focuses on personally relevant reasons to quit, risks associated with continued smoking, rewards for quitting, and roadblocks to successful quitting, with repetition of the counseling at subsequent clinic visits.

Table 3. Medications for Smoking Cessation.

Medication	Dose	Instructions
Sustained-release bupropion	Days 1–3: 150 mg each morning; day 4–end: 150 mg twice daily	Start 1–2 wk before quit date; use for 2–6 mo
Nicotine gum	1 piece every 1–2 hr initially, then taper; up to 24 pieces/day; 2 mg if patient smokes \leq 24 cigarettes/day and 4 mg if patient smokes \geq 25 cigarettes/day	Use up to 12 weeks
Nicotine inhaler	6–16 cartridges/day; inhale 80 times/cartridge	Use up to 6 mo; taper at end
Nicotine lozenges	1 piece every 1–2 hr initially, then taper; 2 mg if patient smokes 30 min or more after waking and 4 mg if patient smokes $<$ 30 min after waking	Use 3–6 mo
Nicotine nasal spray	1 dose is 1 squirt/nostril; 1–2 doses/hr; up to 40 doses/day	Use 3–6 mo
Nicotine patch	If patient smokes \geq 10 cigarettes/day, 21 mg/day for 4 wk, then 14 mg/day for 2 wk, then 7 mg/day for 2 wk; if patient smokes $<$ 10 cigarettes/day, start with 14 mg/day for 6 wk, then 7 mg/day for 2 wk	Use new patch every morning for 8–12 wks
Varenicline	Days 1–3: 0.5 mg every morning; days 4–7: 0.5 mg twice daily; days 8–end: 1 mg twice daily	Start 1 wk before quit date; use 3–6 mo
Combination therapies*		
Patch plus bupropion	Follow instructions for individual medications above	Follow instructions for individual medications above
Patch plus gum, inhalers, or lozenges	Follow instructions for individual medications above	Follow instructions for individual medications above

* Only the nicotine patch plus bupropion is currently approved by the Food and Drug Administration.

most medications for smoking cessation (e.g., nicotine patches, gum, lozenges, nasal spray, inhalers, and sustained-release bupropion) approximately doubled the odds of achieving abstinence. The estimated 6-month abstinence rate among patients randomly assigned to placebo was about 14%, versus 19 to 26% across most pharmacotherapies. (Since some studies included counseling in all the study interventions, these effectiveness rates reflect some counseling benefit.) In contrast, varenicline and combination nicotine-replacement therapy (e.g., the nicotine patch plus a short-term form of nicotine-replacement therapy such as nicotine gum or lozenges) were associated with estimated abstinence rates of 33% and 37%, respectively.² These rates were significantly higher than the rate as-

sociated with a representative monotherapy (the nicotine patch). The superiority of these two medications has also been shown in head-to-head trials in which they were compared with single agents such as the nicotine patch or bupropion.^{33,34} Medications for smoking cessation have been shown to be effective in real-world health care settings and in smokers with various coexisting conditions (e.g., substance abuse and depression).^{2,17}

A potentially beneficial strategy involves the use of a nicotine patch 2 or more weeks before the target quit day (Table 2).^{35,36} A meta-analysis of six randomized trials indicated an increase in 6-month abstinence rates of about 25% over those obtained without the use of a patch before cessation of smoking,³⁶ but effects have been variable.³⁶ An additional agent that

Cautions and Warnings	Side Effects	Availability
Do not use with monoamine oxidase inhibitors or bupropion in any other form or in patients with a history of seizures or eating disorders; see FDA black-box warning on serious mental health events: www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm170100.htm	Insomnia, dry mouth, vivid or abnormal dreams	Prescription only; generic or brand-name drugs (Zyban, Wellbutrin SR)
Patients with dentures should use with caution; patients should not eat or drink 15 min before or during use	Mouth soreness, heartburn	Over-the-counter only; generic or brand-name drug (Nicorette)
May irritate mouth and throat	Mouth and throat irritation	Prescription only (Nicotrol inhaler)
Patients should not eat or drink 15 min before or during use	Hiccups, cough, heartburn	Over-the-counter only; generic or brand-name drug (Commit)
Not for patients with asthma; may irritate nose; may cause dependence	Nasal irritation	Prescription only (Nicotrol NS)
Do not use if patient has severe eczema or psoriasis; patch can be removed at night if sleep is disrupted	Local skin reaction, insomnia	Over-the-counter or prescription; generic or brand-name drugs (Nicoderm CQ, Nicotrol)
Use with caution in patients with clinically significant renal impairment, patients undergoing dialysis, and patients with serious psychiatric illness; see FDA Web sites for black-box warning on serious mental health events and statement on risk of cardiovascular adverse events among patients with cardiovascular disease: www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm170100.htm and www.fda.gov/Drugs/DrugSafety/ucm259161.htm	Nausea, insomnia, vivid or abnormal dreams	Prescription only (Chantix)
See information for individual medications above	See information for individual medications above	See above
See information for individual medications above	See information for individual medications above	See above

warrants consideration in treatment for smoking cessation is the $\alpha_4\beta_2$ nicotinic receptor partial agonist, cytisine. In this issue of the *Journal*, West et al. report on a randomized trial that showed a significantly higher rate of success in smoking cessation with cytisine at 12 months than with placebo (8.4% vs. 2.4%), when both treatments were used with minimal counseling support.³⁷

Choosing among medications requires consideration of the benefits and risks of the various alternatives, with attention to each patient's medical and psychiatric status (Table 3). In 2010, on the basis of postmarketing surveillance, the FDA issued a black-box warning for both varenicline and bupropion concerning serious neuropsychiatric symptoms such as hostility, agitation, depressed mood, and suicidal thoughts and

behavior. The FDA advised that physicians discuss these symptoms with patients, weigh the risk of such symptoms for patients with serious psychiatric illness, monitor patients for the symptoms, and discontinue medication in the event of their occurrence, with monitoring until the symptoms resolve. Also, a recent drug-safety communication from the FDA (based on a randomized, controlled trial that evaluated the safety and effectiveness of varenicline in patients with cardiovascular disease³⁸) noted that varenicline may be associated with a small increase in the risk of cardiovascular events, including heart attack, and it called for physicians to weigh the risks and benefits of the use of varenicline in patients with cardiovascular disease. In addition, bupropion can lower the seizure threshold and

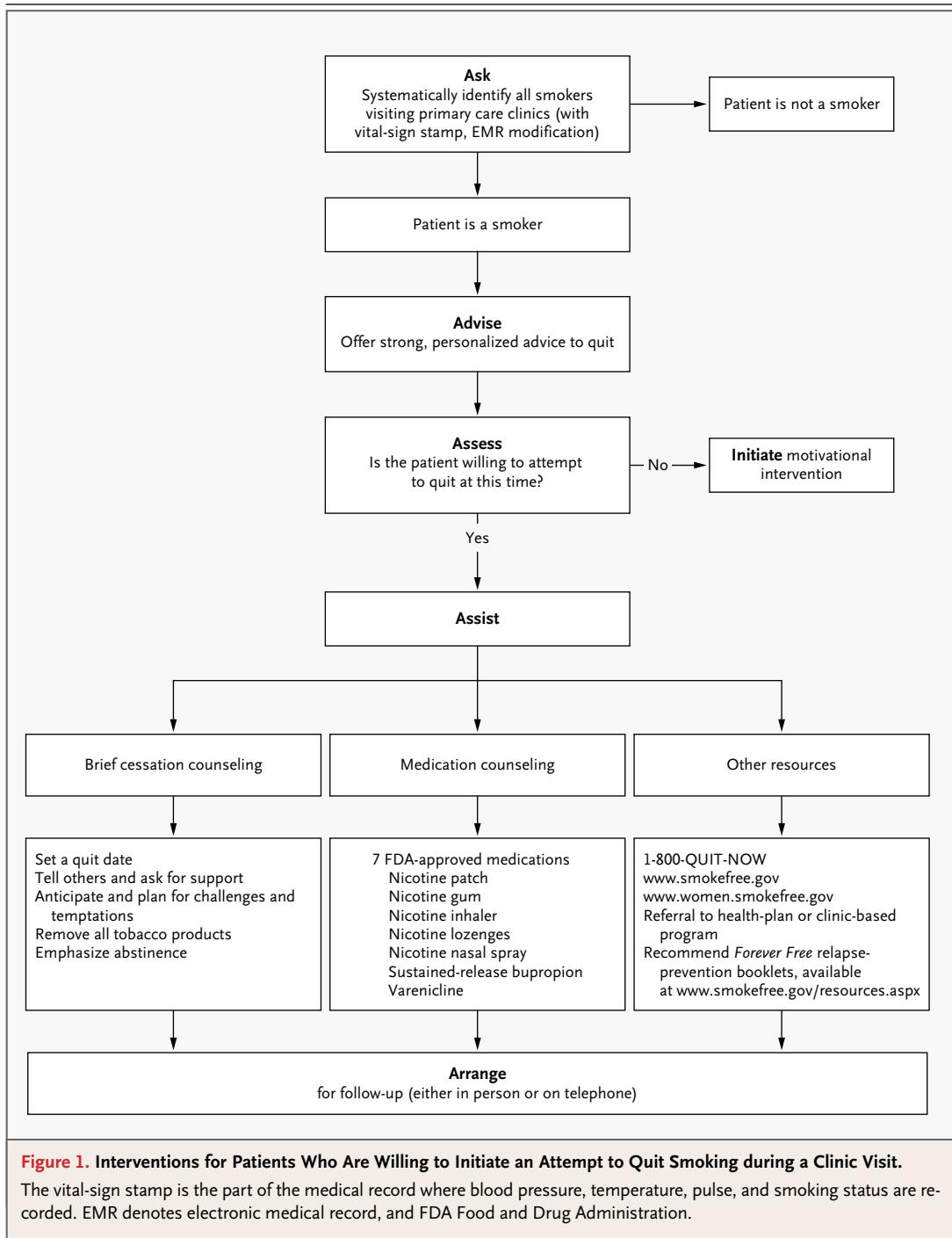


Figure 1. Interventions for Patients Who Are Willing to Initiate an Attempt to Quit Smoking during a Clinic Visit.

The vital-sign stamp is the part of the medical record where blood pressure, temperature, pulse, and smoking status are recorded. EMR denotes electronic medical record, and FDA Food and Drug Administration.

should not be used in patients who have a history of a seizure disorder or who drink heavily.

Nicotine-replacement therapy may cause a local skin reaction (with the nicotine patch) and mouth and throat irritation (with oral nicotine-replacement therapy products). Heavy use of

nicotine-replacement therapy or the use of a combination of nicotine-replacement agents can result in symptoms of nicotine toxicity such as nausea, heart palpitations, and vomiting, but of these symptoms, only nausea is common (occurring in >5% of patients).³³ A meta-analysis of

120 studies showed no significant increase in the risk of serious adverse events with the use of nicotine-replacement therapy.³⁹

TREATMENT USE AND ADHERENCE

Many smokers will not engage in counseling, especially if it involves long sessions or multiple visits.⁴⁰ Therefore, patients should be offered options for quitting, including brief and accessible counseling. Nonadherence to medications for smoking cessation is common and is linked with beliefs that they are dangerous, ineffective, and should not be used if a person has had a relapse.⁴¹ Because nonadherence to medication regimens is related to failure of smoking cessation,¹⁶ the clinician should discuss with the patient any concerns regarding medications for smoking cessation and encourage adherence to the regimen for their use.

CLINICAL STEPS FOR SUCCESSFUL SMOKING CESSATION

A smoker's willingness to try to quit should guide the management plan. Figures 1 and 2 show the respective interventions for patients who are willing and those who are unwilling to attempt to quit at the time of a clinic visit. Although many patients will smoke during an attempt to quit smoking, perhaps 30 to 40% of these patients will not have a full relapse.⁴² Thus, clinicians should encourage patients to keep trying to quit as long as they are willing to do so. Patients who want to abandon the attempt to quit should be encouraged to smoke as little as possible; reduced smoking has been associated with subsequent cessation.²²

HEALTH CARE SYSTEMS APPROACHES

The consistent, effective delivery of an intervention for the cessation of tobacco use requires support from the health care system. Smokers are significantly more likely to make an attempt to quit if tobacco treatment is covered by health insurance.⁴³ Because of the health and cost benefits of smoking cessation, more insurance plans now cover evidence-based treatments for cessation; for example, in 2010, Medicare expanded its counseling coverage to all smokers (4 million persons), not just those with a smoking-related disease.⁴⁴ Moreover, the use of electronic health records to prompt physicians and clinic staff to systematically identify and treat smokers has been associated with increased rates of docu-

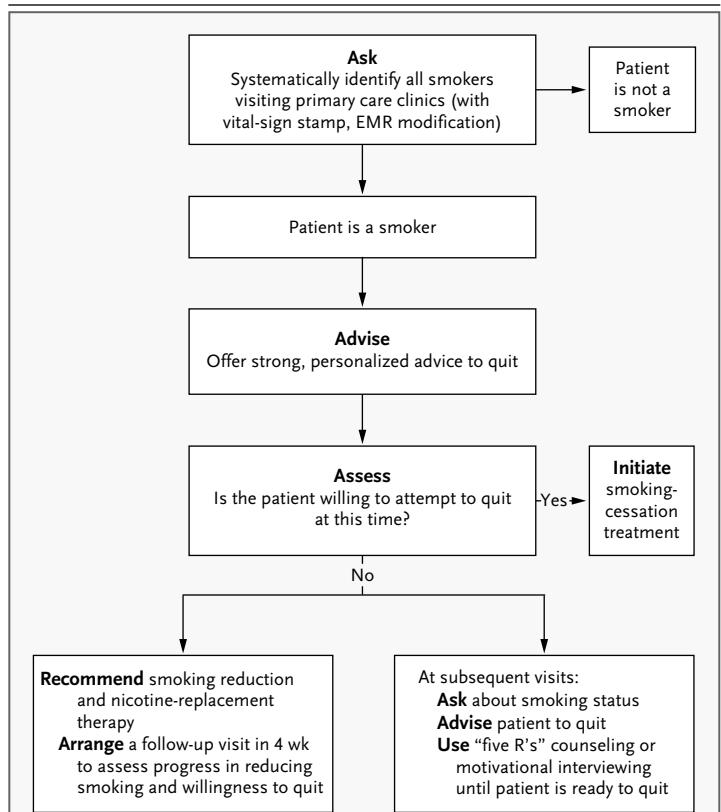


Figure 2. Interventions for Patients Who Are Unwilling to Initiate an Attempt to Quit Smoking during a Clinic Visit.

The vital-sign stamp is the part of the medical record where blood pressure, temperature, pulse, and smoking status are recorded. "Five R's" counseling focuses on personally relevant reasons to quit, risks associated with continued smoking, rewards for quitting, and roadblocks to successful quitting, with repetition of the counseling at subsequent clinic visits. EMR denotes electronic medical record.

mentation of smoking status⁴⁵ and may increase the use of treatments for smoking cessation. Clinician training and performance feedback, dedicated staff to deliver treatments, and "fax to quit" programs that link patients with tobacco quitlines nationwide⁴⁶ also increase cessation rates.

AREAS OF UNCERTAINTY

More research is needed to identify effective strategies for increasing patients' acceptance and use of counseling and pharmacotherapy and to identify optimal combinations of treatments (both before and during attempts to quit smoking). Further research is needed on how to prevent relapse among newly abstinent patients and how best to integrate new forms of technology

(e.g., telephone quitlines and Internet-based treatments) into comprehensive treatment plans for tobacco dependence.

GUIDELINES

The clinical practice guideline of the U.S. Public Health Service, *Treating Tobacco Use and Dependence*,² which was comprehensively updated in 2008, provides evidence-based guidance for clinicians and health systems. The recommendations provided here are generally consistent with this guideline and corroborating analyses.^{31,47} However, other data provide support for the use of nicotine-replacement medication in smokers who are unwilling to quit, in preparation for an attempt to quit,²⁵ and they show a strong link between adherence to the use of such medication and success in quitting.¹⁶

CONCLUSIONS AND RECOMMENDATIONS

At all health care visits, smokers should be encouraged to quit and asked about their willingness to make an attempt to quit. For a patient who is initially unwilling to try to quit smoking, such as the woman in the vignette, either motivational interviewing (Table 1) or the “five Rs” (discussion of personally relevant reasons to quit, risks of continued smoking, rewards for quitting, and roadblocks to successful quitting, with repetition of the counseling at subsequent clinic visits) should be used at each visit. There is more evidence in support of motivational interviewing, but it requires more time and training. In addition, patients who are willing to try to reduce their smoking should be encouraged to do so and

to use nicotine-replacement therapy, generally for at least several months.

For patients who are (or become) willing to attempt to quit, the clinician should provide practical advice on avoiding smoking triggers, such as exposure to other smokers and use of alcohol, and encourage the use of available resources for smoking cessation, including adjunctive counseling through a state quitline (e.g., 1-800-QUIT NOW), online resources (e.g., www.smokefree.gov or www.women.smokefree.gov), or both. The clinician should discuss the benefits and risks associated with various medications and address any misconceptions the patient may have (e.g., that nicotine-replacement therapy is as addictive as smoking).

If the woman described in the vignette became ready to quit, we would recommend combination nicotine-replacement therapy. Nicotine-replacement therapy has been shown to be safe and effective in persons with depressive symptoms⁴⁸ and in persons with high levels of nicotine dependence (e.g., smoking within 5 minutes after awakening^{49,50}) and does not require close monitoring for symptoms. A follow-up visit should be scheduled 2 weeks after the quit day, at which time challenges associated with smoking cessation should be reviewed and support provided. This discussion should be repeated at subsequent visits.

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