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Smoking cessation: Tactics that make a big difference

Quitlines, Web support, text messaging, and drugs improve quit rates—if you and your staff set the stage

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Practice recommendations

- Recommend that your patients take advantage of telephone counseling—it improves both quit rates and long-term abstinence rates (**A**). Web-based cessation programs also help to support smokers in all stages of quitting (**B**).
- Encourage patients to use both pharmacotherapy and counseling to improve abstinence (**A**). Several medications—including bupropion and varenicline—achieve comparable rates of both quitting and long-term abstinence (**A**).
- Train your office staff to assist in the identification and counseling of smokers (**A**).

Strength of recommendation (SOR)
A Good-quality patient-oriented evidence
B Inconsistent or limited-quality patient-oriented evidence
C Consensus, usual practice, opinion, disease-oriented evidence, case series

Ann G. is a 34-year-old mother of 2 who had been coming to the office for her annual Pap smear for several years. Her medical history is significant only for her vaginal deliveries and mild GERD. Her medications include oral contraceptive pills (OCPs) and over-the-counter Zantac as needed. On her most recent annual visit, my medical assistant, Tammy, took Ann's vital signs. The chart had a section about smoking status, and Tammy noted that Ann smoked.

During the office visit, I explained to Ann that her smoking was a serious health risk, and that she needed to quit. She would also need to find a new form of birth control next year, as smoking increases the risks of using OCPs. She nervously laughed off the warning.

The following year, Anne confessed to Tammy that she was still a smoker. Tammy asked her again about quitting. Ann was still adamant: "No way—I can't do it." Nonetheless, during the office visit, I brought up the subject of her smoking. She admitted that she was afraid that quitting smoking would cause her to gain weight. I attempted to address her fears, and then talked about other birth control methods to consider. I gave her a 3-month prescription of OCPs, and told her in 3 months we would discuss what she wanted to do about birth control.

Ann faces an uphill battle. The amount of nicotine in cigarettes is increasing,[1] making it harder for her to quit. The good news is that the treatment of tobacco addiction is constantly improving and the number of tools in our arsenal is growing. In fact, there are many resources that we can try before turning to the prescription pad. However, when needed, pharmacotherapy is an important adjunct for achieving abstinence.

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"5-A" strategy sets stage for success

The Agency for Healthcare Research and Quality (AHRQ) has published *Treating Tobacco Use and Dependence,* a useful guide for helping patients quit.[2,3] These guidelines discuss many aspects of tobacco cessation, from counseling to pharmacotherapy to reimbursement issues. The guidelines break down the smoking cessation process into the 5 A's:

1. **Ask** each patient about her smoking status.
2. **Advise** each patient who smokes that she needs to stop smoking.
3. **Assess** your patient's willingness to make a quit attempt in the next 30 days.
4. **Assist** your patient either in making this quit attempt or in motivating her to consider a quit attempt later.
5. **Arrange** close follow-up of any quit attempts to help prevent relapse.

The Ask and Act program from the American Academy of Family Physicians (AAFP) outlines a similar strategy.[4] The program instructs physicians to **Ask** every patient about her tobacco use and to **Act** to help her quit, via on- or off-site counseling, quitlines, patient education materials, self-help guides or Web sites, cessation classes, and pharmacotherapy.

Take advantage of every opportunity you have to discuss the issue with patients; short conversations can make a difference. A Cochrane Review of 39 trials including 31,000 smokers[5] revealed that even brief advice—simply encouraging patients to quit—was statistically significant (odds ratio [OR]=1.74; 95% confidence interval [CI], 1.48–2.05). The pooled data generated a quit rate difference of 2.5%: for every 40 people who were told to quit, 1 more smoker would.

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Discuss your patient's smoking at every opportunity—one study has shown that even brief advice can help

Empower the office staff

Enlisting the help of the office staff can have a significant impact on the health of the patients. A proactive approach was studied by Fiore et al.[6] Medical assistants, while assessing smoking status, invited all smokers to participate in a cessation study. (The assistants received periodic thank-you gifts for their efforts.)

The participants were randomized to either self-selected treatment or nicotine replacement therapy (NRT) patches, with or without a support program. Some who received the patches and support program also received individual counseling. Fiore et al showed that the majority of smokers were open to attempts to quit smoking. The 13% point-prevalence abstinence rate 1 year out is comparable with the rate obtained (14%) with smokers volunteering for NRT studies in the Cochrane review of 39 trials, noted earlier.

Likewise, in a randomized controlled trial (RCT) involving community-based primary care clinics, Katz[7] demonstrated that intake clinicians could also play an important role in smoking cessation (SOR: **A**). In the study, researchers trained intake clinicians (including registered nurses, license practical nurses, and medical assistants) to identify smokers, provide brief counseling, and assist in their preparation to quit. Patients were offered vouchers for patches and a counselor's business card. Intake clinicians received periodic feedback on their performance based on exit interviews of the patients. The researchers found that these interventions had a statistically significant effect in moderate-to-heavy smokers in quit attempts, quit rates, and continuous abstinence.

Our patient has a change of heart

At the 3-month follow up, Tammy learned that Ann was still smoking—but she now wanted to quit. Ann said that she'd found a pack of cigarettes in her 14-year-old daughter's backpack, and felt that the only way to prevent her from getting hooked was to set a good example.

Tammy gave her the state's quitline number and suggested some online quitting programs. Tammy worked with Ann to choose her target quit date and to pick the Web-based program she was going to use. Ann said that she liked the idea that she

could go online whenever she needed support. She also liked the fact that she could put her quit date into the system, so it would give her timely reminders of all her reasons to quit when she logged on.

I wrote Ann a prescription for varenicline and her OCPs, and told her I wanted to see her in 4 weeks. For her part, Tammy added Ann to her list of patients to call the day after her quit date. Tammy makes this her practice with patients because she knows that one well-timed phone call can be the key to a successful quitting attempt.

Outside support improves abstinence rates

Improving your patients' chances of long-term abstinence hinges, in part, on making the most of outside support. In many cases, your patients can take advantage of them without leaving their homes.

Quitlines increase quit rates, decrease relapse

Telephone counseling is an effective support system.[8] Smokers who call to a single number (800-QUITNOW)—a service provided by the National Cancer Institute—are directed to the quitline for their state. Also, smokers can call the National Cancer Institute directly at their quitline (877-44U-QUIT). Calling a quitline provides smokers with real-time counseling and information about how to quit smoking. Quitlines can be appealing to those patients who are uncomfortable discussing their smoking in a group—and it's free to the patient.

The research supports the use of such help lines. Zhu's study[9] of the California Smokers' Helpline (SOR: **A**) was a proactive protocol where smokers were funneled into a research trial when the help line was overwhelmed. The smokers in the treatment arm of this RCT were assigned a counselor who called the smokers as many as 6 times, following a relapse-sensitive schedule. The 12-month abstinence rate increased from 4.1% to 7.5% ($P<.001$) in the group that had close telephone contact. This improved quit rate reflected both an increase of percentage of smokers who quit and, more importantly, a decrease in quitters who relapsed.

Another prospective RCT[10] (SOR: **A**) enrolled patients from Veterans Affairs (VA) medical centers and involved the same proactive telephone protocol as Zhu used. The treatment group was offered telephone counseling as well as pharmacotherapy; the control group had access to the regular smoking cessation program of the VA system. Regardless of which group an individual was assigned, if that participant used both the counseling and the pharmacotherapy, the quit rate was similar: control (12.7%) and treatment (11.9%). However, only 18% of the controls used both services. The treatment group accessed the combined programs of counseling and medications at a rate of 88%. This led to the difference in 6-month abstinence rates of 13.0% in the treatment group and 4.1% in the control group (OR=3.50; 95% CI, 1.99–6.15). Patients who were directed to and enrolled in treatment programs were therefore more likely to attempt to quit and remain abstinent for up to 6 months.

Web-based programs offer reminders

Like quitlines, Web-based programs offer smokers immediate feedback to help them quit. Many of the programs include links to quitting resources, stories from former smokers and cancer patients, live advice from counselors, and message boards (**TABLE 1**). Web-based programs have been shown to help improve quit rates.

One study[11] compared 2 Web programs involving 11,969 smokers. This RCT (SOR: **B**) looked at an interactive program based, in part, on the AHRQ treatment guidelines. This program generates personalized letters for the participants along with monthly e-mail reminders. A modified program was used as the

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When a counselor called on smokers who were attempting to quit, the abstinence rate climbed from 4.1% to 7.5%

TABLE 1

Web-based support helps smokers quit

www.quitnet.com Boston University School of Public Health	Personalized quit plans
www.ffsonline.org American Lung Association	"Freedom from smoking" modules to guide smokers through quit process
www.whyquit.com Privately supported	Support for "cold turkey" quitting
www.trytostop.org Massachusetts Department of Public Health	Personalized "Quit Wizard" program

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Toll-free quitlines provide patients with personal counseling—appealing to those uncomfortable discussing their smoking in a group

control. The control program was developed by a maker of NRT products, and contained more information about nicotine than about tobacco dependence and cessation. This program was also shorter than the interactive program, which was designed to assist smoking cessation.

Both programs improved quit rates: 10.9% for the interactive program and 8% for the modified/control program, compared with 3.3% for no treatment at all. Although this study was based on participant reports of abstinence over the previous 7 days, and had low follow-up rates (which Internet studies tend to have), the interactive program produced 1 more quitter for every 26 participants than the modified (control) program, using an intent-to-treat analysis (14.6% vs. 10.7%, $P<.001$, OR=1.43, 95% CI, 1.28–1.59).

Another study[12] looked at the use of a more extensive Web site, combining video, audio, and text. This RCT (SOR: **B**) was fully automated and delivered entirely by computer. Again, using the AHRQ guidelines and other sources, researchers designed a series of 5 modules to simulate working with a live counselor. There were 13 different versions, to match the demographics of the participant. The modules ended with a "quit calendar" to pick a date within the next 30 days. The program had 20 hours of video, although no participant saw every section. The intent-to-treat analysis showed a significant difference from the treatment group at 12.3% vs the controls at 5.0% (OR=2.66, 95% CI, 1.18–5.99).

Text messages work

Text messaging may also have a place in supporting smoking cessation efforts. An interesting, although short, study[13] looked at using text messaging to target younger smokers in New Zealand. This RCT (SOR: **B**) involved 1705 smokers who had cell phones with text messaging. Researchers sent participants up to 5 messages daily around their quit date, drawing from over 100 messages that could be personalized with individual names/nicknames. The quit rate was doubled 6 weeks out (28% vs 13%; relative risk=2.20; 95% CI, 1.79–2.70).

Rx in hand, support in place

When Ann left my office, she took with her a prescription for varenicline, the state's quitline number, and the URL for an online support program. Ann was eager to try varenicline: a coworker of hers was using it and doing well. Ann had tried the nicotine patch in the past, but reported that it gave her nightmares. She'd also kept smoking while wearing it. This time, she hoped she'd finally be able to quit for good.

Weighing the drug treatment options

The AHRQ guidelines recommend several types of pharmacotherapy. First-line therapies include different forms of NRT and sustained-release bupropion (Zyban).[2,3]

Nicotine replacement therapy doubles the chances of quitting

With NRT, the nicotine in cigarettes is replaced with nicotine from another source. The thought is that by reducing the withdrawal symptoms, the patient is less likely to relapse and resume smoking. Nicotine replacement is available in several forms: gum, transdermal patches, intranasal spray, inhaler, and lozenges.

A Cochrane meta-analysis of NRT[14] (SOR: **A**) analyzed 123 studies that followed patients for at least 6 months from their quit date. The authors concluded

TABLE 2

Nicotine replacement therapy: Methods are similarly efficacious[11]

THERAPY	OR (95% CI)	N (PARTICIPANTS/ TRIALS)	NNT	DURATION OF THERAPY	COST OF 4 WEEKS (BRAND/GENERIC)†
Nasal spray	2.35 (1.63–3.38)	887/4	8.3	3–6 months	$560/NA
Inhaler	2.14 (1.44–3.18)	976/4	12.5	3 months, then 3-month taper	$504/NA
Lozenges	2.05 (1.62–2.59)	2739/5	14.3	Up to 12 weeks	$300/$240
Patch	1.84 (1.65–2.06)	16,228/37	16.7	8–12 weeks	$110/$92
NRT (all)	1.77 (1.66–1.88)	39,503/105	*		
Gum	1.66 (1.51–1.81)	17,819/52	12.5	Up to 12 weeks	4 mg: $234/$180 2 mg: $204/$150

* Numbers not available.

† Cost based on prices from Walgreen's and Target Pharmacies, May and September 2007.

OR, odds ratio; NNT, number needed to treat; NA, product not available.

that NRT could almost double a patient's chances of quitting smoking. The data from various types of NRT revealed the types to be similarly efficacious (**TABLE 2**). In the treated groups, 17% were abstinent and only 10% were abstinent in the control groups at the various endpoints of the trials. Smokers with higher levels of nicotine dependence as indicated by smoking 10 or more cigarettes daily have higher quit rates using replacement nicotine. Generally, treatments of 8 weeks are as effective as longer courses.

The Cochrane meta-analysis also revealed that:

- Duration of therapy ranges from 3 weeks to 12 months with the various forms of NRT.
- There was no benefit to tapering off the NRT as compared to an abrupt withdrawal.
- Patients are much more likely to relapse after NRT in the first 3 months.
- Combining several forms of NRT may aid a relapsed smoker in another quit attempt. However, the re-attempt should be delayed by a few months, as back-to-back courses are unlikely to improve quit rates.

Sustained-release bupropion: Similar results to NRT

The other first-line therapy suggested by the AHRQ guidelines is sustained-release bupropion.[2,3] A separate Cochrane Review[15] analyzed the data from 36 studies using antidepressants and revealed that two thirds of the studies in this meta-analysis used bupropion. The odds of quitting smoking essentially doubled in the placebo-controlled studies. This is a similar effect as NRT. Neither the AHRQ guidelines nor the Cochrane Review recommend bupropion over NRT or vice-versa.

According to the Cochrane Review, there was no benefit to increasing the dose of bupropion from 150 mg to 300 mg daily. Although the initial multi-dose study of bupropion[16] showed a difference, it was not clinically significant by the end of the study. A larger, open-label randomized trial of 1524 smokers[17] followed for 1 year also showed similar results. At the 3-month evaluation, the higher dose had superior efficacy, but that effect was not statistically significant by the end of the study. Lastly, there is no benefit to continuing the bupropion beyond 7 weeks after the target quit date.

With other antidepressants, results vary

The Cochrane Review also looked at other antidepressants. There were 4 RCTs of nortriptyline (Aventyl/Pamelor) without NRT, totaling 777 smokers followed for at least 6 months.[18–21] The pooled data

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A Cochrane Review found that nicotine replacement may nearly double a smoker's chances of quitting

TABLE 3

Varenicline, nortriptyline, bupropion—strong allies in patients' efforts to quit

THERAPY	OR (95% CI)	N (PARTICIPANTS/ TRIALS)	NNT	DURATION OF THERAPY	COST OF 4 WEEKS (BRAND/GENERIC)*
Varenicline[24,25]	2.80 (2.03–3.88)	1161/2	7.6	12 weeks	$120/NA
Nortriptyline[15]	2.79 (1.70–4.59)	703/4	9.8	12 weeks	$814/$8
Sustained-release bupropion[15]	2.06 (1.77–2.40)	6443/19	10.2	7–12 weeks	$210/$100
Clonidine[23]	1.89 (1.30–2.74)	776/6	9.4	3–4 weeks	$74/$4
Venlafaxine[15]	1.33 (0.59–3.00)	136/1	20.4		$145/NA
Diazepam[23]	1.00 (0.39–2.54)	76/1	No difference		$209/$27
SSRI[15]	0.90 (0.68–1.18)	1768/6	20.7		$170/$4
Buspirone[23]	0.71 (0.34–1.48)	201/3	22.1		$280/$84

* Cost based on prices from Walgreen's and Target Pharmacies, May and September 2007.
OR, odds ratio; NNT, number needed to treat; SSRI, selective serotonin reuptake inhibitors; NA, not available.

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When compared with placebo, bupropion doubled a patient's odds of quitting smoking

essentially doubled the odds of quitting smoking from 7.0% for the controls to 17.2% in the treated groups (OR=2.79; 95% CI, 1.70–4.59). Adding nortriptyline to NRT did increase the quit rates, but not significantly. The dose used in these studies, at 75 to 150 mg is much lower than that used for depression, where significant side effects often interfere with treatment. Generally the starting dose is 25 mg at bedtime. After 1 week, the dose is increased to 50 mg and the following week, it is increased again to 75 mg. Once on the 75 mg dose for a week, the dose is titrated up only if needed. The titration continues at an additional 25 mg weekly.

One of the 4 placebo-controlled studies[20] included an arm of bupropion, producing a head-to-head assessment with nortriptyline (SOR: **A**). The abstinence rates as indicated by no smoking during the final week of treatment were comparable for the 2 groups receiving active medication. Treatment with bupropion or nortriptyline was significantly more efficacious than placebo. However, the effect was lost at the 1 year continuous abstinence mark; the 2 drugs did not differ from each other or placebo (**TABLE 3**).

Other antidepressants were evaluated in the Cochrane study.[15] The tricyclic antidepressants doxepin and imipramine (Tofranil) had no long-term studies and neither showed statistically significant differences in smaller trials. Of the selective serotonin reuptake inhibitors (SSRIs), only fluoxetine (Prozac) had any long-term studies, and none noted statistically significant differences. Likewise, venlafaxine (Effexor) had only 1 trial in which the confidence interval did allow for a potentially useful clinical effect, but failed to show a statistically significant increase in 12-month quit rates.

Clonidine is an option, but side effects are an issue

Another Cochrane Review[22] looked at the effectiveness of clonidine (Catapres) on smoking cessation. Most of the clonidine studies assessed withdrawal symptoms rather than abstinence. Of those that did assess quit rates, the pooled OR for clonidine compares favorably at 1.89 (95% CI, 1.30–2.74). Unfortunately, clonidine has significant side effects: sedation and postural hypotension. The starting dose is 0.1 mg twice daily, and it may be titrated up to a maximum dose of 0.4 mg daily. It should be used for 3 to 4

weeks only to decrease the symptoms of withdrawal. The smoker should then be weaned off the clonidine.

The anxiolytics were the subject of another Cochrane Review.[23] This review, however, did not recommend any anxiolytics, including diazepam and buspirone, for smoking cessation.

A new category of therapy: Nicotinic receptor agonists

With the US Food and Drug Administration's approval of varenicline (Chantix) in May 2006, a new class of drugs became available for treatment of tobacco dependence. This α4β2 nicotinic acetylcholine receptor partial agonist was designed as a smoking cessation drug. By releasing dopamine in the brain like nicotine, it prevents craving. However, it also blocks nicotine from binding, thereby preventing the reinforcing effect of continued smoking.

Two RCTs have assessed varenicline against both bupropion and placebo (**TABLE 3**). Jorenby[24] (SOR: **A**) showed the varenicline-treated participants were significantly more likely to be continuously abstinent at 52 weeks than the placebo- or bupropion-treated groups (23% vs 10.3% placebo [OR=2.66; 95% CI, 1.72–4.11; *P*<.001] and 14.6% bupropion [OR=1.77; 95% CI, 1.19–2.63; *P*=.004]). Gonzales[25] (SOR: **A**) likewise showed the varenicline treated smokers were more likely to be continuously abstinent at 52 weeks than the placebo group (21.9% vs 8.4% [OR=3.09; 95% CI, 1.95–4.91; *P*<.001]). However, the difference between varenicline and bupropion did not reach statistical significance (21.9% vs 16.1% [OR=1.46; 95% CI, 0.99–2.17; *P*=.057]).

As with other medications, varenicline should be started at a low dose. The patient begins with 0.5 mg nightly for the first 3 nights, then increases to 0.5 mg twice a day for 4 days. The second week, the patient begins the 1 mg twice-daily dosing that is continued through treatment.

Vaccines hold the promise of continued abstinence

Several promising ideas for the treatment of tobacco dependence are in development. There are several vaccines being studied.[26] When the immune system produces antibodies to nicotine in response to the vaccine, and when these antibodies bind to the nicotine, the resultant compound is too large to cross the blood-brain barrier. This prevents the reinforcing effect of nicotine. Initial studies of vaccines show that smokers do decrease the amount they smoke, but more importantly, abstinence is easier to maintain. However, the vaccine requires frequent boosters to maintain antibody titers that are effective.

NicVAX from Nabi Biopharmaceuticals was placed on a fast track for approval by the Food and Drug Administration. It is, however, still at least a year away from approval. The other 2 nicotine vaccines are probably several years beyond that for approval.[27]

Researchers are also studying other compounds that block the euphoria associated with smoking.[28] The initial studies of rimonabant (Acomplia), a cannabinoid blocker, have shown it is no better than other treatments already available. With its indication in some European countries for weight loss, it offered promise as an important option for patients who are concerned about the weight gain associated with smoking cessation. However, the FDA did not approve rimonabant for tobacco cessation when issuing its initial approval letter for weight loss in 2006. Because of safety concerns, the manufacturer subsequently withdrew the new drug application for rimonabant in 2007.

With much work, our patient kicks the habit

Ann began taking varenicline the day she left the office, and reached her quit date a week later.

At her 1-month follow-up, Ann reported that it was actually easy for her to stay off

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2 studies suggest that varenicline may be at least as good as—or better than—bupropion for long-term smoking cessation

the cigarettes. With the varenicline, she had lost the desire to smoke. I reminded her to work on the triggers for her smoking: I urged her to make sure that she did not light up when she made her morning coffee or got in the car. I also suggested she put $4 each morning into a jar on her dresser; so she would see how much she saved now that she wasn't buying cigarettes.

At Ann's next annual exam, we marked her in the computer system as a reformed smoker. She was very proud of that label. I asked her what she was doing with all that extra cash. She laughed: "My daughter spends it all! But not on cigarettes!" ■

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Early studies suggest that nicotine vaccines may make abstinence from smoking easier to maintain