

# Smoking cessation: Tactics that make a difference

Telephone “quitlines,” Web support, text messaging, and drugs all boost the quit rate—if you set the stage

## Practice recommendations

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

## CASE Smoker who uses OCs

Ann G. is a 34-year-old mother of two who has 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 gastroesophageal reflux. She takes oral contraceptives (OCs) and uses over-the-counter ranitidine hydrochloride (Zantac) as needed. On Ann’s most recent annual visit, the medical assistant, Tammy, takes her vital signs. The chart has a section about smoking status, and Tammy notes that Ann is a smoker.

During the office visit, the ObGyn explains to Ann that her smoking is a serious health risk and advises her to quit. She also informs Ann that she needs to find a new form of birth

control next year, as smoking increases the risks of using OCs, especially after age 35. Ann nervously laughs off the warning.

When she returns the following year, Ann confesses to Tammy that she is still a smoker. When Tammy asks about quitting, Ann remains adamant: “No way—I can’t do it.” Nonetheless, during the office visit, the ObGyn raises the subject again, and Ann admits that she is afraid that quitting smoking will cause her to gain weight. The physician attempts to address Ann’s fears, talks about other birth control options, and gives her a 3-month prescription for OCs. Before ending the visit, the ObGyn tells Ann that they will discuss what to do about birth control when she returns in 3 months.

Ann faces an uphill battle. The amount of nicotine in cigarettes is increasing,<sup>1</sup> making it harder 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 in a patient’s struggle to achieve abstinence.

## “5-A” strategy sets stage for success

*Treating Tobacco Use and Dependence*, a useful publication from the Agency

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for Healthcare Research and Quality (AHRQ), offers guidelines on many aspects of tobacco cessation, from counseling to pharmacotherapy to reimbursement.<sup>2,3</sup> The guidelines break the smoking cessation process into five 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 in making this quit attempt or encourage 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 outlines a similar strategy.<sup>4</sup> 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, telephone "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 revealed that even brief advice—simply encouraging patients to quit—was statistically significant in helping the smoker quit (odds ratio [OR] = 1.74; 95% confidence interval [CI], 1.48–2.05).<sup>5</sup> The pooled data generated a quit rate difference of 2.5%: for every 40 people who were told to quit, one more smoker would.

#### **Empower the office staff**

Enlisting the help of the office staff can have a significant impact on the health of patients. Fiore and colleagues evaluated a proactive approach in which medical assistants, while assessing smoking status, invited all smokers to participate in a cessation study.<sup>6</sup> (The assistants received periodic thank-you gifts for their efforts.)

Participants were randomized to 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. The result: Most smokers were open to encouragement to quit smoking. The 13% point-prevalence abstinence rate 1 year out was comparable to the rate observed (14%) in smokers volunteering for NRT studies in the Cochrane review of 39 trials noted earlier.<sup>5</sup>

Likewise, in a randomized controlled trial (RCT) involving community-based primary care clinics, Katz and associates demonstrated that intake clinicians can also play an important role in smoking cessation.<sup>7</sup> In the study, researchers trained intake clinicians (including registered nurses, licensed 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. These interventions had a statistically significant effect in moderate-to-heavy smokers in quit attempts, quit rates, and continuous abstinence.

#### **CASE...continued A change of heart**

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

Tammy gives her the state's quitline number, suggests some online quitting programs, and works with Ann to choose her target quit date and to pick the Web-based program she is going to use. Ann likes the fact that she can go online whenever she needs support. She also likes being able to put her quit date into the system so that the program will give her timely reminders of all her reasons to quit when she logs on.

#### **FAST TRACK**

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

The ObGyn writes prescriptions for varenicline (Chantix) and OCs and tells Ann to come back in 4 weeks. For her part, Tammy adds Ann to the list of patients she calls and will get in touch the day after Ann's 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 quit 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 it without leaving their homes.

### Quitlines increase quit rates, reduce relapse

Telephone counseling is an effective support system.<sup>8</sup> Smokers who call to a single number (800-QUITNOW)—a service provided by the National Cancer Institute (NCI)—are directed to the quitline for their state. Smokers can also call the NCI directly at its 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 patients who are uncomfortable discussing their smoking in a group—and they are free to the patient.

Evidence supports the use of such help lines. In their study of the California Smokers' Helpline, Zhu and colleagues tested a proactive protocol where smokers were funneled into a research trial when the help line was overwhelmed.<sup>9</sup> The smokers in the treatment arm of this RCT were assigned a counselor who called the smokers as many as six 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 reflects both an increase in the percentage of smokers who quit and, more importantly, a decrease in quitters who relapsed.

Another prospective RCT enrolled patients from Veterans Affairs (VA) medical centers and involved the same proactive telephone protocol that Zhu and associates used.<sup>10</sup> 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. Quit rates were similar in both groups if the participant utilized both counseling and pharmacotherapy: 12.7% in the control group and 11.9% in the treatment group. However, only 18% of patients in the control group used both services. Among patients in the treatment group, 88% utilized both counseling and medication. This led to 6-month abstinence rates of 13% in the treatment group versus 4.1% in the control group (OR = 3.5; 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, page 38). Web-based programs have been shown to help improve quit rates.

One study compared two Web programs involving 11,969 smokers.<sup>11</sup> This RCT 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, developed by a maker of NRT products, served as the control; it 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.

CONTINUED

### FAST TRACK

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

**TABLE 1**

| <b>Web-based support helps smokers quit</b>                           |  |
|---|--|
| <b>www.quitnet.com</b><br>Boston University School of Public Health   | Personalized quit plans  |
| <b>www.ffsonline.org</b><br>American Lung Association                 | “Freedom from smoking” modules to guide smokers through quit process |
| <b>www.whyquit.com</b><br>Privately supported                         | Support for “cold turkey” quitting                                   |
| <b>www.trytostop.org</b><br>Massachusetts Department of Public Health | Personalized “Quit Wizard” program                                   |

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 one more quitter for every 26 participants than the modified (control) program did, according to an intent-to-treat analysis (14.6% vs 10.7%,  $P < .001$ ; OR = 1.43; 95% CI, 1.28–1.59).

Another RCT looked at the use of a more extensive Web site, combining video, audio, and text.<sup>12</sup> This program was fully automated and delivered entirely by computer. Again, using the AHRQ guidelines and other sources, researchers designed a series of five modules to simulate work with a live counselor. There were 13 different versions to match the demographics of the participant. The modules ended with a “quit calendar” for use by the participant to pick a date within the next 30 days. The program included 20 hours of video, although no participant saw every section. The intent-to-treat analysis showed a significant difference between groups: 12.3% in the treatment group versus 5% in the control group (OR = 2.66; 95% CI, 1.18–5.99).

### **Text messages work**

A short but interesting study used text

messaging to target younger smokers in New Zealand.<sup>13</sup> This RCT involved 1,705 smokers who had cell phones with text messaging. Researchers sent participants up to five messages daily around their quit date, drawing from over 100 messages that could be personalized with individual names/nicknames. The quit rate doubled 6 weeks out (28% vs 13%; relative risk = 2.2; 95% CI, 1.79–2.70).

### **CASE...continued Support in place**

Ann leaves the office with her prescription for varenicline and OCs, the state’s quitline number, and the URL for an online support program. She is eager to try varenicline: A coworker of hers is using it and doing well. Ann has tried the nicotine patch in the past, but says that it gave her nightmares. (She kept smoking while wearing it.) This time, she hopes she’ll 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).<sup>2,3</sup>

### **Nicotine replacement therapy doubles the chance of quitting**

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

A Cochrane meta-analysis of NRT analyzed 123 studies that followed patients for at least 6 months after their quit date.<sup>14</sup> The authors concluded that NRT could almost double a patient’s chance of quitting smoking. The data from various types of NRT revealed the types to be similarly effective (TABLE 2, page 41). In the treated groups, 17% were abstinent, compared with only 10% in the control groups at the various endpoints of the

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

TABLE 2

**Nicotine replacement therapy: Methods are similarly effective<sup>11</sup>**

| THERAPY     | ODDS RATIO (95% CI) | NO. OF PARTICIPANTS/TRIALS | NNT  | DURATION OF THERAPY          | COST OF 4 WEEKS (BRAND/GENERIC) <sup>†</sup> |
|-------------|---------------------|----------------------------|------|------------------------------|--|
| 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)    | 2,739/5                    | 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<br>2 mg: \$204/\$150       |

\* Numbers not available.

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

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

trials. Smokers who had higher levels of nicotine dependence, as indicated by smoking 10 or more cigarettes daily, had higher quit rates using replacement nicotine. Generally, treatment for 8 weeks was as effective as a longer course.

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, compared with 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 (Wellbutrin).<sup>2,3</sup> A separate Cochrane Review analyzed the data from 36 studies using antidepressants and revealed that two thirds of the studies used

bupropion.<sup>15</sup> The odds of quitting smoking essentially doubled in the placebo-controlled studies when the patient used bupropion. This effect is similar to that of 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 dosage of bupropion from 150 mg to 300 mg daily.<sup>15</sup> Although the initial multidose study of bupropion showed a difference between dosages, it was not clinically significant by the end of the study.<sup>16</sup> A larger, open-label randomized trial of 1,524 smokers followed for 1 year had similar results.<sup>17</sup> At the 3-month evaluation, the higher dosage 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 four RCTs of nortriptyline (Aventyl/Pamelor) without NRT, totaling 777 smokers followed for at least 6 months.<sup>18–21</sup> The

### FAST TRACK

**A Cochrane Review found that nicotine replacement nearly doubles a smoker's chance of quitting**

**TABLE 3**

| <b>Varenicline, nortriptyline, bupropion—strong allies in patients' efforts to quit</b> |                            |                                   |               |                            |   |
|---|----------------------------|-----------------------------------|---------------|----------------------------|---|
| <b>THERAPY</b>  | <b>ODDS RATIO (95% CI)</b> | <b>NO. OF PARTICIPANTS/TRIALS</b> | <b>NNT</b>    | <b>DURATION OF THERAPY</b> | <b>COST OF 4 WEEKS (BRAND/GENERIC)*</b> |
| <b>Varenicline</b> <sup>24,25</sup>   | 2.80 (2.03–3.88)           | 1,161/2                           | 7.6           | 12 weeks                   | \$120/NA                                |
| <b>Nortriptyline</b> <sup>15</sup>  | 2.79 (1.70–4.59)           | 703/4                             | 9.8           | 12 weeks                   | \$814/\$8                               |
| <b>Sustained-release bupropion</b> <sup>15</sup>  | 2.06 (1.77–2.40)           | 6,443/19                          | 10.2          | 7–12 weeks                 | \$210/\$100                             |
| <b>Clonidine</b> <sup>23</sup>  | 1.89 (1.30–2.74)           | 776/6                             | 9.4           | 3–4 weeks                  | \$74/\$4                                |
| <b>Venlafaxine</b> <sup>15</sup>  | 1.33 (0.59–3.00)           | 136/1                             | 20.4          |                            | \$145/NA                                |
| <b>Diazepam</b> <sup>23</sup>   | 1.00 (0.39–2.54)           | 76/1                              | No difference |                            | \$209/\$27                              |
| <b>SSRI</b> <sup>15</sup>   | 0.90 (0.68–1.18)           | 1,768/6                           | 20.7          |                            | \$170/\$4                               |
| <b>Buspirone</b> <sup>23</sup>  | 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. NNT, number needed to treat; SSRI, selective serotonin reuptake inhibitors; NA, not available.

**FAST TRACK**

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

pooled data essentially showed a doubling of the odds of quitting from 7% among 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 rate, but not significantly. The dosage used in these studies (75–150 mg) is much lower than that used for depression, where significant side effects often interfere with treatment. Generally, the starting dosage for smoking cessation is 25 mg at bedtime. After 1 week, the dosage is increased to 50 mg, and the following week it is increased again to 75 mg. After a week at 75 mg, the dose is titrated upward only if necessary. The titration continues at an additional 25 mg weekly.

One of the four placebo-controlled studies included both nortriptyline and bupropion arms.<sup>20</sup> The abstinence rates, as indicated by no smoking during the final week of treatment, were comparable for the two groups that received active medication. Treatment with bupropion or nortriptyline was significantly more effective than placebo. However, the effect was lost at the 1-year continuous-absti-

nence mark; the two drugs did not differ from each other or placebo (TABLE 3).

Other antidepressants were evaluated in the Cochrane study.<sup>15</sup> Long-term studies of the tricyclic antidepressants doxepin and imipramine (Tofranil) were lacking. Nor were there statistically significant differences in smaller trials. Of the selective serotonin reuptake inhibitors, only fluoxetine (Prozac) had been studied in long-term trials, and none noted statistically significant differences. Likewise, venlafaxine (Effexor) was studied in only one trial in which the confidence interval allowed for a potentially useful clinical effect, but there was no statistically significant increase in 12-month quit rates.

**Clonidine is an option, but side effects are an issue**

Another Cochrane Review looked at the effectiveness of clonidine (Catapres) on smoking cessation.<sup>22</sup> Most of the 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 dosage is 0.1 mg twice daily, and it may be titrated to a maximum dose of 0.4 mg daily. It should be used for 3 to 4 weeks only to decrease withdrawal symptoms. The smoker is then weaned off the drug.

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

### **A new category of therapy: Nicotinic receptor agonists**

With US Food and Drug Administration (FDA) approval of varenicline in May 2006, a new class of drugs became available for tobacco dependence. This  $\alpha 4\beta 2$  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 and colleagues showed that 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;  $P = .004$ ]).<sup>24</sup> Gonzales and associates also showed that 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;  $P < .001$ ]).<sup>25</sup> However, when compared with varenicline, bupropion's effects were no longer statically significant at 52 weeks (21.9% vs 16.1% [OR = 1.46; 95% CI, 0.99–2.17;  $P = .057$ ]).

The patient initiating varenicline begins by taking 0.5 mg nightly for 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 dosage that is continued through treatment.

### **Vaccines hold promise**

Several promising ideas for the treatment of tobacco dependence are in development, including several vaccines.<sup>26</sup> 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 decrease the amount they smoke and find abstinence easier to maintain. However, the vaccine requires frequent boosters to maintain effective antibody titers.

NicVAX from Nabi Biopharmaceuticals was placed on a fast track for approval by the FDA, which is still at least 1 year away. The other two nicotine vaccines are unlikely to be approved for several years.<sup>27</sup>

Researchers are also studying other compounds that block the euphoria associated with smoking.<sup>28</sup> The initial studies of rimonabant (Acomplia), a cannabinoid blocker, have shown that 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 it issued 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.

### **CASE...resolved She kicks the habit**

Ann begins taking varenicline the day she leaves the office, and reaches her quit date a week later.

At her 1-month follow-up, she reports that it was easy for her to stay off the cigarettes. With the varenicline, she lost

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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 desire to smoke. The ObGyn reminds her to work on the triggers for her smoking, urging her not to light up when she makes her morning coffee or gets in the car. The physician also suggests that Ann put \$4 each morning into a jar on her dresser, so she can see how much she saves now that she isn't buying cigarettes.

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

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