



*Oncologists can help their patients quit smoking through simple and proven pharmacologic and behavioral intervention.*

Gary Ernest Smith. *Winter Field*. Oil on canvas, 36" × 60". Reprinted by permission of Gary Ernest Smith, Overland Gallery, Scottsdale, Arizona.

# Contemporary Smoking Cessation

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**Background:** Tobacco smoking is the single most preventable cause of death in the United States today. Oncologists are in a unique position to affect the health and economic burdens of smoking by encouraging cessation among their patients who smoke.

**Methods:** The authors describe and review the effectiveness of current smoking cessation interventions as well as strategies that can be used to encourage cessation among patients. Three types of smoking cessation interventions are described: minimal (or self-help) interventions, behavioral interventions, and pharmacotherapy. The effectiveness of combinations of these types of treatments is also discussed.

**Results:** Oncology professionals can improve their patients' chances for success by implementing various cost-effective and easily executed smoking cessation interventions. Advice from a physician to quit smoking has resulted in long-term quit rates of up to 10.2%, and nicotine transdermal patches, nicotine gum, inhalers, and nasal sprays are also effective.

**Conclusions:** Oncologists are encouraged to adopt the "4As" treatment protocol recommended by the National Cancer Institute: ask patients about their smoking status, advise them to quit, assist by recommending pharmacotherapy, counseling, and psychosocial self-help materials, and arrange follow-up.

## Introduction

Tobacco smoking is the single most preventable cause of death in the United States today, claiming at least 419,000 lives every year.<sup>1</sup> In addition to contributing to gastric ulcers, chronic bronchitis, emphysema, cerebrovascular disease, and heart disease, cigarette smoking is responsible for at least 29% of all cancer deaths.<sup>2</sup> These include cancers of the mouth, larynx, pharynx, bladder, pancreas, esophagus, stomach, kidney, and uterine cervix. Smoking is responsible for 90% of lung cancer cases.<sup>3</sup> Compared with never-

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smokers, current men smokers are 23 times more likely to die of lung cancer, and current women smokers are 13 times more likely.<sup>4</sup> As of 1987, lung cancer due to smoking has surpassed breast cancer as the leading cause of cancer death among women.<sup>5</sup>

The economic burden to society of smoking-related illnesses and death is enormous. Smokers lose between 15 and 25 years of life expectancy, resulting in billions of dollars of lost productivity. In addition, the costs of treating smoking-related diseases in 1993 amounted to \$50 billion, according to the Centers for Disease Control and Prevention.<sup>6</sup>

## Smoking Cessation: Benefits and Difficulties

In 1990, the US Surgeon General's report concluded that smoking cessation produces substantial and immediate health benefits and that benefits apply to persons with and without smoking-related disease.<sup>7</sup> According to the report, after 10 years of abstinence, former smokers' risk of lung cancer is reduced to between 30% to 50% of the risk in continuing smokers. With increasing years of abstinence, risk continues to decline. Furthermore, the reduction in risk occurs for both men and women and for all histological types of cancer. Recent data also indicate that smoking cessation substantially reduces the risk of developing a second primary cancer after successful treatment of small-cell lung cancer.<sup>8</sup>

Quitting smoking is a difficult task, however. According to results from the 1994 National Health Interview Supplement (NHIS-2000), 70% of smokers indicated a strong desire to quit, and 46.6% had tried to quit smoking in the year prior to completing the survey.<sup>9</sup> However, only 5.7% of smokers were able to maintain abstinence for 12 months.

## Why People Smoke

Several theories have been advanced to explain the initiation and maintenance of nicotine dependence. In the 1970s, addiction models that emphasized relief of nicotine withdrawal symptoms comprised the dominant paradigm. However, researchers subsequently recognized the importance of other motivating influences. For example, studies suggested that some individuals smoked not only to relieve withdrawal symptoms, but also to enhance attention, to attain pleasurable feelings of relaxation, or to relieve anxiety or other negative affective states.<sup>10</sup> These subjective effects are consistent with the demonstrated pharmacological effects of

inhaled nicotine on a number of neuroregulatory systems. Social influences such as peer pressure or images of smoking portrayed in movies and advertising also played a role, especially in explaining initiation into smoking among younger individuals.<sup>9</sup> In addition, the pairing of cues (eg, coffee, stress, etc) with the reinforcing effects of nicotine has been recognized as an important factor maintaining nicotine dependence.

## Smoking Cessation: A Role for Oncologists

Although quitting smoking is inherently difficult for the majority of smokers, oncology professionals can help improve patients' chances for success. Oncologists and other health professionals are in a unique position to foster cessation because they are a credible source of health information and have access to large numbers of smokers who may be reluctant to seek help for smoking cessation. In addition, there is evidence to suggest that most smokers believe it is their physician's responsibility to ask about their smoking status and to advise them to quit.<sup>11</sup> Smokers have also reported that advice from a physician to stop smoking would increase their motivation to quit.<sup>12,13</sup> Clinical trials have shown that brief advice to quit from a physician produces abstinence rates of between 5% and 10%, which rises to between 20% to 36% when physicians are more involved in providing counseling and advice.<sup>14</sup> Because physicians and other health professionals see a large number of patients on a routine basis, such involvement can have a substantial public health impact.

In recognition of this fact, some hospitals have begun to assess smoking status as a vital sign.<sup>15</sup> Similarly, data from the National Ambulatory Medical Care Survey found that in 1991, 67% of 3,254 physicians surveyed reported having asked about patients' smoking status.<sup>16</sup> Other data, however, suggest that many physicians are missing opportunities to provide simple cessation advice and treatment to smokers,<sup>17</sup> particularly those patients whose diagnoses are nonsmoking-related.<sup>15</sup> The physician's task of aiding cessation among patients is simpler now that effective and easy-to-administer treatments (eg, nicotine replacement therapy and brief counseling) are available.

## Review of Contemporary Smoking Cessation Interventions

For this review, we report and update conclusions reached by the United States Agency for Health Care Policy and Research (AHCPR). With the aim of developing

clinical guidelines for treating tobacco dependence, the AHCPR convened an expert panel to evaluate the efficacies of available smoking cessation treatments. The panel reviewed more than 3,000 randomized, controlled evaluations of cessation interventions. Inclusion criteria for studies were the report of follow-up data at least 5 months after a quit date and publication in English-language, peer-reviewed journals between the years 1975 and 1994. The panel also conducted random-effects logistic regression analyses to yield effect size estimates for the various treatments. The guidelines for treatment were published in April 1996 by AHCPR.<sup>18</sup> Subsequently, a summary paper of the guideline findings was published,<sup>19</sup> and an update is now in progress. Other review papers have since appeared that have addressed the efficacy of recently developed smoking cessation aids or treatments.<sup>20,21</sup> In the following sections, we briefly describe three main types of intervention: minimal (or self-help) interventions, behavioral interventions, and pharmacotherapy. We also discuss the effectiveness of combinations of these types of treatments.

### *Minimal Interventions*

**Brief advice to quit by a physician:** As a part of their meta-analyses, the AHCPR Panel evaluated seven studies in which physicians took 3 minutes or less to advise patients to quit smoking. Their analysis revealed that, on average, advice raised long-term quit rates from 7.9% to 10.2%. This increase translates to a significant public health impact, considering the large number of patients with whom physicians have contact. Also illustrating the substantial public health impact of brief advice, a 1999 analysis by the Centers for Disease Control and Prevention estimated that brief physician counseling costs between \$705 to \$988 per life-year gained for men and between \$1,204 to \$2,058 for women, depending on a patient's age.<sup>22</sup> This compares favorably to cost-effectiveness statistics for prevention therapies for other illnesses. For example, mammography screening for breast cancer costs approximately \$60,000 per life-year gained. Thus, simple, clear advice from a physician can be regarded as an easy, cost-effective intervention that not only moves smokers closer to the decision to quit, but may also motivate some smokers to make an actual attempt. In a later section, we describe specific advice that oncologists and other physicians can provide to patients.

**Self-help interventions for unassisted quitters:** According to meta-analyses conducted by the AHCPR panel, written materials (pamphlets, booklets, manuals) by themselves do not enhance quit rates among self-quitters, compared to no intervention. A similar conclusion was reached for the use of audiotapes and videotapes as well as for the provision of referral lists

for community-based smoking cessation programs. Results, however, were better for telephone hotlines that potential quitters can call for counseling or aid (reactive counseling). The overall cessation rate for such hotlines approached 11.1%. In a study by Ossip-Klein and colleagues,<sup>23</sup> the simple availability of a hotline had a significant impact on cessation rates. This controlled trial sampled participants from 10 counties who all received self-help manuals. The percentage of participants who were abstinent from smoking for at least 90 days at the 12-month follow-up was significantly higher among smokers who had the option of calling the hotline (10%) vs those who received only self-help materials (7.1%).

Telephone advice may also be proactive, whereby a trained clinician provides telephone counseling at specified times during a smoker's attempt to quit. In a recent study published subsequent to the AHCPR review,<sup>24</sup> researchers compared proactive telephone counseling consisting of two calls spaced over a three-month period, with a condition in which smokers received two letters encouraging them to use a hotline. All participants received a standard self-help manual. The six-month abstinence rate for both interventions was approximately 20%. Although the sample for this study was composed of smokers 60 years of age or over, the results are consistent with other research using different samples that point to improved cessation rates when proactive or reactive telephone counseling is combined with self-help manuals.<sup>25</sup> Research also suggests that a greater number of proactive telephone contacts may improve abstinence rates. In one study, 3,030 smokers received one of three interventions: a self-help quit kit only or a quit kit plus either one telephone counseling session or up to six telephone counseling sessions. The abstinence rate at 12 months was 5.4% for participants who did not receive calls, 7.5% for those who received only one follow-up call, and 9.9% for smokers who received multiple follow-up calls.<sup>26</sup> These results are consistent with the AHCPR panel's findings that more intensive person-to-person counseling, such as longer individual sessions or a greater number of treatment sessions, is more beneficial than less intensive interventions.

Because of the relatively small number of evaluations of self-help interventions conducted thus far, the AHCPR advocated greater study of self-help modalities, especially those utilizing innovative strategies. One recent innovative approach compared cessation rates among smokers who received (1) a standard self-help manual, (2) manuals matched to individual smokers' readiness to quit smoking (ie, stage-matched), (3) stage-matched manuals plus personalized computer feedback, or (4) stage-matched manuals, computer feedback,

and four follow-up counselor calls.<sup>27</sup> Results of comparisons showed that smokers who received computer feedback plus stage-matched manuals achieved the highest abstinence rate at 18 months posttreatment (approximately 25%). This rate was more than twice that achieved by smokers who received only standardized nonstage-matched manuals. Other innovative interventions worthy of future investigation include the use of automated telephone systems that ask questions and provide smokers with counseling, reinforcement, feedback, and suggestions for behavioral change.<sup>28</sup>

### *Behavioral Interventions*

The AHCPR panel reviewed 39 studies of behavioral interventions. These interventions consisted of a number of treatment components, the most prevalent being problem solving/skills training and strategies to increase motivation to quit. A number of studies also included relaxation training, contingency contracting, manipulation of smoking dynamics (eg, gradual reduction of nicotine administration), and social support as provided by treatment or by external sources. The AHCPR panel's meta-analysis concluded that two features of behavioral interventions were associated with more positive cessation outcomes: (1) supportive care by a clinician and (2) training in problem solving or coping. Treatments incorporating these components produced estimated six-month abstinence rates as high as 15.2%. Elements of supportive care include expressing care and concern by a clinician, providing information about quitting, and encouraging patients to talk about their feelings and concerns regarding quitting. Important features of problem solving and skills training were training smokers to recognize and learn to cope with internal and external states that increase the risk of relapse.

A small number of studies separately reviewed by the AHCPR panel examined the use of hypnosis, acupuncture, and cue-exposure in treatments. The panel concluded that there was insufficient data to justify conclusions about the efficacy of these specific components.

There have been recent attempts to match behavioral interventions to smoker characteristics. Data on matching is preliminary, however, with the role of individual differences limited to smokers' predisposition toward depression and their degree of nicotine dependence.<sup>29-31</sup>

### *Pharmacotherapy*

**Nicotine transdermal patch:** The nicotine transdermal patch, like all nicotine replacement thera-

pies (NRTs), improves cessation rates by reducing withdrawal symptoms and cravings for cigarettes. Several brands of nicotine patches are available either over the counter or by prescription. An AHCPR summary of five meta-analyses found that the nicotine patch at least doubled 6- and 12-month cessation rates relative to placebo-patch comparison groups. For example, a recent study found a 24-week abstinence rate of 11.0% with a nicotine patch compared with a rate of 4.2% with a placebo patch.<sup>32</sup>

The package insert for all nicotine patch brands includes instructions for use. Brands vary in terms of recommended duration of treatment and whether tapering to lower patch doses is suggested. Tapering does not appear to confer an advantage, according to a recent meta-analysis,<sup>33</sup> but the notion may appeal to patients. Pregnant women and individuals with heart disease are advised to use the patch only with physician approval and supervision. Other considerations are skin reactions, which according to package inserts can occur in up to 50% of patients. These reactions usually are not severe enough to warrant discontinuation of patch treatment and can be ameliorated by the use of medicated creams and by changing patch sites. More detailed suggestions for clinical use of the patch are provided elsewhere.<sup>18</sup>

**Nicotine gum:** The AHCPR Guideline Panel recommends use of the patch over gum because of potential problems with adherence to the gum regimen. According to the panel, gum is likely to be the better choice when patients express a preference for gum, when previous use of the patch has failed, or when severe reactions occur (such as skin irritation) specific to the use of the patch. Nevertheless, as reported by the AHCPR panel, three meta-analyses of the effectiveness of nicotine gum found that gum increased 12-month abstinence rates by between 40% and 60% compared with placebo-gum or no-gum conditions.

**Nicotine inhaler:** The nicotine inhaler, available only by prescription, is a plastic device shaped like a cigarette that produces a vapor of nicotine when puffed. The term *inhaler* is a misnomer, however, because the nicotine vapor is not inhaled but rather is absorbed through the oral cavity, much like nicotine gum. An advantage of the inhaler is that its shape and manner of use may satisfy some of the behavioral aspects of smoking implicated in cravings. The inhaler may cause some users to experience sore throat or coughing, but these reactions are usually mild.

Because the inhaler is relatively new on the market, its efficacy in smoking cessation was not evaluated by the AHCPR panel. At least three recent studies, how-

ever, have found six-month abstinence rates of between 17% and 28% compared with rates of between 6% and 9% for placebo.<sup>34-36</sup>

**Nicotine nasal spray:** The nicotine nasal spray provides a dose of nicotine much more rapidly than any of the previous NRTs described but less rapidly than cigarettes.<sup>37</sup> Some of its side effects include irritation of the throat and nasal passages, sneezing, coughing, and tearing, but these reactions tend to diminish after the first week of use. Nicotine nasal sprays also appear to double quit rates compared with placebo<sup>38</sup> and may be particularly effective for heavy smokers.<sup>39</sup>

**Choice of NRTs:** Patients have several options for NRT, and more are currently under development. Because all NRTs are safe and effective, the choice of which type of NRT to recommend is a matter of patient preference, previous experience, and potential side effects. In addition, long-term use of NRT does not appear to exacerbate existing conditions or create additional health problems.

**Combination NRT:** Recent studies have examined the concurrent use of more than one type of NRT. One study found that the combination of gum and patch significantly increased abstinence rates relative to either method alone (ie, active gum plus placebo patch or placebo gum plus active patch). The combination obtained a six-month abstinence rate of 27.5% and a 12-month rate of 18.1%.<sup>40</sup> The combination of nicotine spray with the patch has also been evaluated. At 12 months, the combination spray and patch treatment resulted in abstinence of 27% compared to a patch-only abstinence rate of 11%.<sup>41</sup> At six years of follow-up, 16% of participants who received the combined treatment were abstinent, whereas 9% of the patch-only group were abstinent. (It should be noted that all participants attended four supportive group meetings.) An advantage of using the spray in conjunction with slower-acting NRTs such as the patch is that the spray can more effectively satisfy immediate cravings.

NRTs have also been used in combination with psychosocial treatments. According to the results of meta-analyses conducted by the AHCPR panel, counseling interventions combined with the use of NRTs increase the chances of cessation; the greatest improvement occurs with intensive therapy as opposed to brief counseling.

**Bupropion:** Several nonnicotinic medications have been investigated for their ability in helping smokers to reduce cravings and other withdrawal symptoms. The efficacy of many of these medications in aiding ces-

sation, however, has not been clearly demonstrated.<sup>19</sup> Two exceptions are bupropion and nortriptyline hydrochloride. Bupropion is a sustained-release antidepressant (a dopamine reuptake inhibitor) that has been shown to increase quit rates relative to placebo.<sup>42</sup> In a recent study,<sup>43</sup> bupropion nearly doubled 12-month point-prevalent abstinence rates (30.3%) relative to placebo (15.6%) or the patch (16.4%). The combination of bupropion and the patch was also more efficacious (35.5%) than placebo or the patch. Although 12-month point-prevalent rates were similar for the patch and placebo groups, the authors reported that 12-month continuous rates were superior for the nicotine patch (odds ratio 1.1). Future research will determine whether the effectiveness of the patch alone has dropped as low as that found in this study.

Bupropion may be an effective alternative for smokers who do not wish to use the patch or for those in whom patch treatment was ineffective. Some patients may suffer side effects of insomnia or dry mouth, but side effects generally are mild. Contraindications include a history of seizure, head trauma, anorexia, and alcohol abuse. The dosage recommended for smoking cessation is 300 mg/d for 7 to 12 weeks, with treatment beginning at least one week prior to cessation.

**Nortriptyline hydrochloride:** Nortriptyline hydrochloride, a tricyclic antidepressant, has also been evaluated for its effectiveness as a smoking cessation aid. A study conducted by Prochazka and colleagues<sup>44</sup> showed that among patients receiving a standard behavioral treatment and follow-up visits, six-month point-prevalence abstinence rates were 14% for patients receiving nortriptyline vs 3% for placebo. Other research has confirmed the superiority of nortriptyline over placebo. For example, Hall and colleagues<sup>45</sup> found a continuous abstinence rate of 24% for nortriptyline and 12% for placebo over a 64-week study period. Nortriptyline thus appears promising as a smoking cessation aid, although side effects such as dry mouth and dysgeusia have been reported.<sup>44</sup> Other antidepressants are currently under investigation as smoking cessation aids.

## How Oncology Practitioners Can Aid Cessation

Oncology professionals can help to reduce the societal burden of smoking by adopting the "4As" treatment strategy (ask, advise, assist, arrange) recommended by the National Cancer Institute (NCI).<sup>46</sup> The first "A" is to ask patients about their smoking status at every visit and record this information. The second "A" is to

advise smokers to quit. For physicians with extreme time pressures, this level of intervention may be all that is feasible. The third "A" is to assist patients' cessation attempts where possible by helping them to set a quit date, providing self-help materials, prescribing pharmacological treatment, and recommending counseling. Specific useful suggestions are to quit "cold turkey" instead of gradually reducing smoking, to make abstinence the goal, to change one's daily routine, to avoid cues associated with smoking (eg, alcohol, other smokers), and to use distraction when urges to smoke arise. It may be useful for smokers to know that whereas most withdrawal symptoms last one to two weeks, urges to smoke decline more gradually. The final "A" is to arrange follow-up contact. Follow-up contact should occur within a week of the quit date and can occur either in person or by telephone. During a follow-up session, the physician should congratulate successful abstinence or, if smoking has occurred, urge a recommitment to total abstinence. Circumstances surrounding the relapse should be examined and the event viewed as a learning experience that can be used in anticipating future challenges. Smokers who relapse should be advised that it may take several attempts to achieve abstinence, and they should be encouraged to try again soon.

Gritz and colleagues<sup>47</sup> implemented components of the NCI model in a controlled intervention geared specifically for cancer patients. Participants consisted of 186 smokers (133 inpatients and 53 outpatients) who were receiving treatment for primary squamous cell carcinomas of the head and neck. Both intervention and usual-care (control) patients received strong cessation advice, but intervention patients also received self-help booklets, monthly advice, and reminder postcards for follow-up visits. Absolute outcomes from the trial were encouraging, with at least 64% of smokers from each group achieving 12-month continuous abstinence. There were no significant differences in abstinence rates between the intervention and control group, however. Possible reasons include the provision of strong initial cessation advice to all patients, contamination of the intervention to control group participants, a ceiling effect due to high quit rates in cancer patients, and a small sample size. Further research testing models of smoking cessation interventions targeting cancer patients is needed.

To enhance motivation among smokers who are less inclined to want to quit, clinicians can follow the "4Rs" strategy (risk, rewards, relevance, repetition) suggested by the AHCPR panel.<sup>17</sup> The first "R" is to emphasize the risks of continued smoking, which can be acute (eg, shortness of breath, impotence, exacerbation of asthma) or long-term (eg, heart attack, stroke, lung and

other cancers, and chronic obstructive pulmonary diseases). The second "R" involves the rewards of quitting, which include improving physical and overall health, enhancing sense of smell and taste, being a good role model for children, and saving money. The third "R" is relevance; these risks and rewards may vary in importance depending on a smoker's age, gender, health status, or other important patient characteristics. The final "R" represents repetition of the risks and rewards until smokers are committed to making a genuine attempt to quit. According to a recent analysis, these recommendations for physician interventions are extremely cost effective compared with other medical interventions.<sup>48</sup>

## Conclusions

Helping patients to quit smoking is an important strategy in cancer control. At the very minimum, an assessment by oncologists of their patients' smoking status and providing strong, clear advice to quit can help substantially. In further assisting patients to quit, physicians should encourage pharmacotherapy consisting of either bupropion or the patch, and possibly their combination, with clear descriptions of both types of medications. Where possible, psychosocial treatment should be advised. If not possible, self-help materials should be made available to patients.

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