

# Treatment of Tobacco Use and Dependence: The Role of the Dental Professional

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*Abstract:* The purpose of this article is to discuss tobacco use and dependence, effective treatments, and the role of the dental professional. Tobacco dependence is discussed as a chronic condition characterized by a vulnerability to relapse that persists for perhaps years. The need for ongoing rather than just acute care is highlighted. Effective treatments for tobacco dependence exist. Brief clinical intervention makes a difference. It is recommended that every dental patient who uses tobacco be offered at least one of the effective treatments available. In so doing, dental professionals can play an important role in primary prevention of adverse health effects and can have an important public health impact by helping to counter tobacco use.

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*Key words:* tobacco, dental professionals, nicotine dependence

The purpose of this article is to discuss tobacco use and dependence, effective treatments, and the role of the dental professional. To this end, a brief overview of popular types of tobacco, their prevalence of use, health and economic consequences of use, benefits of quitting, and challenges to quitting will be provided. In addition, effective treatments implemented in clinical practice, how to approach tobacco users in different stages of readiness to quit, and pharmacological aids will be presented. Finally, some of the current frontier areas of research in the area of treatment will be addressed.

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## Types of Tobacco and Prevalence and Consequences of Use

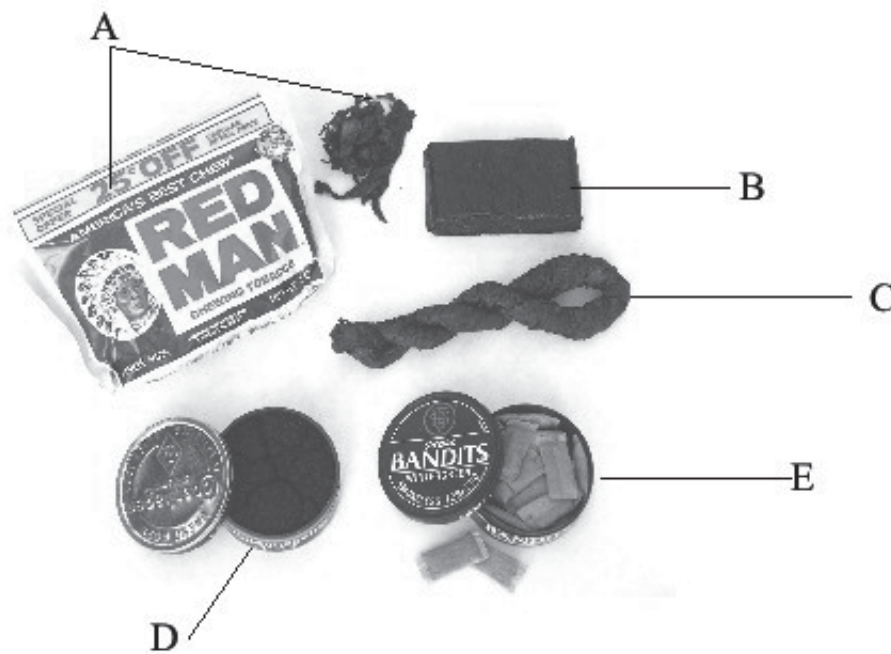
There are two basic types of tobacco: smoked and unsmoked. Among smoked tobacco, the most popular forms in the United States are cigarettes, pipes, cigars, clove cigarettes, and bidis. Cigarettes are the most common form of tobacco used in the United States. In 2002, U.S. smokers consumed an estimated 420 billion cigarettes.<sup>1</sup> Clove cigarettes are from Indonesia and contain 30-40 percent minced cloves. They deliver twice as much nicotine, tar, and carbon monoxide as moderate-tar U.S. cigarettes.<sup>2</sup> Bidis are small, brown, hand-rolled cigarettes imported primarily from India and other southeast Asian countries. They consist of tobacco wrapped in a

temburni leaf.<sup>3</sup> Because of the low combustibility of the temburni leaf, bidis must be puffed constantly to remain lit. Consequently, bidi smokers inhale more frequently and more deeply, increasing the delivery of tar and other toxins.<sup>3,4</sup>

Unsmoked tobacco—also known as spit tobacco (ST) and by the industry-coined term “smokeless” tobacco—includes chewing tobacco and moist oral snuff. Chewing tobacco is a more coarsely cut tobacco leaf. It is marketed as either looseleaf, plug, or twist (Figure 1). It is chewed and then held in place in the mouth. Moist oral snuff, also known as “dip,” is a finely ground tobacco leaf. It is sold either loose or packaged in sachets and is placed in the cheek or lip without chewing for about thirty minutes. Nicotine in ST products is absorbed through the oral mucosa.

Among adults in the United States, 22.5 percent, or 45.8 million, smoke cigarettes. Prevalence of smoking is highest among Native Americans/Alaskan Natives (40.8 percent), followed by white non-Hispanics (23.6 percent), black non-Hispanics (22.4 percent), Hispanics (16.7 percent), and Asian/Pacific Islanders (13.3 percent).<sup>5</sup> Although adult smoking has declined substantially from 40 percent in 1960, an estimated 3,000 children and adolescents become regular users of tobacco every day.<sup>6</sup> The prevalence of smoking among high school students in 2003 was an estimated 21.9 percent, and the prevalence of ST use was 11 percent among high school males.<sup>7</sup>

The prevalence of tobacco use is of concern because of the adverse health effects associated with its use. Smoking is the leading preventable cause of death in the United States. Each year, approximately



**Figure 1. Forms of spit tobacco commonly used in the United States: A. Looseleaf chewing tobacco and pouch used for packaging. B. Plug chewing tobacco. C. Twist chewing tobacco. D. Moist snuff. E. Moist snuff packaged in sachets.**

440,000 deaths are directly attributable to smoking, and secondhand smoke kills as many as 35,053 people per year<sup>8</sup> (Table 1). In addition, numerous oral diseases and conditions clearly are caused by smoking. These include oral, pharyngeal, and esophageal cancers<sup>9</sup> and adult periodontitis.<sup>10</sup> Fifty percent of adult periodontitis cases in the United States have been attributed to cigarette smoking.<sup>11</sup>

Smoking also is a significant predictor of failure of periodontal therapy<sup>12</sup> and of failure of the osseointegration of dental implants.<sup>13</sup> In addition,

**Table 1. Annual U.S. deaths attributable to smoking, 1995-99**

CV diseases	148,605	34%
Lung cancer	124,813	28%
Respiratory diseases	98,007	22%
Second-hand	35,053	9%
Other cancers	30,948	7%
Other	1,917	<1%
Total	439,343	100%

Source: Centers for Disease Control and Prevention, MMWR 2002;51(14):300-3.

smoking is associated with impaired oral wound healing,<sup>14,15</sup> increased risk of root caries,<sup>16</sup> oral pain,<sup>17</sup> and a wide range of other oral soft tissue changes (e.g., nicotine stomatitis, oral leukoplakia, ANUG, halitosis, dental plaque, calculus, and staining).<sup>18</sup> Moreover, the economic burden of tobacco use is enormous. For example, the societal costs of tobacco-related diseases and deaths in 1998-99 was \$157 billion.<sup>19</sup>

Spit tobacco (ST) use also is associated with oral cancer.<sup>20-22</sup> In addition, ST users, compared to nonusers, have significantly more gingival recession<sup>23</sup> and oral leukoplakia in the area they hold their tobacco.<sup>24-26</sup> The

malignant transformation of these lesions is estimated to be 2 percent to 18 percent.<sup>27-29</sup> In addition, ST use is associated with increased risk of oral pain,<sup>17</sup> heart rate,<sup>30</sup> blood pressure,<sup>31</sup> and hypercholesterolemia,<sup>32</sup> compared to nonusers. ST use also produces blood nicotine concentrations similar to regular smoking<sup>33</sup> and is associated with nicotine addiction. Figure 2 shows that peak blood nicotine concentrations are higher and are achieved more rapidly when nicotine is delivered by a cigarette. Although nicotine from ST products is absorbed a little more slowly than from cigarettes, eventually similar blood nicotine concentrations are achieved. Thus, all these tobacco products are addictive.

## Benefits of Quitting

Although there are long-term health problems associated with long-term smoking, the benefits of quitting smoking are numerous and substantial.<sup>4,34</sup> For example, two weeks to three months after quitting, circulation improves and lung function increases up to 30 percent. Lung ciliary function is restored one to nine months after quitting, which increases

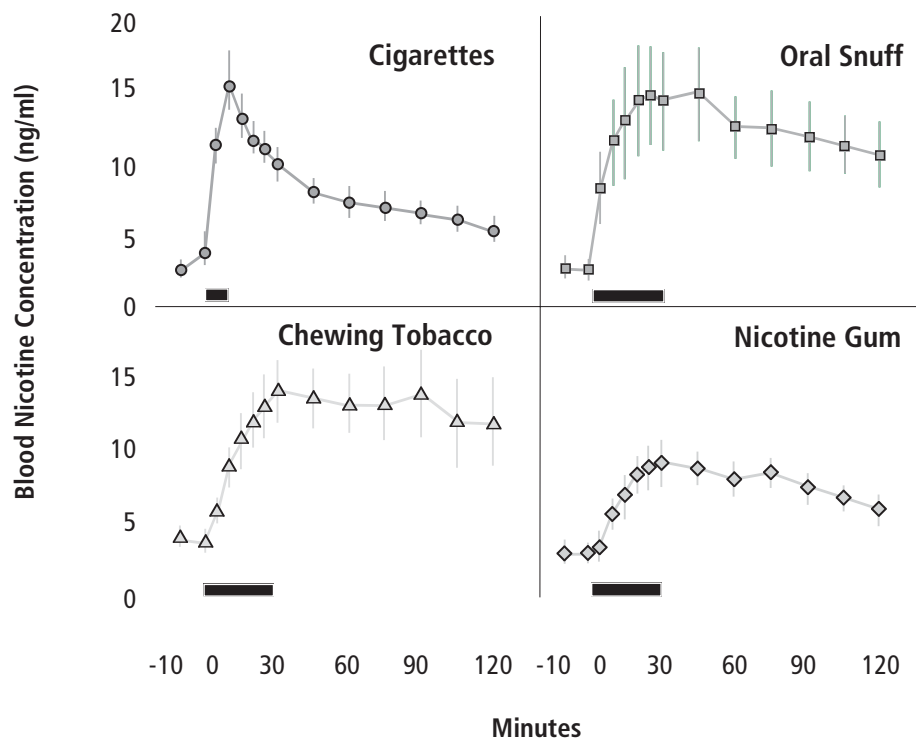
the individual's ability to clear the lungs of mucous and decreases the risk of infection.

In addition, one year after smoking cessation, risk of coronary heart disease is decreased to half that of a smoker; five to fifteen years after smoking cessation, risk of stroke is reduced to that of individuals who have never smoked; and ten years after quitting, an individual's risk of dying from lung cancer is about half that of a continuing smoker, and the risk of cancer of the mouth, throat, esophagus, bladder, kidney, and pancreas decrease. Finally, fifteen years after one stops smoking, risk of coronary heart disease becomes that of a never smoker.<sup>34</sup>

Moreover, with cessation of ST use, many oral conditions are arrested or improved by cessation. For example, ST-associated oral mucosal lesions,<sup>35</sup> ANUG, and nicotine stomatitis generally resolve clinically.<sup>36</sup> In addition, acceleration of periodontal disease, plaque biofilm, dental calculus, tooth stain, halitosis, and the rate and incidence of tooth loss decrease.<sup>36</sup> Osseointegration of dental implants im-

proves.<sup>37</sup> Most importantly, oral cancer survival rates improve, and risk of recurrent oral cancer decreases.<sup>38</sup>

Given the benefits of quitting, it has been said that "we need to encourage a culture of health care in which failure to treat tobacco use—the chief cause of preventable death and disease—constitutes an inappropriate standard of care."<sup>39</sup> Although dentists perceive "patient resistance" and "fear of patients leaving their dental practice" as barriers to providing tobacco cessation counseling in the dental setting,<sup>40</sup> studies report that patients prefer smoking cessation counseling from a health professional over support groups, self-help, and telephone counseling.<sup>41</sup> A survey of 3,088 dental patients in fifty-three dental practices revealed that 58.5 percent believed that dental offices should provide tobacco cessation treatment services. There was equal support among tobacco users and nonusers.<sup>42</sup> Moreover, a survey of patients in independent dental practices and HMO clinics revealed that 40-67 percent of ST users reported interest in receiving cessation from their den-



**Figure 2. Blood nicotine concentrations with cigarette smoking and the use of smokeless tobacco in single doses**

Source: Adapted from Benowitz NL. Systemic absorption and effects of nicotine from smokeless tobacco. *Adv Dent Res* 1997;11(3):336-41.

tists. Patients not only expected oral health professionals to advise them on smoking-related matters, but welcomed such involvement.<sup>43</sup>

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## Challenges to Quitting: The Nature of Nicotine Addiction

Stopping tobacco use, however, is not easy. Tobacco dependence is a chronic disorder, characterized by multiple periods of relapse and remission.<sup>44</sup> For example, among smokers in the United States, data suggest that 70 percent have made at least one attempt to quit, and each year about 46 percent try to quit.<sup>45</sup> Among the 17 million adults who made a quit attempt in 1991, only 7 percent were abstinent one year later.<sup>46</sup> Although some tobacco users achieve permanent abstinence after their first quit attempt, most who wish to quit continue to use tobacco for many years, going in and out of remission and relapse. Therefore, most quitters require multiple attempts before succeeding.<sup>44</sup> It is important for clinicians to understand that relapse is likely and that it reflects the chronicity of tobacco dependence, not their personal failure nor the failure of their patients.<sup>44</sup> Appreciating the nature of nicotine dependence can enhance the clinician's motivation to treat tobacco use consistently with ongoing rather than just acute care.

All forms of tobacco contain nicotine, a highly addictive substance. Hallmarks for addiction to nicotine and other addictive drugs are:<sup>47</sup>

- compulsive use
- use despite harmful effects
- pleasant (euphoric) effects
- difficulty in quitting or controlling use
- recurrent drug cravings
- tolerance
- physical dependence
- relapse following abstinence

Aspects of nicotine addiction are categorized as physical, psychological, behavioral, sensory, and social.<sup>48</sup>

### Physical Aspects of Nicotine Addiction

The physical aspects of nicotine addiction include the reinforcing effects of nicotine and the potential for the brain to develop tolerance for, and physical dependence on, nicotine.

The neurochemical rewards that nicotine provides the tobacco user are known as its reinforcing effects. Nicotine acts on the mesolimbic area of the brain to cause the release of chemicals such as dopamine, norepinephrine, acetylcholine, vasopressin, serotonin, and beta-endorphins. Dopamine causes the experience of pleasure; serotonin reduces stress; norepinephrine causes appetite suppression; acetylcholine stimulates cognitive arousal; vasopressin enhances short-term memory; and beta-endorphin reduces anxiety and tension. Nicotine is a unique drug because it interacts with the brain depending on the tobacco user's need. For example, if individuals are "blue," nicotine can perk them up; if they are tired, nicotine can wake them up; and if they are stressed, nicotine can calm them down. Thus, the reinforcing effects of nicotine—mood modulation, enhanced short-term cognitive performance, and weight reduction—make it difficult for individuals to stop their tobacco use.<sup>49</sup>

With chronic exposure to nicotine, brain cells adapt to compensate for the actions of nicotine. This process is called neuroadaptation.<sup>50</sup> Tolerance results from neuroadaptation, so that a given level of nicotine eventually has less of an effect on the brain and a larger dose is needed to produce the rewarding effects that lower doses formerly produced. Thus, the longer clients use tobacco, the more product they need to achieve the desired physiologic effect or psychological response.<sup>49</sup>

Even though the brain adapts to function normally in the presence of nicotine, it also becomes physically dependent on nicotine for that normal functioning. When nicotine is not available, the brain function becomes disturbed, resulting in withdrawal symptoms. Nicotine withdrawal symptoms include cravings, irritability, frustration, anger, anxiety, difficulty concentrating, increased appetite and weight gain, depressed or sad mood, insomnia, headache, and gastrointestinal problems.<sup>49</sup> Thus, the nicotine addiction cycle<sup>49</sup> begins when an individual uses nicotine for pleasure, enhanced performance, or mood regulation. Then tolerance and physical dependence develop, and nicotine abstinence produces withdrawal symptoms. The individual then uses nicotine to self-medicate withdrawal symptoms.

Not everyone experiences withdrawal symptoms, and the degree of discomfort among abstainers also varies. When one is trying to stop tobacco use, specific strategies can be recommended for coping with specific nicotine withdrawal symptoms and temptations to use. Although withdrawal symp-

toms only last about three to four weeks and are the brain's attempt to heal itself, they can be a barrier to success with the quitting process.<sup>51</sup>

## Psychological, Behavioral, Sensory, and Sociocultural Aspects of Nicotine Addiction

Psychological, behavioral, and sensory aspects of nicotine addiction also sustain tobacco use. These factors provide a sense of comfort level and add to the complexity and difficulty of stopping tobacco use.<sup>48</sup>

Psychological aspects of nicotine addiction relate to the sense of well-being and comfort level associated with the use of nicotine. As a result, many tobacco users view their tobacco as their best friend. As one major league baseball player once stated, "When I'm at bat with a dip in my mouth, I feel like I'm not alone."<sup>52</sup> Tobacco use also may serve as passive entertainment to decrease boredom<sup>48</sup> or as a diversion from a strife-filled existence.<sup>53</sup>

Behavioral aspects of nicotine addiction derive from the direct effects of nicotine withdrawal,<sup>48</sup> as well as from the learned anticipatory responses.<sup>50</sup> These learned anticipatory responses develop from having experienced various forms of gratification from tobacco use in the presence of certain environmental cues.<sup>50</sup> For example, when a user encounters a situational reminder of tobacco use (e.g., after a meal or when drinking alcohol, or in the case of a professional baseball player, the sight of the baseball field), these stimuli are associated with pleasure or other reinforcing effects that then generate the urge to use tobacco. Such recurrent anticipatory responses can last six months or longer after physical dependence has been overcome and are responsible for relapse that occurs beyond the first few weeks of cessation. In order to become abstinent, a tobacco user must learn to cope with not only the loss of the physiologic pleasures associated with nicotine, but also with those aspects of tobacco-using behavior that have become pleasurable as a result of anticipatory mechanisms.<sup>50</sup>

Having a cigarette, or a dip in one's mouth of a specific size and texture, often provides oral gratification that relates to the sensory aspect of nicotine addiction. Because of the sense of well-being this oral gratification provides, the use of non-tobacco oral substitutes (e.g., chewing gum, sunflower seeds) are important to the quitting process, especially for ST users. In addition, because nicotine is an appetite

suppressant, individuals often increase their food intake when they reduce their nicotine exposures. Individuals who successfully stop their tobacco use gain on average ten pounds. Drinking a lot of water, exercise, and a balanced low fat diet can help avoid this weight gain.<sup>48</sup>

Sociocultural aspects of nicotine addiction that pose challenges to abstinence include peer pressure, the influence of family members and significant others who use tobacco, and a social network that supports, accepts, and allows the habit.<sup>53</sup> Thus, users frequent environments where tobacco use is considered acceptable and often associate with other users. As a result, users trying to stop their tobacco use often need to avoid situations where they will be tempted to use until they are secure that they can cope with these situations.<sup>51</sup>

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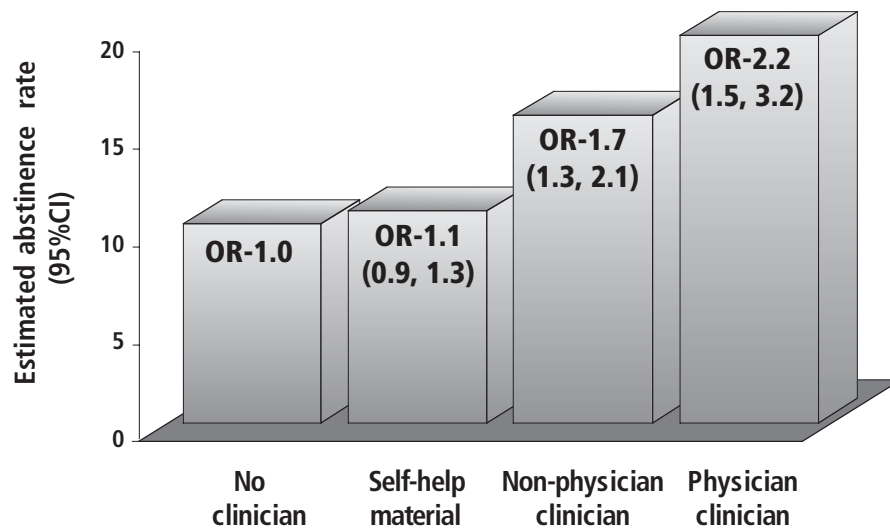
## Effects of Low-Cost/Low-Contact Intervention and Other Treatments

The Public Health Service (PHS) clinical guidelines for treating tobacco use and dependence in primary care settings provide evidence-based, practical methods for dental professionals to incorporate into their practices.<sup>44</sup> These guidelines are supported by evidence from two systematic reviews of the literature. The first included literature published from 1975 through 1994; the second included literature from 1995 through January 1999. The two reviews were then combined into one database, and various meta-analyses were conducted to estimate the impact of a treatment or variable across a set of related investigations. Random effects modeling was used to accommodate variations among studies<sup>44</sup> and to identify clearly efficacious treatment strategies. For example, a meta-analysis of seven studies showed physicians' brief advice to quit smoking significantly increased long-term smoking abstinence rates by about 10 percent.<sup>44</sup> The modal time physicians spent in these studies was three minutes or less. A meta-analysis of twenty-nine studies showed an increase in long-term smoking cessation rates (five or more months post-intervention) by about 20 percent when brief interventions were delivered by physicians and 16 percent when delivered by non-physician clinicians, many of whom were dental professionals. These findings indicate that patients who receive

these interventions are about twice as likely to quit compared to patients who receive no intervention or only self-help materials (Figure 3).<sup>44</sup> Although studies assessing the efficacy of interventions delivered specifically by dentists and dental hygienists are too few to be separated out for specific meta-analysis evaluation, it should be noted that several studies have demonstrated that brief cessation interventions

by dental professionals are effective in helping patients stop ST use (Table 2).<sup>54-59</sup>

Moreover, as reported in the PHS guidelines, in two separate meta-analyses of time spent in person-to-person counseling and of the number of sessions provided respectively, there was a strong dose-response relation between the intensity of tobacco dependence counseling and its effectiveness (Figures 4 and 5).<sup>44</sup> For person-to-person contact of more than



**Figure 3. Efficacy of clinical intervention at 5+ months (n=29 studies)**

Source: Fiore MC, Bailey WC, Cohen SJ, et al. Treating tobacco use and dependence: clinical practice guideline. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service, June 2000.

**Table 2. ST studies of behavioral spit tobacco treatments provided by dental professionals**

	Sample Size (Population)	Follow-Up	% Quit	
			Intervention	Control
Stevens et al. (1991) <sup>1</sup>	I=273 C=245 (adolescent & adult males)	1 year	34	25
Severson et al. (1998) <sup>2</sup>	I=239 C=394 (adult males)	1 year	17	9
Walsh et al. (2000) <sup>3</sup>	I=171 C=189	1 year	35	16
Walsh et al. (2002) <sup>4</sup>	I=141 C=166	1 year 2 year	27 23	14 13

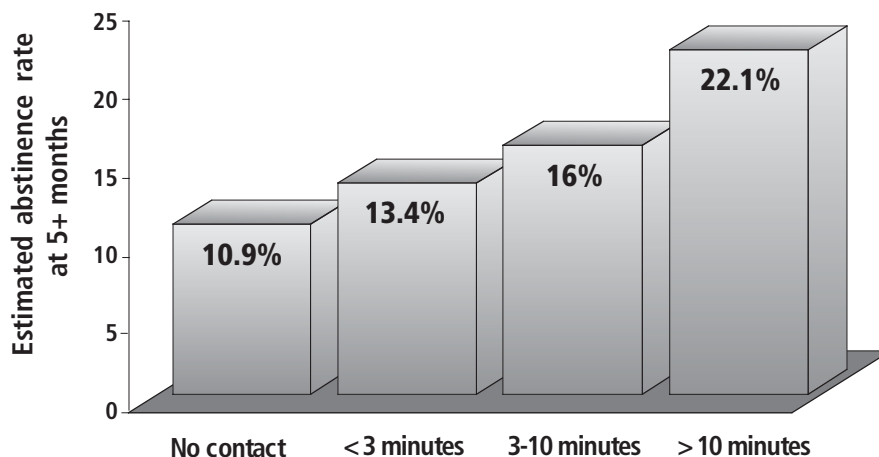
1. Usual care vs oral exam, feedback, advice, video, phone calls, monthly mailings
2. Oral exam, feedback, quit materials vs previous + quit date, video, phone call
3. Oral exam, feedback, quit materials, brief counseling, phone call
4. Oral exam, feedback, quit materials, brief counseling, phone call + educational session

ten minutes, long-term cessation rates were around 22 percent, compared to 13 percent for less than three minutes. Moreover, results from additional meta-analyses indicated that the greater the number of treatment sessions, as well as the greater the number of different types of clinicians delivering brief tobacco

cessation interventions, the higher the abstinence rates reported.

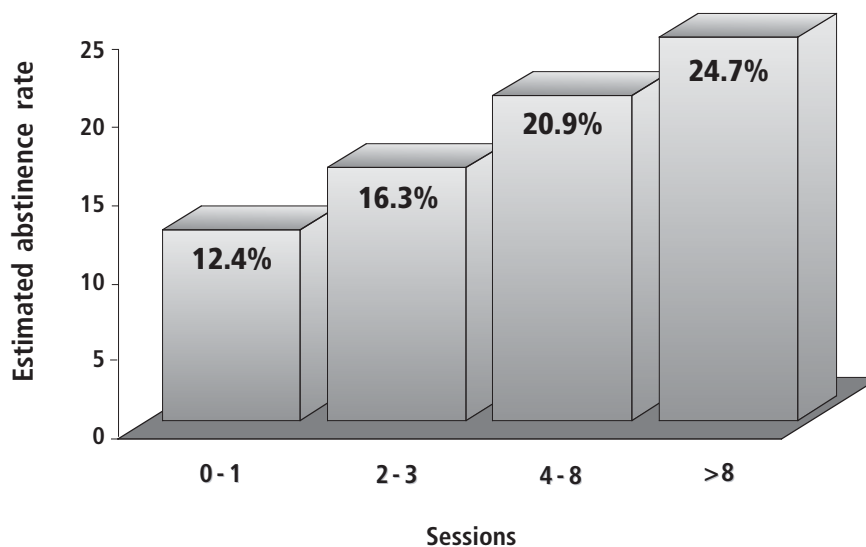
Based on this and other evidence,<sup>44</sup> implementation of the following five strategies by dental professionals at each clinical visit is recommended:

- Ask: Systematically identify and document all to-



**Figure 4. Abstinence rates for various intensity levels of contact as measured by time spent in person-to-person counseling (n=43 studies)**

Source: Adapted from Fiore MC, Bailey WC, Cohen SJ, et al. Treating tobacco use and dependence: clinical practice guideline. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service, June 2000.



**Figure 5. Abstinence rates for number of person-to-person treatment sessions (n=45 studies)**

Source: Adapted from Fiore MC, Bailey WC, Cohen SJ, et al. Treating tobacco use and dependence: clinical practice guideline. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service, June 2000.

bacco users at every visit. Also, verbally ask patients about their tobacco use (e.g., “Do you ever smoke or use any type of tobacco? I take time to ask all my patients about tobacco use because it’s important.”).<sup>44</sup>

- Advise: In a clear, strong, nonjudgmental, and personalized manner, urge every tobacco user to quit (e.g., “I need you to know that quitting smoking is the most important thing you can do to protect your current and future health.”).
- Assess: Assess willingness to make a quit attempt in the next month (e.g., “Would you be willing to try to quit in the next month? If so, we can help.”).
- Assist: Help with the quitting process.
- Arrange: Schedule follow-up contact and note in chart to ask again at next visit.

Given the evidence that minimal interventions lasting less than three minutes increase overall tobacco abstinence rates, the PHS guidelines recommend that every tobacco user be offered at least a minimal intervention whether or not he or she is referred to a more intensive intervention. These interventions can be offered by any member of the oral health team. Training the oral health team to implement these guidelines has been shown to be effective.<sup>60</sup>

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## Helping Patients to Quit: When and How

To be most effective in assisting patients with tobacco cessation, it is important for dental professionals to tailor their approach based on the patient’s readiness or willingness to quit. The concept of readiness to quit relates to the stages of change theory.<sup>61</sup> According to this theory, any behavior change moves through a series of five stages, and tobacco cessation is no exception. The first stage of change is precontemplation, in which the individual may think tobacco use is not a problem or at least is less of a problem than others think it is, has no thought of quitting tobacco use in the next six months, and may resent outside pressure to do so. The second stage of change is contemplation, in which the individual is aware that tobacco use is a problem and is seriously thinking about quitting some day but not in the next six months. The third stage of change is preparation, in which the individual has been making small changes to try to cut down and to stop tobacco use, would like to quit in the next month or so, or may even have quit recently but returned to tobacco use

at a reduced rate. The fourth stage is action, in which the individual has quit smoking within the last six months. The fifth stage is maintenance, in which the individual has quit for more than six months.

For individuals in stages 1 and 2, the important goal for treatment is to motivate the individual to begin to weigh the pros and cons of tobacco use. The PHS clinical guidelines for the treatment of tobacco use and dependence suggest that the dental professional conduct a motivational interview designed to increase motivation to quit (see Table 3 for details).<sup>44</sup> Thus the clinician should personalize benefits of quitting and continued risks of tobacco use (e.g., disease status or risk, health concerns, age), ask the patient to identify barriers to quitting, note elements of treatment that could address barriers, and make a note in the chart to repeat at the next visit.

For individuals in stage 3, it is important to suggest that it is clearly time to make a commitment by setting a quit date, encourage the patient to tell family and friends for social support, provide a self-help guide, refer for treatment to an external resource (e.g., state-supported telephone quit lines described below or community-based cessation programs) or to an in-office treatment program in the dental setting consisting of four appointments or more (see Table 3 and Figure 6 for details), and make a note in the chart to follow up at the next visit.

For individuals in stages 4 and 5, it is important to provide congratulations and make suggestions for relapse prevention to help them cope with withdrawal symptoms, weight gain, and negative moods experienced as a result of the quitting process. In addition, a note should be made in the patient chart to repeat this intervention at the next visit.

## Statewide Tobacco Use Quit Lines

Excellent external resources for referral for tobacco cessation assistance are tobacco use telephone quit lines. Currently there are statewide tobacco use quit lines in thirty-four states in the United States.<sup>62,63</sup> They offer easy access at no cost to the client and address ethnic and geographic disparities. Many tobacco users prefer quit lines to face-to-face programs because telephone counseling is more convenient and provides anonymity.<sup>64</sup> Key factors that increase quit line effectiveness include the use of trained counselors, use of proactive quit lines where staff initiate contact and follow-up, and use in combination with client self-help materials and/or FDA-approved pharmaceuticals.<sup>64</sup> In clinical trials, pro-

**Table 3. Tobacco cessation assistance**

Patients Not Ready to Quit	Patients Ready to Quit	Patients Ready to Quit
<p><b>Motivational Interview</b></p> <p><b>Relevance and Risks:</b></p> <ul style="list-style-type: none"> <li>• Ask about negative consequences and point out those that are relevant (e.g., “Have you been experiencing problems associated with your tobacco use?”).</li> </ul> <p><b>Relevance and Rewards:</b></p> <ul style="list-style-type: none"> <li>• Ask about benefits of quitting and point out those that are relevant.</li> </ul> <p><b>Roadblocks:</b></p> <ul style="list-style-type: none"> <li>• Ask about barriers to quitting; point out how treatment can help.</li> </ul> <p><b>Repetition:</b></p> <ul style="list-style-type: none"> <li>• Provide a supportive clinical environment: “My staff and I are available to assist you when you are ready.” Repeat at every appointment.</li> </ul>	<p><b>Brief Intervention (three to ten minutes)</b></p> <ul style="list-style-type: none"> <li>• Reinforce motivation to quit.</li> <li>• Ask about reasons and reinforce benefits of quitting.</li> <li>• Reassure about past failures (e.g., “Most people have to try three or four times before they are ultimately successful. But each time you try, you learn something new about the quitting process that makes you better prepared to quit this time. As long as you are trying, you are not failing.”).</li> <li>• Encourage patient to tell family and friends.</li> <li>• Provide self-help booklet.</li> <li>• Refer internally or externally.</li> <li>• Follow up at next visit; make a note to do so in chart.</li> </ul>	<p><b>Elements of More Intense In-Office Treatment Program (at least four one-hour appointments)</b></p> <ul style="list-style-type: none"> <li>• Assessment <ul style="list-style-type: none"> <li>—reasons for quitting</li> <li>—nicotine dependence (e.g., use within thirty minutes of waking indicates dependence)</li> <li>—mood (e.g., Center for Epidemiologic Studies NIMH 20-item Depression Scale: refer patients who score 16 or higher to physician for management of possible underlying depression)</li> <li>—previous quit attempt</li> <li>—contraindications to pharmacological aids</li> <li>—patterns of use (Figure 6)</li> </ul> </li> <li>• Motivation enhancement</li> <li>• Education (e.g., the nature of nicotine addiction)</li> <li>• Setting a quit date</li> <li>• Choosing a plan</li> <li>• Training for coping with withdrawal symptoms and temptation to use (e.g., avoidance of high risk situations, relaxation techniques, distraction and delaying techniques, positive thinking, rewards, oral substitutes)</li> <li>• Social support</li> <li>• Relapse prevention (e.g., identifying trigger situations and planning ahead on how to deal with the urge to use tobacco, and turning slips into a learning opportunity)</li> <li>• Pharmacotherapy</li> <li>• Follow up for several visits specifically for cessation assistance</li> <li>• Referral to external program if indicated</li> </ul>

active telephone counseling increases the probability of quitting smoking to about 13 percent.<sup>65</sup> Randomized trials of the California quit line show that telephone counseling doubles quit rates compared with the use of self-help materials alone.<sup>63-65</sup>

## Pharmacological Aids to Tobacco Dependence Treatment

There are two general classes of FDA-approved drugs for treatment of tobacco dependence: nicotine

replacement therapy (nicotine gum, patch, nasal spray, inhaler, and lozenge) and the non-nicotine medication, sustained release bupropion (Table 4).<sup>44</sup> The comparative daily costs of these pharmacotherapy aids are similar to that of a pack of cigarettes. Based on results of a meta-analysis of fifty-eight studies,<sup>44</sup> Figure 7 shows estimated abstinence rates of 30.5 percent for Bupropion SR, 23.7 percent for nicotine gum, 22.8 percent for nicotine inhaler, 30.5 percent for nicotine nasal spray, and 17.7 percent for nicotine patch compared to placebo.

Time	Craving	Place/Activity	Mood

Score craving on a scale of 1-10 where 1=you don't need it at all and 10=you just have to have it.  
 Score mood: 1=relaxed; 2=bored; 3=angry; 4=happy; 5=stressed; 6=excited; 7=tired; 8=sad; 9=hungry; 10=irritable

**Figure 6. Assessment of patterns of tobacco use in a typical day**

Source: Adapted from Jensen J, Hatsukami D. Tough enough to quit using snuff. University of Minnesota, Tobacco Research Laboratory, 2002.

*Nicotine Replacement Therapy.* The rationale for the use of nicotine replacement therapy (NRT) in tobacco dependence treatment is to provide some blood concentration of nicotine to reduce symptoms of physical nicotine withdrawal. This reduction in withdrawal symptoms allows the client to focus on the psychological and behavioral changes necessary for successful tobacco cessation. Peak blood nicotine concentrations are higher and are achieved more rapidly when nicotine is delivered by a cigarette compared to the available NRT products.<sup>4</sup> Among the nicotine replacement products, however, absorption is fastest with the nasal spray, followed by the inhaler, lozenge, gum, and patch.<sup>66</sup> The magnitude and rapidity of the effect are significant since they are factors that contribute to abuse liability. That is to say, the faster nicotine reaches the brain and the greater the magnitude of effect, the more likely the NRT product will be abused.<sup>67</sup> Nevertheless, when compared to tobacco products, nicotine replacement products deliver nicotine more slowly and at lower levels (30-75 percent of those achieved by smoking) and are less likely to be associated with dependence.<sup>4</sup>

Nicotine replacement therapy has been identified as effective for increasing smoking abstinence rates compared to placebo (Figure 7). In general,

patients using NRT are two times more likely to successfully quit smoking than are those receiving placebo.<sup>68</sup> Moreover, patients using NRT are not exposed to the carcinogens and other toxins found in tobacco and tobacco smoke. It should be noted, however, that the success rates of smoking cessation significantly improve when the use of NRT is combined with psychological counseling.<sup>69</sup> General contraindications/precautions related to NRT are patients with underlying cardiovascular disease such as recent myocardial infarction, life-threatening arrhythmias, and severe or worsening angina. The following is a brief overview of each of the NRT products.

Nicotine gum, a sugar-free chewing gum base with buffering agents to enhance buccal absorption, is available over-the-counter (OTC) in 2 or 4 mg doses. A common brand name is Nicorette. Nicotine gum is used on a fixed schedule (every one to two hours) for at least thirty minutes. The recommended limit is twenty-four pieces per day. Nicotine gum is not used like general chewing gum; instead the patient is instructed to chew it very slowly, to stop chewing and place it against the buccal mucosa after the first sign of a peppery taste or a tingling sensation, and to chew it again when the taste or tingling fades. These instructions are based on the rationale that

nicotine is best absorbed through the buccal mucosa and not the stomach.

The initial recommended dose is dependent on the individual's smoking habit. Heavier smokers (>20 cigarettes per day) begin with 4 mg gum and later switch to 2 mg gum. The goal is to gradually discontinue use over a period of one to three months. Contraindications for use of nicotine gum are a recent or severe myocardial infarction, stomach ulcers, TMJ problems, dentures, dental work to which the gum may stick, or any oral problems that the gum may exacerbate.

Transdermal nicotine patches, depending on brand, are either twenty-four or sixteen hours. For example, Nicoderm CQ is available OTC in 7, 14, and 21 mg doses. They are worn up to twenty-four hours per day to provide steady flow of nicotine. The initial recommended dose is dependent on the individual's smoking habit. Regular smokers (>10 cigarettes per day) begin with the 21 mg patch and gradually move to 14 mg, then to 7 mg. The goal is to gradually discontinue use. Contraindications to the nicotine patch use are recent severe myocardial infarction, psoriasis, eczema, and skin sensitivity to the patch.

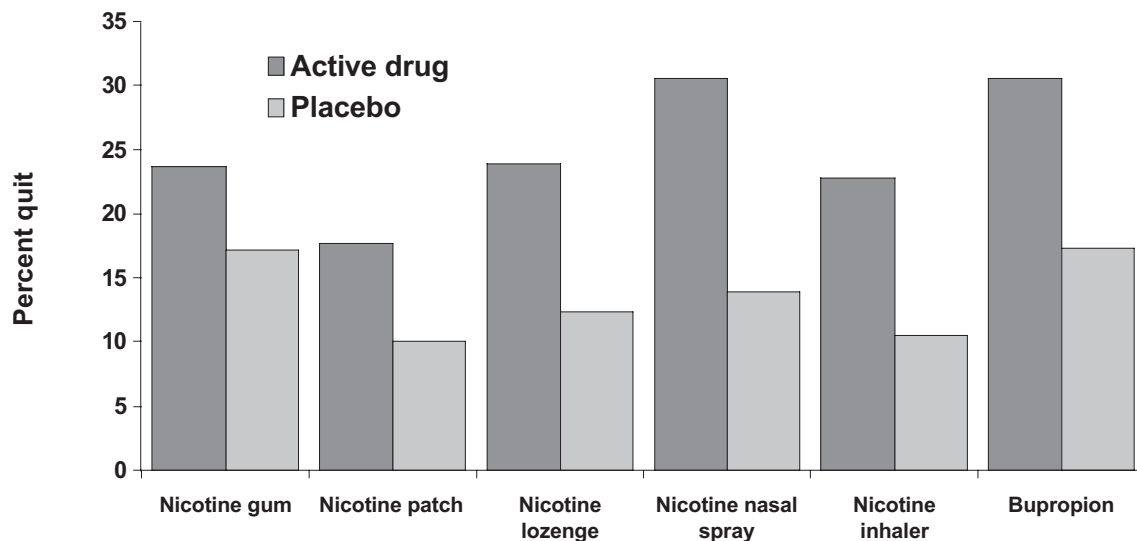
**Table 4. Pharmacologic aids to smoking cessation treatment**

Pharmacologic Aid	Year Introduced	Availability
Nicotine Gum	1984	OTC
Nicotine Transdermal System	1991	OTC/Rx
Nicotine Nasal Spray	1996	Rx
Nicotine Inhaler	1997	Rx
Lozenge	2000	OTC
Bupropion HCl	1997	Rx

Source: Adapted from Hudmon K, Corellie R. Rx for change: clinician-assisted tobacco cessation curriculum content. University of California, San Francisco, School of Pharmacy, 2002.

Nicotine nasal spray is available by prescription only. Each 10 ml spray bottle contains 100 mg nicotine. A 1.0 mg nicotine dose is delivered with one spray (0.5 mg nicotine) in each nostril. Recommended use depends on individual smoking habit, but should not exceed five doses in one hour or forty doses in twenty-four hours. The goal is to gradually discontinue use.

The nicotine inhaler is available by prescription only. It consists of a mouthpiece and cartridge



**Figure 7. Long-term (>5 month) quit rates for available cessation medications**

Source: Fiore MC, Bailey WC, Cohen SJ, et al. Treating tobacco use and dependence: clinical practice guidelines. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service, June 2000. As adapted by Hudmon K, Corellie R. Rx for change: clinician-assisted tobacco cessation curriculum content. University of California, San Francisco, School of Pharmacy, 2002.

with porous plug containing 10 mg nicotine. When inhaled or puffed through the mouthpiece for approximately twenty minutes, 4 mg of nicotine vapor is absorbed across the oropharyngeal mucosa. Recommended use depends on an individual's smoking habit, starting at six cartridges per day, but not exceeding sixteen cartridges per day for a minimum of three weeks to a maximum of twelve weeks.

The nicotine lozenge is available OTC in 2 or 4 mg doses. It is used on a fixed schedule (every one to two hours) for at least thirty minutes. The lozenge is placed in the mouth and allowed to dissolve slowly for twenty to thirty minutes. It is not chewed or swallowed. Because the nicotine lozenge is dissolved completely, it delivers approximately 25 percent more nicotine than the equivalent gum dose. The recommended limit is twenty lozenges per day.

The initial recommended dose is based on the "time to first cigarette after waking" as an indicator of nicotine addiction. Smokers who have their first cigarette more than thirty minutes after waking use the 2 mg lozenge; and those who have their first cigarette within thirty minutes use the 4 mg lozenge. The goal is to gradually discontinue use over a period of ten to twelve weeks.

*Non-Nicotine Medication.* Sustained-release bupropion (brand names: Zyban, Wellbutrin) is a sustained-release, but atypical, antidepressant provided in tablet form that has been shown to be efficacious for smoking cessation (Figure 7).<sup>4</sup> It is the only non-nicotinic drug with an FDA indication for smoking cessation. Bupropion is thought to increase levels of dopamine and norepinephrine released from the brain. The clinical effects are a reduced craving for tobacco and reduced symptoms of nicotine withdrawal.

The maximum dose for smoking cessation is 300 mg per day for seven to twelve weeks. Therapy is initiated seventeen to fourteen days before stopping tobacco use. It is recommended that the individual start by taking one 150 mg tablet every morning for three days. If it is well tolerated, then the dosage is increased to 150 mg twice per day. One 150 mg tablet is taken in the morning followed by another 150 mg tablet taken at least eight hours later. A dosage greater than 300 mg per day should not be used.

Contraindications to use are seizure risk, history of head injury, anorexia or bulimia nervosa, MAO inhibitor use within the last two weeks, the use of other forms of bupropion (Wellbutrin), and

patients undergoing abrupt discontinuation of alcohol or sedatives. Common side effects include insomnia and dry mouth. Less common but reported side effects are tremor and skin rash. Also, there are age-related differences with respect to bupropion. For example, there is concern that youth who smoke also are more likely to use illicit stimulants. Since stimulants are thought to increase the seizure risk of bupropion, adolescents are a special case, as they are with respect to smoking in general.<sup>93</sup>

Sustained-release bupropion can be used safely with NRT with very dependent tobacco users. Figure 8 shows that combination therapy is more effective than either bupropion or nicotine patch therapy alone.<sup>4</sup> Dose tapering is not necessary when discontinuing treatment. If no significant progress towards abstinence is observed by the seventh week of use, therapy is unlikely to be effective and to be discontinued.<sup>4</sup>

Two second-line pharmacotherapies,<sup>44</sup> Clonidine and Nortriptyline, have been identified as efficacious and should be considered if first-line pharmacotherapies are not effective with an individual patient. Clonidine is an antihypertensive that has been reported to reduce nicotine withdrawal symptoms. Precaution/contraindication to use is rebound hypertension, and side effects are dry mouth, drowsiness, dizziness, and sedation.

Nortriptyline is an antidepressant that increases serotonin and/or norepinephrine in the CNS. Precaution/contraindication is risk of arrhythmias, and side effects are sedation and dry mouth.<sup>44</sup>

## Use of ST as a Harm Reduction Method for Smokers

Use of ST as a smoking cessation method or as a means to reduce cigarette use has been actively debated,<sup>70</sup> despite the availability of safe, effective, and regulated pharmacological products to promote smoking cessation (e.g., nicotine replacement products).<sup>44</sup> Arguments to support the use of ST as a harm reduction approach include the following:

- 1) reports that ST use leads to less morbidity and mortality than cigarette smoking;<sup>71</sup>
- 2) findings from two studies<sup>72,73</sup> supported by the tobacco industry indicating no statistical association between oral cancer and Swedish oral snuff (snus); and
- 3) reports that the concentration of tobacco specific nitrosamines (carcinogens) in Swedish snuff is much lower than that found in American brands.<sup>74</sup>

Arguments against the use of ST as a current harm reduction approach include the following:

- 1) The impact of using it as such is relatively unknown.<sup>75</sup> Research needs to determine the extent of smoking reduction achieved, whether it is associated with a significant reduction in disease risk, and/or with harm at the population level.<sup>76,77</sup> It is important that such investigations be conducted on regulated ST products by organizations that are independent of the producers and marketers of ST products.<sup>76</sup> Currently, ST products in the United States are not regulated by the FDA and there is considerable variation in cancer-associated tobacco specific nitrosamines between types, brands, and storage conditions of the tobacco.<sup>78</sup>
- 2) Caution should be exercised in generalizing the findings in Sweden of Schlidt et al.<sup>72</sup> and Lewin et al.<sup>73</sup> to other ST products and populations. In addition, the Schlidt study also failed to detect an association between cigarette smoking and oral cancer. Moreover, the Lewin study reported a statistical association between snus and all head and neck cancer in a small group of snus users that had never smoked cigarettes (nine cases and ten controls, RR= 4.7 [95 percent CI, 1.6-13.8]).<sup>73-79</sup>
- 3) Although ST use leads to less morbidity and mortality than cigarette smoking,<sup>71</sup> ST products contain carcinogens, which come in direct con-

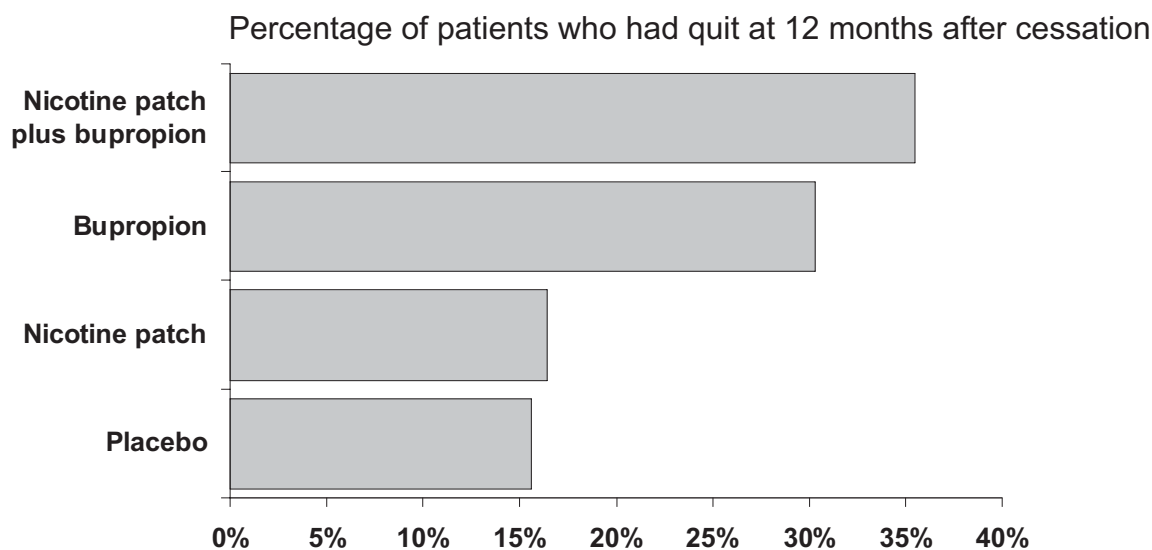
tact with the oral mucosa for prolonged periods.<sup>80</sup> Thus, no form of tobacco is safe.

- 4) Studies have shown that, in the United States, using ST is more likely to lead to smoking than not using ST.<sup>75</sup>
- 5) Findings from an epidemiological study<sup>81</sup> indicated that combined tobacco product users smoked more cigarettes than exclusive smokers and that combined use of ST and cigarettes led to a doubling of the lung cancer mortality rate compared to exclusive smokers.
- 6) There may be legal and liability implications associated with recommending the use of a product known to contain carcinogens and other tobacco-related toxins that is associated with cardiovascular risk factors and has great potential for addiction.<sup>75</sup>

This harm-reduction debate relative to the use of ST as a smoking cessation method or as a means to reduce cigarette use is ongoing.

## Current Frontier Areas of Research

Studies of identical and fraternal twins report a higher concordance of tobacco use for identical than for fraternal twins. The estimated heritability for smoking reported was 0.53 indicating that approximately half of the variance in smoking is due to genetic factors.<sup>82,83</sup>



**Figure 8. Combination therapy: nicotine patch + bupropion**

Sources: Hudmon K, Corellie R. Rx for change: clinician-assisted tobacco cessation curriculum content. University of California, San Francisco, School of Pharmacy, 2002; Jorenby et al. A controlled trial of sustained-released bupropion, a nicotine patch, or both for smoking cessation. *N Engl J Med* 1999;340(9):685-91.

Genetic studies suggest smoking is altered by variable nicotine metabolism. For example, CYP2A6 is an enzyme responsible for the metabolism of nicotine. People who have low CYP2A6 activity appear to be slow metabolizers of nicotine.<sup>4</sup> In a genetic study of nonsmokers and smokers, it was demonstrated that low activity of CYP2A6 was less frequent in smokers than nonsmokers and less frequent in dependent smokers than nondependent smokers. These findings suggest that low activity of CYP2A6 is associated with decreased risk of smoking and nicotine dependence.<sup>84</sup> Other genetic studies have shown that low activity of CYP2A6 decreases risk for tobacco dependence, decreases number of cigarettes/day smoked, decreases the duration of tobacco dependence, increases success of quitting, increases levels of nicotine from NRT, and decreases activation of procarcinogens.<sup>85-88</sup> As a result, increased research is aimed at identifying genetic variants that might enhance current pharmacologic treatments of tobacco dependence. Examples of pharmacotherapy currently under study include CYP2A6 inhibitors, cannabinoid receptor inhibitors, and nicotine vaccine.<sup>84</sup>

A CYP2A6 inhibitor, methoxsalen, is a drug being studied to enhance the effects of nicotine replacement therapy. Researchers have found that methoxsalen blocks the body's ability to break down nicotine and thus significantly improves the effectiveness of oral nicotine replacement in reducing a smoker's urge for nicotine.<sup>89,90</sup> In one study, seventeen smokers (eight men and nine women) received methoxsalen or placebo in combination with oral nicotine replacement. Blood levels of nicotine were measured in samples taken at thirty-minute intervals for three hours. Participants who received either 10 or 30 mg of methoxsalen had mean nicotine levels roughly twice as high as those given placebo. The participants also were asked at hourly intervals to rate their urge to smoke. Those who received methoxsalen reported far less desire to smoke. As stated in *NIDA Notes*: "These results suggest that methoxsalen, or other medications that act at the primary site of nicotine metabolism, may represent part of a potent new treatment for nicotine addiction."<sup>89,90</sup>

As described earlier, nicotine triggers release of endocannabinoids (dopamine and other chemicals) that produce reinforcing effects. Rimonabant, a cannabinoid receptor inhibitor, blocks nicotine-induced reinforcement and reduces nicotine self-administration.<sup>91</sup> It also produces weight loss. In a Phase 2 randomized placebo controlled trial, subjects in the 40 mg Rimonabant group (N=185) had significantly

greater twenty-eight-day abstinence, weekly point-prevalence abstinence, and continuous abstinence. In addition, in the Rimonabant group, there was 75 percent reduction in post-cessation weight gain among quitters and reduced craving compared to subjects in the placebo group (N=183).<sup>84</sup>

To improve the treatment for tobacco dependence, researchers are studying ways to affect the movement of nicotine across the blood-brain barrier to prevent the reinforcing effects of the chemicals released by the brain that are evoked by smoking. Among these is the development of a nicotine vaccine that produces antibodies that bind to nicotine and prevent it from crossing the blood-brain barrier.<sup>92</sup> Potential uses for nicotine vaccine would reduce the neurochemical rewards associated with nicotine. It is not expected to decrease neuroadaptive changes such as craving or withdrawal. In addition, it could be used as an adjunct to counseling and/or other medications. Also, it could be used in relapse prevention; however, its use in primary prevention is unlikely.<sup>84</sup>

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## Conclusion

Tobacco dependence is an addictive disorder characterized by vulnerability to relapse and requiring ongoing rather than just acute care.<sup>44</sup> To identify and treat tobacco users, all members of the health care system must be involved. Dentists and dental hygienists are important in this process. Effective treatments for tobacco dependence exist. Brief interventions make a difference. Repeated interventions make a difference.<sup>44,93</sup> Although effective pharmacotherapy is available for some, more effective medications are needed.<sup>84</sup> Increased attention is being devoted to the study of genetic variants that might improve current approaches to pharmacologic treatments of tobacco dependence.<sup>89</sup>

In 1982, Former U.S. Surgeon General C. Everett Koop said: "Cigarette smoking is the chief, single, avoidable cause of death in our society and the most important public health issue of our time."<sup>94</sup> Working together, dental professionals not only can play an important role in preventing adverse health effects by promoting cessation of tobacco use, but also can have an important public health impact by helping to counter tobacco use. For example, one third of all smokers die prematurely.<sup>94</sup> Dental professionals are favorably positioned to provide tobacco cessation treatment since more than 50 percent of

smokers see a dentist during a year.<sup>95</sup> Thus, 25 million of the estimated 50 million adult smokers in the United States<sup>96</sup> could be treated by a dental professional to quit smoking in a single year. If 10 percent of smokers who see a dentist could be influenced to consider quitting, each year 2.5 million U.S. tobacco users could be treated and an estimated 600,000 premature deaths from smoking could be prevented.<sup>97</sup>

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