reimbursed for clinical and pharmacologic treatments to help patients quit smoking (Group Health Association of America, Inc. 1993; Schauffler and Parkinson 1993). Appropriate reimbursement may be essential to ensuring greater clinical attention to tobacco addiction (Schauffler and Parkinson 1993; Fiore and Baker 1995; Kaplan et al. 1995).

The Public Health Service-sponsored Clinical Practice Guideline *Treating Tobacco Use and Dependence* has recommended that health care professionals use the "five A's" to help their patients quit smoking: (1) *ask* about smoking, (2) *advise* all smokers to quit, (3) *address* willingness to make a quit attempt, (4) *assist* patients who want to quit, and (5) *arrange* follow-up visits (Manley et al. 1991; Glynn and Manley 1993; Orleans et al. 1993; Houston et al. 1994; Fiore et al. 2000). These recommendations, based on a comprehensive review of the empirical literature, constitute a proscriptive algorithm for clinical interventions (see the text box).

Additional follow-up visits, at increasing intervals, with patients who continue not to smoke have been associated with greater long-term abstinence (Kottke et al. 1988; Wilson et al. 1988; Orleans et al. 1991). Patients who have relapsed should be helped to quit again at follow-up visits and subsequent visits.

The Five A's

To help their patients quit smoking, clinicians can use the "five A's" approach: (1) *ask* patients about smoking, (2) *advise* all smokers to quit, (3) *assess* willingness to make a quit attempt, (4) *assist* those who want to quit, and (5) *arrange* follow-up visits with those trying to quit (Glynn and Manley 1993). These brief clinician interventions, which are described in this text box, can be completed within two to three minutes at each visit and have been associated with a cessation prevalence of 5 percent (Glynn 1988) to 8 percent (Kottke et al. 1988).

All patients seen in a primary care setting should be routinely *asked* about their smoking status. One means of institutionalizing the identification of smokers is to expand the vital signs to include smoking status (Fiore 1991). Another means is to use stickers or other markers to clearly identify charts and prompt clinicians to help their patients who smoke quit (Cohen et al. 1989b; Ockene et al. 1991).

All patients who smoke should be *advised* to quit. This advice should be clearly stated and personalized. After giving this advice, clinicians should *assess* whether smokers desire to quit at the present time. Clinicians should provide motivational materials and messages to those not willing to quit. These patients should be asked about smoking and advised to quit at all subsequent visits.

Clinicians should *assist* patients who want to quit. The clinician should work together with the patient to set a date to quit (preferably within two weeks of the clinic visit) and should provide the patient with practical advice about how to quit and self-help materials.

Clinicians should determine whether the patient is likely to require adjunctive help and whether the patient is a candidate for pharmacotherapy. Pharmacotherapy should be considered for all patients motivated to make a quit attempt, except in the presence of specific contraindications (Fiore et al. 2000). The choice may take into account previous patient experience, preferences, and other factors (see "Pharmacologic Interventions," later in this chapter). Clinicians should also present other treatment options to their patients who want to quit. In particular, patients should be made aware of community cessation resources (such as those offered by the American Cancer Society and the American Lung Association) and of intensive clinical interventions (see "Intensive Clinical Interventions," later in this chapter) available in the community. The primary care clinician, however, should continue to monitor and assist those patients who elect to undergo intensive treatments.

Clinicians should *arrange* for a follow-up visit to discuss smoking cessation within two weeks of the chosen date to quit. Researchers have documented that scheduling follow-up visits or making follow-up telephone calls improves cessation success (Kottke et al. 1988; Wilson et al. 1988; Ockene et al. 1991, 1992; Orleans et al. 1991). Follow-up visits should be arranged whether the patient has been referred to another clinic or treated by the primary care clinician.

Modifications in treatment, including a discussion of more intensive efforts, should be considered for relapsing patients at each iteration.

An area of current active research in minimal interventions is the use of computer-tailored messages for individual smokers who want to quit. Computer software that approximates deductive or inductive human reasoning has been proposed as an efficient and cost-effective mechanism for this modality (Velicer et al. 1993). In a large trial of one such system, interactive computer reports plus individualized manuals produced higher current abstinence (20 percent) and prolonged abstinence (11 percent) than did standard manuals, individualized manuals alone, or personalized counselor calls (Prochaska et al. 1993). Similarly, analyses of two separate controlled trials found that computer-tailored letters generated significantly greater cessation proportions in groups receiving them than in control groups (Strecher et al. 1994). Although these mechanisms have not been extensively evaluated, they are a promising avenue for further investigation.

Efficacy

Kottke and colleagues (1988) performed a meta-analysis of 39 smoking cessation trials conducted in medical practice settings. Most of these trials involved relatively minimal interventions, but some more intensive treatments were included. Participants had a mean of 4.8 (standard deviation = ±4.4) contacts with these clinic-based programs. The major conclusion of this analysis was that success increased with the number of intervention modalities employed, the number of health care professionals involved in the effort, and the number of follow-up assessments. Duration of follow-up (as opposed to number of follow-ups) was not predictive of success. Using diverse techniques may be a key characteristic of successful clinic-based smoking cessation programs (Fiore et al. 2000). A successful program might be one in which face-to-face counseling or advice is given; dates for quitting are set; pamphlets are distributed; reminders by telephone are made; smokers are advised and counseled on quitting by physicians, nurses, and other health professionals; and multiple clinic visits or telephone calls are made after the smoker's quitting day. In the meta-analysis by Kottke and colleagues (1988), cessation assistance delivered by nonphysicians tended to be slightly more effective than that performed by physicians, but a more recent meta-analysis (Fiore et al. 2000) found no difference in effectiveness between physicians and nonphysicians. Both individual and group counseling was effective (Fiore et al. 2000).

The meta-analysis by Kottke and colleagues (1988) also suggested, however, that complex interventions are not necessary for clinic-based success. Compared with smokers who received no assistance, smokers who received help consisting of advice only or brief counseling had a 13.1-percentage point increase in cessation 6 months after treatment and a 3.8-percentage point increase after 12 months. Comparable estimates for smokers whose only treatment was to receive written self-help materials from health care professionals were 1.6 percent at 6 months and 2.0 percent at 12 months. The impact of brief intervention is illustrated in one study by Russell and colleagues (1979), who found that providing advice in a primary care setting produced a biochemically confirmed increase in abstinence of 3.3 percentage points; when smokers were told they would be followed up and when self-help materials were distributed in conjunction with the advice, the resulting one-year increase in abstinence was 5.1 percentage points.

Trials postdating the meta-analysis of Kottke and colleagues (1988) have also indicated that brief clinical interventions have a small but reliable impact on smoking cessation success (Cummings et al. 1989a; Risser and Belcher 1990; Taylor et al. 1990; Ockene et al. 1991, 1994; Weissfeld and Holloway 1991; Hollis et al. 1993; Strecher et al. 1994). A meta-analysis of seven studies found that physician advice to quit increases cessation by 30 percent (Fiore et al. 2000). The consistency of these findings over a considerable time span and in multiple settings lends credence to the usefulness of minimal interventions.

Smokeless tobacco use may be particularly amenable to minimal clinical interventions, especially in dental office settings. Oral lesions caused by smokeless tobacco are quite common among users of these products (Ernster et al. 1990; Tomar et al. 1997) and provide the opportunity for the dentist to point out the direct adverse health effects of smokeless tobacco. Several trials have examined the efficacy of minimal clinical interventions in smokeless tobacco cessation.

In a randomized trial conducted in a dental health maintenance office clinic to test a minimal clinical intervention, Stevens and colleagues (1995) reported significantly higher smokeless tobacco quit rates in the intervention group than in the usual-care group at both 3 months (32.2 vs. 21.3 percent) and 12 months (33.5 vs. 24.5 percent). In a randomized clinical trial conducted in private dental offices, Severson and colleagues (1998) also found that a minimal intervention significantly increased smokeless tobacco quit rates in the intervention group compared with rates in the usual-care group at 3 months (17.8 vs. 8.8

percent) and 12 months (10.2 vs. 3.3 percent). A minimal intervention trial for smokeless tobacco use among college athletes, which included dental examinations to demonstrate oral lesions, 15–20 minutes of counseling by dental hygienists, and follow-up telephone calls, found that three-month biochemically assayed quit rates were 24 percent in the intervention group and 16 percent in the control group (Masouredis et al. 1997).

Relevant Process Measures

Although minimal clinical interventions provide smokers with some practical advice about quitting, their primary purpose is to increase smokers' motivation to quit. Specific process measures—such as measures of this motivation—are seldom incorporated into minimal clinical interventions. The nonspecific measures some investigators use do not associate clinical success with changes (such as greater awareness of disease risk or enhanced belief in one's ability to quit). Nonetheless, the available evidence suggests that minimal clinical interventions can enhance smokers' desire and intention to quit (Russell et al. 1979), decrease the number of cigarettes smoked per day (Folsom and Grimm 1987), and increase the number of attempts to quit smoking (Folsom and Grimm 1987; Cummings et al. 1989b; Strecher et al. 1991). In addition, patients have reported that physicians trained to perform more intensive interventions are more helpful than physicians without such training (Ockene et al. 1991).

Summary

Substantial evidence suggests that minimal clinical interventions (e.g., a health care provider's repeated advice to quit) foster smoking cessation and that the more multifactorial or intensive interventions produce the best outcomes. These findings highlight the importance of cessation assistance by clinicians, who have a unique access to more than 70 percent of smokers each year. Moreover, minimal clinical interventions have been found to be effective in increasing smokers' motivation to quit and are cost-effective (see "Cost-Effectiveness," later in this chapter). However, research has not clarified fully the specific elements of minimal interventions that are most important to clinical success nor the specific types of changes they produce in smokers that lead to abstinence.

Intensive Clinical Interventions

Intensive clinical interventions (sometimes called "formal" or "organized" cessation treatments) are multisession counseling programs involving extensive contact between a health care provider and a smoker. The value of intensive interventions has been questioned because they are more expensive and reach fewer smokers than self-help and minimal clinical interventions do (Chapman 1985). However, more intensive interventions continue to attract interest because they are more successful at helping people quit smoking (Schwartz 1987). Despite their comparatively high cost, they are cost-effective (Elixhauser 1990), and they may be especially well-suited for treating the most addicted smokers (Lichtenstein and Glasgow 1992; Orleans 1993).

Intensive clinical interventions may be characterized by structure and content. Structural variables include providers' credentials and training; individual, telephone, or group format; session length; total number of sessions; and duration of follow-up. Relatively little research into intensive treatments has been designed to assess the effects of different structural variables (Lichtenstein and Glasgow 1992). Increased patient contact results in better outcomes (Lando 1981; Decker and Evans 1989; Lichtenstein and Glasgow 1992; Fiore et al. 2000). In a meta-analysis of research on the nicotine patch (Fiore et al. 1994c), researchers found that the following counseling features were associated with significant increases in six-month abstinence rates: counseling being a main reason for clinician-patient contact, at least weekly clinician-patient meetings during the first 4 weeks of treatment, and more than six clinician-patient meetings in the first 12 weeks of treatment. A more recent meta-analysis that was not restricted to nicotine patch studies (Fiore et al. 2000) found that quitting success increased with increasing contact time (up to 90 minutes of total contact) and that there was a dose-response relationship between number of sessions and treatment efficacy (Fiore et al. 2000). Thirty to 90 minutes of total counseling and four or more sessions were two to three times more effective in producing long-term smoking cessation than no contact controls. This research supports the notion that in general, as the intensity of clinician-patient counseling increases, so does the long-term effectiveness of treatment.

Because so little information is available on how structural variables affect intensive treatment outcomes, this section concentrates on a review of content variables. Content refers to the specific information, materials, and techniques to which smokers are

exposed during the course of treatment. The various contents of intensive smoking cessation interventions are not easy to evaluate, partly because the methodological quality of clinical trials tends to differ across content areas. For example, trials of relatively unorthodox treatments, such as acupuncture and hypnosis, tend to use shorter follow-up periods than assessments of efforts involving pharmacologic and behavioral treatments (Schwartz 1987; Ter Riet et al. 1990); inflated efficacy estimates may thus result for unorthodox treatments. These methodological concerns are handled here by limiting the review primarily to studies reporting outcomes with at least five months of follow-up.

Another problem in evaluating the content of intensive interventions is that the evolution of treatments over the past 40 years prevents a cumulative assessment of specific intensive interventions. Moreover, changing research interests and methodologies make it difficult to integrate findings from over the entire period. For instance, pharmacotherapies have changed greatly during this period and are now incorporated routinely into intensive treatments. In addition, treatment response may be affected by changes in the nature of the smoking population; for instance, compared with 40 years ago, a higher proportion of today's smokers are women. Methodological and statistical changes have also altered the nature of the studies themselves: sample sizes are larger to increase statistical power, and biochemical confirmation of abstinence is now routine, as is the application of the "intent to treat" principle in analyses. Because of these refinements, early cessation research is now often neglected, perhaps because it is difficult to integrate with newer work. On the other hand, some apparently effective methods, such as rapid smoking, have often not been evaluated by newer methods. The older literature on such strategies is included selectively in this review.

A related problem, complicating the interpretation of relatively recent research, arises from what Lichtenstein and Glasgow (1992) have referred to as a shift from a "clinical" to a "public health" (p. 518) orientation among smoking cessation researchers. This shift has resulted in a dearth of theory-driven research into intensive interventions. In fact, one observer has suggested that the long-term research trajectory favors modifying established models over applying innovation in the basic approach to treatment (Shiffman 1993b). Recent emphasis on public health has also produced a research climate that favors the evaluation of treatment packages and minimal interventions over treatment components (Lichtenstein and Glasgow 1992). One reason for this shift is the high cost and large sample sizes required to evaluate individual components. Thus clinical trials rarely allow assessment of a given treatment's independent contribution. Smoking cessation trials now tend to combine specific treatment components into multicomponent interventions. Moreover, within the same study, not only may groups receive different treatment packages but the packages may differ in their structural components.

Finally, the question of selection bias remains a challenge to interpreting the literature on intensive interventions. Investigators typically recruit highly motivated volunteers to serve as subjects, because the efficacy of intensive interventions can be tested only if the patients under study actually receive the entire treatment. Efficacy estimates derived from this atypical population may not be appropriate for making predictions about the larger population of smokers. The principal types of intensive interventions must be evaluated in the context of these limitations stemming from the nature of the available evidence.

Problem Solving/Skills Training

Various strategies try to impart to smokers the knowledge and skills necessary to cope with cessation—that is, both to attain and to maintain abstinence when confronted with withdrawal symptoms or the temptation to smoke (Marlatt and Gordon 1985; Curry and McBride 1994). This approach (hereafter referred to as problem solving/skills training) springs from the observation that most relapse efforts seem to be associated with a finite number of factors, such as alcohol use, negative affect (e.g., depression), and the presence of others smoking (Shiffman 1982; Baer and Lichtenstein 1988; Brandon et al. 1990). Problem solving/skills training tries to help people who have recently quit smoking anticipate these "high-risk" situations and learn to cope with them when they arise. Such interventions also train participants to cope with withdrawal symptoms, replace positive reinforcements they had linked to smoking, and meet other challenges that might be encountered during or after an attempt to quit smoking.

General problem solving/skills training targets challenges that occur early in the quitting process (e.g., withdrawal discomfort). Because newly abstinent smokers often return to regular smoking (Curry and McBride 1994), one specialized type of intervention teaches skills to help the former smoker maintain abstinence (Marlatt and Gordon 1985). These interventions also train former smokers to prevent any relapse from becoming a long-term return to smoking. Former smokers are encouraged to view relapses as a normal

part of the quitting process rather than as an indication of failure (Curry et al. 1988).

Another type of problem solving/skills training focuses on coping with the immediate negative affects of quitting smoking. The growing body of research on dysphoria (feeling unhappy or unwell) after smoking cessation (Glassman et al. 1988; Covey et al. 1990; Brandon 1994; Hall et al. 1994) suggests that strategies that help smokers who have just quit resist negative moods may be particularly successful (Shiffman 1993b). However, a recent meta-analysis (Fiore et al. 2000) did not find that interventions that targeted negative affect improved cessation rates. These interventions were used with the general population as well as smokers with a history of depression. It is possible that the results might be more positive if the studies were restricted to high-risk populations.

Efficacy

Because nearly every state-of-the-art smoking cessation program contains elements of problem solving/skills training (Curry and McBride 1994), the technique is difficult to assess as an individual treatment. Some investigators have failed to uncover evidence that this technique increases cessation success relative to comparison groups (Curry et al. 1988; Emmons et al. 1988; Omenn et al. 1988; Minneker-Hügel et al. 1992; Zelman et al. 1992). Other studies have found beneficial effects, but these benefits have often been modest and have come only through protracted treatment (Hall et al. 1984b; Davis and Glaros 1986; Goldstein et al. 1989; Stevens and Hollis 1989). Even in studies that report success in long-term abstinence through skills training, the overall relapse curves for treatment subjects have paralleled those for comparison groups (Glasgow and Lichtenstein 1987; Goldstein et al. 1989; Stevens and Hollis 1989; Mermelstein et al. 1992; Minneker-Hügel et al. 1992; Gruder et al. 1993). A recent meta-analysis (Fiore et al. 2000) of 104 studies, however, reported that problem solving/skills training increased quitting success by 50 percent. Some evidence suggests that problem solving/skills training may be particularly useful for female smokers (Curry et al. 1988), those who smoke fewer cigarettes (Hall et al. 1984b), those who smoke to cope with emotional stress (O'Connor and Stravynski 1982), and those who are less prone to negative affect (Zelman et al. 1992).

Although multicomponent skills-training programs have sometimes included information about managing the dysphoria associated with smoking cessation (Tiffany et al. 1986; Kristeller et al. 1993), relevant behavioral interventions have only recently begun (Hall et al. 1994). Initial results suggest that such strategies are promising, but these findings require replication and extension.

In sum, the evidence on problem solving/skills training suggests a beneficial impact (Fiore et al. 2000). Such training can offer practical strategies about quitting and inculcate desired coping skills.

Relevant Process Measures

Skills training rests heavily on two assumptions: (1) coping skills will help former smokers remain abstinent in the face of temptation, and (2) smokers can be taught these skills. Some cross-sectional research (Shiffman 1984) and skills-training intervention trials (Hall et al. 1984b; Davis and Glaros 1986; Zelman et al. 1992) have suggested that coping strategies help avert relapse. The available evidence also indicates that patients given skills training acquire coping skills (Hall et al. 1984b; Davis and Glaros 1986; Zelman et al. 1992), and there is evidence that the level of skill acquisition predicts long-term abstinence (Zelman et al. 1992). Although the results of one trial suggest that coping skills are not retained for very long (Davis and Glaros 1986), consistent self-monitoring of smoking during treatment is associated with longer-term maintenance (Kamarck and Lichtenstein 1988); this finding suggests the importance of behavioral characteristics that foster maintenance.

One of the goals of skills training is to encourage relapsed former smokers to renew their efforts to quit smoking. Curry and colleagues (1988) found evidence that smokers who had received skills training were more likely to try quitting again if they relapsed.

Rapid Smoking

Rapid-smoking strategies typically require that smokers inhale deeply from a cigarette about every six seconds until they become nauseated. In theory, this aversive conditioning transforms the subject's perception of smoking from a pleasurable activity into an unpleasant one, thereby making it easier for smokers to give up cigarettes.

Medical complications produced by rapid smoking can include elevations in heart rate, blood pressure, and carboxyhemoglobin blood levels as well as electrocardiogram abnormalities (Horan et al. 1977). Because of these potential problems, candidates for rapid smoking should be selected carefully (Lichtenstein and Glasgow 1977). Older persons and persons with cardiovascular or pulmonary conditions are generally excluded from rapid-smoking strategies,

but some evidence suggests that rapid smoking can be conducted with these persons if appropriate precautions are taken (Hall et al. 1984a).

Efficacy

The 1988 Surgeon General's report on smoking and health (USDHHS 1988) reviewed the literature on rapid smoking and reached two conclusions: (1) although its effectiveness is variable when used alone, rapid smoking yields moderately high long-term abstinence success (40 percent of subjects were abstinent 6–12 months after treatment) when incorporated in multicomponent behavioral interventions, and (2) auxiliary treatment factors, such as patient expectations, patient-therapist rapport, and admonitions not to smoke between sessions, can influence how successful rapid-smoking strategies are. Few rapid-smoking trials have appeared since the 1988 report.

The mid-1980s advent of pharmacologic treatments for smoking cessation greatly reduced research interest in rapid smoking. Pharmacologic aids, such as nicotine gum, appear as efficacious as rapid smoking (Zelman et al. 1992) and are probably more acceptable to smokers and program administrators. Nonetheless, the doubling of long-term success associated with rapid smoking (Fiore et al. 2000) suggests that it may remain an option for smokers who are unable to quit through other methods and for whom such aversive conditioning is acceptable.

Relevant Process Measures

Rapid smoking is intended to produce aversive conditioned responses to stimuli associated with smoking (USDHHS 1988). The technique reliably produces tachycardiac responses to cigarettes, and the magnitude of these responses is directly related to treatment outcome (Tiffany et al. 1986; Zelman et al. 1992). More easily observable variables, such as the number of cigarettes smoked during a rapid-smoking session or the degree of nausea reported by patients, have not been shown to be consistently related to outcome (USDHHS 1988).

Other Aversive-Smoking Strategies

Three other techniques intended to produce aversion to cigarettes have been investigated: satiation therapy, rapid puffing, and focused smoking. Concern over the safety of rapid smoking (Horan et al. 1977) was partly responsible for investigation of these alternative aversion techniques. Some evidence suggests that they are less unpleasant and less risky than rapid smoking (Glasgow et al. 1981; Tiffany et al. 1986). Satiation therapy requires that patients smoke many more cigarettes per day than they normally do, usually about twice as many (Best et al. 1978). Rapid puffing is similar to rapid smoking, but patients are instructed not to inhale cigarette smoke (Tiffany et al. 1986). Focused smoking requires patients to smoke for an extended period of time at a normal rate while concentrating on the negative sensations smoking produces (Lowe et al. 1980).

Efficacy

Satiation therapy alone produces relatively little cessation success (15 percent at one year) (Lando 1982), but the technique may be more effective when incorporated into multicomponent programs (USDHHS 1988). Focused smoking and rapid puffing produce long-term abstinence rates that are equivalent to, or slightly lower than, those produced by rapid smoking (USDHHS 1988; Fiore et al. 2000). Because these techniques do not appear to result in significant tachycardiac responses (USDHHS 1988), their efficacy is probably accounted for by mechanisms other than aversive conditioning.

Cue Exposure

Cue exposure therapy is based on the premise that smokers become conditioned to certain cues or contextual signals correlated with smoking behavior. When persons who have recently quit smoking are exposed to these cues, they are motivated to begin smoking again (Rohsenow et al. 1990–91; Brandon et al. 1995). In cue exposure therapy, persons trying to quit smoking are repeatedly exposed to these signals in a therapeutic context in which smoking is prohibited; the resulting reduced association between smoking and previous cues is hypothesized to reduce some of the temptation for relapse that former smokers will face in the natural environment.

Because cue exposure therapy has produced promising results with other addictive disorders (Monti et al. 1993), several researchers have suggested that such strategies be developed for smoking cessation (Hodgson 1989; Heather and Bradley 1990). These strategies may be particularly important for women, whose responsiveness to nicotine replacement therapy appears to be less than that of men (Perkins 1996). Women may be less controlled by nicotine and more influenced by nonnicotine factors (sensory stimuli, environmental factors) (Perkins et al. 1999) and may therefore respond better than men to behavioral approaches.

Efficacy

Studies conducted to date that have evaluated cue exposure have failed to find significant differences in outcome between cue exposure and comparison interventions (Lowe et al. 1980; Raw and Russell 1980; Götestam and Melin 1983; Corty and McFall 1984). However, clinical research on cue exposure for smoking cessation is sparse, and interpretation of most existing trials is hampered by methodological flaws (Brandon et al. 1995).

Relevant Process Measures

Environmental associations with cigarette smoking can be strong enough to provoke the desire to smoke (Herman 1974; Rickard-Figueroa and Zeichner 1985; Tiffany and Hakenewerth 1991). These provoked responses may affect treatment outcome (Niaura et al. 1989). However, because cue reactivity has not been assessed in existing clinical trials of cue exposure therapy, it is impossible to determine whether such interventions extinguish motivational responses to smoking-related cues.

Nicotine Fading

Nicotine fading is based on the assumption that withdrawal symptoms will be lessened through a gradual reduction of nicotine intake (Foxx and Brown 1979; McGovern and Lando 1991). Nicotine fading can be accomplished either by progressively switching to brands of cigarettes yielding less nicotine or by using a series of graduated filters (McGovern and Lando 1991). Once the lowest nicotine level is reached, cessation is attempted. Nicotine fading should be distinguished from cigarette fading, in which the number of cigarettes smoked per day is gradually reduced. Cigarette fading has generally not been shown to be an effective smoking cessation technique; participants generally reach a level beyond which they find it difficult to reduce cigarette consumption (Lando 1993; Fiore et al. 2000).

Efficacy

Foxx and Brown (1979) reported that 4 of 10 subjects who tried nicotine fading had quit smoking at 18 months, but subsequent investigations have found more modest long-term results (usually around 20 percent) (Beaver et al. 1981; Lando and McGovern 1985; Burling et al. 1989). Some evidence suggests that nicotine fading can increase abstinence success independently within a larger smoking cessation program (Burling et al. 1989). In a community setting where participants were allowed to select their treatment, about 25–30 percent of those who chose multicomponent interventions containing nicotine fading achieved long-term abstinence (Lando et al. 1990; Lando 1993). Brand switching and graduated filters have produced equivalent outcomes (McGovern and Lando 1991). Cinciripini and colleagues (1995) found that 44 percent of persons using a combined nicotine fading and skills-training package were abstinent from nicotine at one year, a proportion significantly higher than that produced by matched conditions.

Relevant Process Measures

Nicotine fading is presumed to exert its effects by gradually weaning smokers from nicotine, thereby reducing withdrawal symptoms. Reductions in nicotine intake and withdrawal indexes are thus the process measures of primary importance to nicotine fading. One early study suggests that nicotine fading reduces the severity of withdrawal symptoms (West et al. 1984a,b).

The process measure of reduced nicotine intake is problematic, because smokers' nicotine consumption seldom matches a given brand's machine-rated nicotine yields (McMorrow and Foxx 1983). Smokers are able to compensate for reduced nicotine yield by adjusting how they smoke—by inhaling more strongly, holding smoke in longer before exhaling, inhaling more frequently, or smoking the cigarette closer to its high-yield butt (Benowitz et al. 1983; Kozlowski et al. 1988). Smokers can also compensate for nicotine fading by blocking the air inlet holes on the filters that are used to decrease nicotine intake (McGovern and Lando 1991). The best available evidence indicates that although nicotine consumption is indeed reduced by nicotine fading, the extent of these reductions is smaller than would be expected (i.e., based on machine ratings); apparently, some compensatory smoking occurs (Lando 1993). For example, one study (McGovern and Lando 1991) compared two nicotine fading regimens, brand switching and graduated filter use, each of which was designed to reduce nicotine intake by 80 percent by the final stage. Each regimen significantly reduced nicotine consumption but by far less than 80 percent: brand switching reduced intake by 42.5 percent and graduated filters by 55.2 percent.

Lando and McGovern (1985) suggested that nicotine fading increases smokers' self-efficacy by providing them with a series of concrete steps that are mastered before cessation. Self-efficacy does increase during the fading process (McGovern and Lando 1991),

although no more than with comparison treatments (Burling et al. 1989). Moreover, increased self-efficacy has not been shown to predict treatment outcome for nicotine fading (McGovern and Lando 1991).

Motivational Rewards

Strategies that use motivational rewards are rooted in operant conditioning theory. These efforts are designed to provide reasons for remaining abstinent to smokers who have just quit—reasons more tangible and immediate than the important but delayed outcomes that typically motivate cessation attempts (e.g., improvements in health). In a typical motivational rewards intervention, the provider collects a deposit from each participant at the outset of treatment and refunds a portion of this sum at each follow-up assessment at which the participant demonstrates abstinence (Paxton 1983). Other variations of this technique have used nonmonetary rewards (Lando 1982), punished smokers for every cigarette smoked (Murray and Hobbs 1981), instructed participants to reward themselves for abstinence (Tiffany et al. 1986), and rewarded participants who had reduced their carbon monoxide levels (Stitzer and Bigelow 1985). Curry and colleagues (1991) used a theoretical framework that tested intrinsic motivation (personalized feedback) against extrinsic motivation (financial incentive). Abstinence at 3 and 12 months was two times higher in the intrinsically motivated groups.

Efficacy

When used alone, motivational rewards foster relatively high abstinence success in the short term, but these gains do not appear to be durable (Antonuccio et al. 1992). Participants often return to smoking after the term of the contract expires (Paxton 1980, 1981). Attempts to prolong abstinence by varying factors such as duration and frequency of reward have generally been unsuccessful (Paxton 1981, 1983). Multicomponent treatments using motivational rewards have sometimes fared better than comparison treatments, but these comparisons are generally confounded by other factors (Jason et al. 1990; Lando et al. 1990) and may lead to type II errors. A meta-analysis of 62 studies comparing components of behavioral controls found that motivational rewards (contingency contracting) did not significantly alter long-term cessation rates (Fiore et al. 2000). In the final results of the Minnesota Heart Health Program, the failure of community education methods (which included motivational rewards for smoking cessation) to produce results that exceeded secular trends is an important demonstration of the difficulties in evaluating such modalities (Lando et al. 1995).

Relevant Process Measures

The process measures most relevant to this strategy are presumably motivational; making rewards contingent on abstinence should increase a smoker's resolution to remain abstinent. However, motivational measures have been neglected in research on this intervention. Many programs require participants to administer their own rewards or punishments. Evaluations of these strategies should routinely assess how well participants take on this responsibility; to date, evaluations have not made this assessment.

Social Support

Social support interventions try to ease the smoking cessation process by enlisting the support of significant persons in smokers' lives (extratreatment social support) and by providing support from clinicians (intratreatment social support). Both strategies may range from intense and pervasive to relatively minimal and limited. Intensive extratreatment social support may train participants to elicit aid and support of family and friends, whereas training clinicians to communicate caring, concern, and encouragement increases intratreatment social support. Increasing the cohesiveness of smoking cessation groups can enhance both forms of social support (Hajek et al. 1985; Lando and McGovern 1991). At the basic level, the simple use of a group rather than an individual format can be viewed as a social support intervention.

Efficacy

Strategies that add social support to pharmacologic treatment appear to significantly increase long-term quit rates compared to treatments without social support, although some intensive interventions have reported mixed results (Glasgow et al. 1986; McIntyre-Kingsolver et al. 1986). A recent meta-analysis of 19 studies (Fiore et al. 2000) reported that interventions to increase social support in the smoker's environment increase long-term cessation by 50 percent. A meta-analysis of 50 studies (Fiore et al. 2000) reported that within-treatment social support increased cessation by 30 percent. The importance of intratreatment social support may well be reflected in the finding that individual and group counseling are both much more effective than no contact interventions (Kottke et al. 1988; Fiore et al. 1996).

Relevant Process Measures

Studies of intensive social support interventions have regularly included measures of smokers' perceived support. These investigations have found that the amount of support a smoker perceives is directly related to outcome (Malott et al. 1984; Glasgow et al. 1986; McIntyre-Kingsolver et al. 1986; Gruder et al. 1993), but the trials have typically failed to find evidence that the support itself has increased this perception (Malott et al. 1984; Glasgow et al. 1986). In one study that found social support intervention to be effective, the strategy was itself associated with an increase in received support (Gruder et al. 1993). Moreover, this increase in support was statistically related to the differential outcome. Because support measures have rarely been incorporated into the evaluation of group treatments for smoking cessation, little is known about whether group formats enhance perceived support and about what influence such support has on treatment outcome (Hajek et al. 1985).

Weight Control

Most people who quit smoking gain weight (Klesges et al. 1989), and this effect may be greater for women than for men (Williamson et al. 1991; Fant 1996). This effect has been hypothesized to result from nicotine's ability to modify various mechanisms in the central nervous system that regulate body weight (Schwid et al. 1992; Perkins 1993). Apprehension about weight gain may serve as a barrier to cessation attempts, especially among young women (Gritz et al. 1989). Cessation strategies that address this barrier have only recently begun to be assessed.

Efficacy

Two important trials have examined the contribution of a weight control component to a multicomponent smoking cessation program. One study (Hall et al. 1992) compared a specialized weight control program with both a nonspecific weight control program and a standard program. Patients in the specialized group learned behavioral self-management, reduced their caloric intake under the direction of a dietitian, and received an individualized activity plan from an exercise counselor. Patients in the nonspecific group attended several group sessions devoted to discussing weight-related issues. Results showed that participants in both of these weight control programs were less likely to be abstinent after one year (21 percent success for both groups combined) than participants treated with the standard protocol (35 percent success).

Another study (Pirie et al. 1992) examined the effects of adding nicotine gum, weight control counseling, both, or neither to a standardized smoking cessation program in a sample of women who had indicated that they were concerned about postcessation weight gain. After 12 months, the group that added nicotine gum to the standard program had much greater success (44.4 percent had quit smoking) than the groups that added weight control counseling to the standard package (27.8 percent success for the group that added weight control only and 27.6 percent success for the group that added both weight control and nicotine gum). However, the standard package alone was the least successful program (19.4 percent had quit smoking) and was viewed by participants as less appealing than the weight control component (Pirie et al. 1992).

A meta-analysis of six studies (Fiore et al. 2000) that looked at the effect of dieting and physical activity on smoking cessation did not find that these interventions increased cessation success. A recent single study (Marcus et al. 1999) found that vigorous physical activity increased quit rates.

Relevant Process Measures

Weight gain has not been a consistent predictor of smoking relapse (Gritz et al. 1989), and it has predicted abstinence as well (Hall et al. 1986; Gritz et al. 1989; Hughes et al. 1991b). Nonetheless, actual control of weight is an important process measure for weight control interventions—the primary purpose of which is relapse prevention—because they explicitly assume that preventing weight gain will boost abstinence rates (Hall et al. 1992; Pirie et al. 1992). Neither published trial of weight control interventions found differences in weight gain among abstinent subjects across treatment conditions (Hall et al. 1992; Pirie et al. 1992). One of the studies (Hall et al. 1992) found evidence for lower caloric intake in specialized weight control interventions, especially among women, but failed to find differences in activity levels across treatment conditions. In sum, despite the intuitive appeal of weight control interventions to promote smoking cessation, there is mixed evidence relating such interventions to cessation success (Fiore et al. 2000). Hall and colleagues (1992) suggested that such interventions may interfere with cessation. However, Marcus and colleagues (1999) found that a vigorous exercise intervention increased quit rates while contributing to weight management. Pharmacotherapies, including bupropion sustained release (SR) and nicotine gum, may help to delay weight gain after cessation (Emont and Cummings 1987; Doherty et al. 1996; Jorenby et al. 1999).

Hypnosis

Some smokers try hypnosis therapy to help them quit (Schwartz 1987). Strategies for hypnosis interventions include direct hypnotic suggestions to quit, suggestions intended to produce aversion to smoking, and training in self-hypnosis to reinforce formal treatment (Simon and Salzberg 1982).

Efficacy

The methodological shortcomings of hypnosis research make it difficult to estimate the value of this therapy for smoking cessation (Schwartz 1987). Reviewers have noted that, in general, hypnosis is not very effective when used alone, but it may be useful as part of a multicomponent intervention in which subjects see a therapist many times (Holroyd 1980; Schwartz 1987). In methodologically sound studies, hypnosis often fails to outperform comparison techniques, such as self-help strategies (Rabkin et al. 1984; Lambe et al. 1986). Hypnosis techniques may work best for the relatively small proportion of people highly susceptible to hypnosis (Barabasz et al. 1986; USDHHS 1988). Since the late 1980s, there have been only two trials of hypnosis in smoking cessation, with inconclusive results. Johnson and Karkut (1994) conducted an uncontrolled clinical trial of hypnosis plus aversion treatment and reported about 90 percent abstinence at three months. A similar uncontrolled study of 226 smokers reported a 23-percent abstinence at two years (Spiegel et al. 1993). A recent review of hypnosis by the Cochrane group (Abbot et al. 2000) found insufficient evidence to support hypnosis as a treatment for smoking cessation.

Relevant Process Measures

Appropriate process measures for studies of hypnosis are those that assess the various means of hypnotic induction and the motivational changes that are presumed to accrue from them. Because measures have rarely been collected, little is known about the mechanisms of hypnotic treatments for smoking cessation (Holroyd 1980; Schwartz 1987; USDHHS 1988).

Acupuncture

The typical acupuncture treatment for smoking cessation involves the insertion of needles or staples into the outer ear, but a number of other techniques have been investigated (Schwartz 1988). The most commonly cited rationale for using acupuncture is that it relieves the discomfort of nicotine withdrawal.

Efficacy

The available evidence suggests that acupuncture is no more effective in smoking cessation than placebo treatments (Schwartz 1987). For example, Schwartz (1988) reviewed eight studies in which acupuncture at a theoretically appropriate site was contrasted with acupuncture at a placebo site. Only one of these studies found greater success among participants undergoing the procedure with theoretically appropriate sites (MacHovec and Man 1978). A recent meta-analysis of five studies (Fiore et al. 2000) found that acupuncture was no more effective than placebo.

Relevant Process Measures

Acupuncture is commonly presumed to exert its effects by easing tobacco withdrawal. At present there is no evidence that acupuncture is capable of relieving withdrawal symptoms associated with smoking cessation (Clavel et al. 1987; Schwartz 1987; USDHHS 1988).

Summary of Intensive Clinical Interventions

Intensive programs serve an important function in the nation's efforts to reduce smoking, despite the resources the programs demand and the relatively small population of smokers who use them. Such programs may be particularly useful in treating smokers who find it most difficult to quit.

Because intensive smoking cessation programs differ in structure and content, evaluation is often hampered by variation in methodology and by a lack of research addressing specific treatment techniques. Because few studies have chosen to isolate single treatments, assessment of the effectiveness of specific approaches is difficult. Nonetheless, skills training, rapid smoking, and both intratreatment and extratreatment social support have been associated with successful smoking cessation. When such treatments are shown to be effective, they are usually part of a multifactorial intervention. Little clear evidence has implicated particular psychological, behavioral, or cognitive mechanisms as the agents of change. The specific impact of intensive interventions may be masked by the efficacy of several multicomponent programs, some of which have achieved cessation proportions of 30–50 percent (Lando 1993).

Thus, in their positive effect on smoking cessation and long-term abstinence rates (Kottke et al. 1988; Fiore et al. 1994a), intensive interventions seem little different from other forms of counseling or psychotherapy. With intensive interventions, as with counseling, it is difficult to attribute the efficacy to

specific characteristics of the interventions or to specific change mechanisms (Luborsky et al. 1975; Elkin et al. 1989).

Pharmacologic Interventions

At first look, nicotine replacement therapy appears to be the treatment of a disease with its cause. The rationale, however, is well established. Observations on the beneficial effects of nicotine replacement in abstinent smokers were first made in 1967 (Lucchesi et al. 1967), and the process has its medical precedent in the use of methadone for opiate dependence. Nicotine use, in the form of 10 or more cigarettes a day, provides continuous neuroexposure (Benowitz 1993). The resulting tolerance and physical dependence produce classic withdrawal symptoms (USDHHS 1988). As Benowitz (1993) has summarized, "Nicotine replacement therapy serves primarily to break the daily addiction cycle by relieving withdrawal symptoms, thereby facilitating behavioural modification that is necessary for permanent smoking cessation" (p. 158). However, as will be discussed later in this chapter, recent data suggest that nicotine replacement may be effective without behavioral support or counseling. A number of candidate delivery systems have now been extensively evaluated with clear and consistent results. In addition, nonnicotine pharmacotherapies for treatment of tobacco use are now available.

Nicotine Polacrilex

Nicotine polacrilex (nicotine gum) was approved by the Food and Drug Administration (FDA) for use as an aid to smoking cessation in a 2-mg dose in 1984 and in a 4-mg dose in 1994. The nicotine in the gum is bound to an ion-exchange resin. Chewing the gum liberates the nicotine, which is absorbed through the buccal mucosa. Currently, both doses of nicotine polacrilex are approved for use as over-the-counter preparations by adults. The package insert instructs patients to use the gum as needed with the constraint that they not exceed a daily dose of 20 pieces of 4-mg gum or 30 pieces of 2-mg gum.

Efficacy

With more than 50 studies on its efficacy, nicotine gum is the most extensively investigated pharmacologic treatment for smoking cessation. This body of research has been summarized by several major meta-analyses (Lam et al. 1987; Cepeda-Benito 1993; Silagy et al. 1994; Tang et al. 1994). The most recent meta-analysis (Fiore et al. 2000) is summarized in Table 4.3. All meta-analyses found the gum to be effective in helping smokers quit.

Lam and colleagues (1987) performed a meta-analysis of nine randomized, controlled trials of the 2-mg nicotine gum. These authors performed separate analyses on the trials conducted in specialized smoking cessation clinics and on those conducted in general medical settings. In the specialized clinics, cessation success was greater with nicotine gum than with placebo gum. In general medical practice settings, however, nicotine gum was no more successful than placebo gum; both types of gum were more successful than usual care. The authors suggested that participants at the specialized cessation clinics had greater success because such participants may have been more motivated to quit and may have received more intensive adjuvant behavioral support than those at the generalized settings. The authors also speculated that patients who seek treatment in specialized clinics may be more physically dependent on nicotine and thus more likely to benefit from nicotine replacement than the average patient seen in a general medical clinic.

Cepeda-Benito (1993) performed a meta-analysis of 33 trials of the 2-mg gum. As in the review by Lam and colleagues (1987), the trials were categorized according to whether the adjuvant behavioral support was intensive or brief and according to whether the control group used placebo gum or no gum. Pooled estimates of efficacy were derived for short-term (0–8 weeks after treatment) and long-term (12 ± 2 months) outcome measures within each category. Effect sizes were not systematically related to the type of control treatment used but were related to the intensity of behavioral support provided. When used in intensive interventions, the gum was associated with greater abstinence success than the control treatments at both long-term and short-term follow-up. When used in brief behavioral interventions, however, the gum outperformed the control interventions only at short-term follow-up. The author concluded that nicotine gum is an effective aid to smoking cessation but questioned its long-term value in the absence of adjuvant psychosocial support.

In the context of a larger review of available nicotine replacement therapies, Tang and colleagues (1994) performed a meta-analysis of 28 randomized, controlled trials of the 2-mg gum and 6 randomized, controlled trials of the 4-mg gum. The authors found that among participants recruited through advertisements to attend specialized cessation clinics, the 2-mg gum was associated with an 11-percent increase in success over control treatments. However, among

smokers who were directly invited to participate in a general smoking cessation trial conducted by a nonspecialist physician, the 2-mg gum increased abstinence success by only 3 percentage points over control conditions. Consistent with the analysis by Lam and colleagues (1987), the authors suggested that these findings reflect (1) the greater motivation of the smokers who referred themselves (i.e., responded to advertisements instead of being directly invited), (2) the greater degree of nicotine dependence in the self-referred group, and (3) the more extensive encouragement and more detailed instructions provided by therapists in the specialized settings in which the self-referred smokers were treated.

Six of the 28 trials of the 2-mg gum (Fagerström 1982, 1984; Jarvik and Schneider 1984; Areechon and Punnotock 1988; Hughes et al. 1989b; Jensen et al. 1990) reported abstinence success as a function of nicotine dependence as assessed by the Fagerström Tolerance Questionnaire (described later in this chapter). The authors aggregated these data and found that the 2-mg gum improved cessation success by 16 percentage points among smokers scoring high (indicating considerable nicotine dependence) on the

Table 4.3. Meta-analyses of efficacy (estimated odds ratio and abstinence rates) for seven pharmacotherapies used in tobacco dependence treatment

Pharmacotherapy	Number of study groups	Estimated odds ratio (95% CI*)	Estimated abstinence rate (95% CI)
Bupropion SR† (n = 2‡)			
Placebo	2	1.0	17.3
Bupropion SR	4	2.1 (1.5, 3.0)	30.5 (23.2, 37.8)
Nicotine gum, 2 mg (n = 13)			
Placebo	16	1.0	17.1
Nicotine gum	18	1.5 (1.3, 1.8)	23.7 (20.6, 26.7)
Nicotine inhaler (n = 4)			
Placebo	4	1.0	10.5
Nicotine inhaler	4	2.5 (1.7, 3.6)	22.8 (16.4, 29.2)
Nicotine nasal spray (n = 3)			
Placebo	3	1.0	13.9
Nicotine spray	3	2.7 (1.8, 4.1)	30.5 (21.8, 39.2)
Transdermal nicotine (the nicotine patch) (n = 27)			
Placebo	28	1.0	10.0
Transdermal nicotine	32	1.9 (1.7, 2.2)	17.7 (16.0, 19.5)
Clonidine (n = 5)			
Placebo	6	1.0	13.9
Clonidine	8	2.1 (1.4, 3.2)	25.6 (17.7, 33.6)
Nortriptyline (n = 2)			
Placebo	3	1.0	11.7
Nortriptyline	3	3.2 (1.8, 5.7)	30.1 (18.1, 41.6)

*Confidence interval.
†SR = sustained release.
‡Number of studies.
Source: Fiore et al. 2000.

questionnaire but produced only a 2-percentage point increase among smokers whose scores indicated low levels of nicotine dependence.

When data from the 4-mg gum trials (Puska et al. 1979; Kornitzer et al. 1987; Tønnesen et al. 1988a,b; Blöndal 1989; Hughes et al. 1990a) were aggregated, the influence of nicotine dependence paralleled that seen in trials using the lower dose. Among smokers highly dependent on nicotine, those who used the 4-mg gum had a 21-percent greater success at cessation than those using the 2-mg gum. In contrast, among smokers low in nicotine dependence, those who used the 4-mg gum had an 18-percent lower success than those using the 2-mg gum. Highly dependent participants using the 4-mg gum had a 35-percent greater success than those using the placebo gum, but this comparative improvement was only 5 percent greater among less dependent participants.

Tang and colleagues (1994) concluded that nicotine gum is an effective aid to smoking cessation and suggested that its efficacy is a direct function of the dependence of the smoker. On the basis of their review of other nicotine replacement therapies (including the nicotine patch), the authors concluded that the 4-mg gum is the most effective form of nicotine replacement for highly dependent smokers.

Silagy and colleagues (1994) examined 42 nicotine gum trials in their meta-analysis of nicotine replacement interventions. To compute effect sizes for each analysis, the authors combined data from the longest follow-up assessments (mainly 12 months) from available trials, regardless of gum dose or type of control treatment. Across all 42 trials, 42 percent of participants using nicotine gum quit smoking, whereas only 18 percent of participants in the control groups, who used either placebo gum or no gum, succeeded in quitting. The pooled odds ratio (OR) for the gum-to-control comparison across all trials was 1.61 (95 percent confidence interval [CI], 1.46–1.78). Differences between gum and control conditions did not vary according to the intensity of adjuvant behavioral support.

Fiore and colleagues (1990) conducted a meta-analysis of 13 randomized controlled trials of 2-mg nicotine gum therapy with at least five months of follow-up (Table 4.3). Nicotine gum treatment was associated with a 50-percent increase in quit rates (23.7 percent quit rate vs. 17.1 percent) in the control group. There were too few studies done in the over-the-counter setting to allow meta-analysis of the over-the-counter effect of nicotine gum.

Taken together, these meta-analyses suggest that nicotine chewing gum is an effective aid to smoking cessation. This conclusion continues to be borne out as evidence continues to accumulate. In an ongoing project, Silagy and colleagues (1999) have been regularly searching medical databases for new nicotine replacement trials, recalculating effect sizes as new data sources are identified, and frequently publishing the updated meta-analyses. In the most recent edition of this meta-analysis, the pooled gum-to-control OR was estimated at 1.63. That in most settings nicotine-containing gum is associated with greater cessation success than placebo gum suggests that the gum's efficacy is due to its pharmacologic properties. Some evidence indicates that the efficacy of the 2-mg gum depends on the presence of intensive adjuvant behavioral support. The meta-analysis by Silagy and colleagues (1994) suggests that nicotine gum may be beneficial even without intensive adjuvant therapy. In this analysis, however, because 2-mg and 4-mg gum studies are combined, definitive conclusions about the efficacy of either dose alone in the absence of behavioral support cannot be drawn. This finding underscores the importance of selecting those smokers for whom nicotine gum is likely to be beneficial. The available evidence suggests that traditional measures of nicotine dependence may be a useful basis for selecting gum candidates. Both doses of the gum appear to be of greater value to smokers who are more dependent on nicotine. The 4-mg gum may be particularly effective for the most dependent smokers.

Relevant Process Measures

Nicotine gum is presumed to exert its effects by replacing a portion of the nicotine that smokers usually obtain through smoking; in therapy, the gum ameliorates aversive tobacco withdrawal (Benowitz 1991; Hughes 1993). Some evidence suggests that nicotine gum reliably reduces some withdrawal symptoms.

Patients receiving the 2-mg nicotine gum have consistently reported having less total withdrawal discomfort than patients treated with placebo gum (Jarvis et al. 1982; Hughes et al. 1984, 1989a, 1991b; Gross and Stitzer 1989; Hatsukami et al. 1991). However, studies have found that withdrawal severity is not consistently related to smoking relapse (West 1992; Hughes 1993), and the withdrawal suppression produced by nicotine gum appears to be somewhat independent of its efficacy. Moreover, the suppression reported seems to accrue through the lessening of a relatively small subset of withdrawal symptoms (Hughes et al. 1990b). The 2-mg gum consistently alleviates symptoms such as

anxiety and irritability but does not appear to reliably ameliorate craving, hunger, sleep disturbance, or difficulty concentrating (West et al. 1984a,b; Gross and Stitzer 1989; Hughes et al. 1989a, 1990a; Hatsukami et al. 1991). One trial (Hughes et al. 1990a) has found that the 4-mg gum was no more effective than the 2-mg gum either in suppressing total withdrawal severity or in relieving any of the individual symptoms of withdrawal. Future research must explore whether these counterintuitive findings are a result of poor measurement of withdrawal severity or whether other mechanisms explain how nicotine gum produces clinical success (Hughes 1993).

Effect on Postcessation Change in Body Weight

Evidence suggests that the 2-mg gum is capable of delaying, but not preventing, postcessation weight gain. Early in the cessation process, smokers given the 2-mg gum tend to gain less weight than smokers treated with placebo gum (Gross et al. 1989). During this period, weight gain among the 2-mg gum users is inversely related to the amount of gum used (Emont and Cummings 1987; Fagerström 1987; Killen et al. 1990a; Nides et al. 1994). However, differences in weight gain between smokers using the 2-mg gum, using placebo gum, and using no gum (Gross et al. 1989; Nides et al. 1994) disappear when follow-up is conducted after gum therapy has ended.

Relatively little is known about the weight-related effects of the 4-mg gum. Early trials did not show it to diminish weight gain any more than either the 2-mg gum (Kornitzer et al. 1987; Tønnesen et al. 1988a) or the placebo gum (Puska et al. 1979; Tønnesen et al. 1988a). These trials, however, tended to use different weight measures and more distal end points than the typical trial with 2-mg gum, and one trial used a mixed-dose regimen (Tønnesen et al. 1988a). A more recent study, however, reported that nicotine gum suppressed weight gain with greater suppression occurring with the 4-mg dose (Doherty et al. 1996). Analysis of salivary cotinine showed that smokers who replaced a greater percentage of their baseline cotinine levels gained less weight.

Side Effects and Likelihood of Inappropriate Use

Common side effects reported by the 2-mg gum users include mouth soreness, hiccups, indigestion, jaw ache, and unpleasant taste (American Medical Association [AMA] 1993; Tang et al. 1994). Most of these symptoms are relatively mild and transient, and many can be resolved by correcting the user's chewing technique. Symptoms observed less frequently (in less than 2 percent of patients) include irritability, lightheadedness, headache, excessive salivation, and anorexia (AMA 1993). Moreover, absorption of nicotine from the gum is highly dependent on the pH of the mouth (Henningfield et al. 1990). Because nicotine is inactivated by an acidic environment, patients are urged to refrain from eating or drinking anything but water for 30 minutes before using the gum. Approximately 10–25 percent of successful abstainers continue to use the gum for one year or longer (Hajek et al. 1988; Hughes 1988; Hughes et al. 1991a). Although discontinuance of use should be encouraged, continued use confers a substantial reduced health risk compared to a return to smoking. The 4-mg gum appears to have similar side effects, but it may produce slightly more dyspepsia and hiccuping than does the 2-mg gum (Tønnesen et al. 1988a,b).

Transdermal Nicotine

In 1991, the FDA approved the use of transdermal nicotine patches as an aid to smoking cessation. Nicotine patches contain a reservoir of nicotine that diffuses through the skin and into the wearer's bloodstream at a constant rate. Patients are usually instructed to apply one patch each day. Specific dosing regimen may vary.

All currently marketed brands are designed to deliver approximately 0.9 mg per hour of nicotine over the weaning period. Most are intended for 24-hour wear and deliver 21–22 mg of nicotine; one is intended for waking hours wear (16 hours per day) and delivers 15 mg of nicotine. Full-strength patches typically produce serum nicotine levels similar to trough levels of serum nicotine in moderate to heavy smokers (Mulligan et al. 1990). On July 3, 1996, the FDA approved the transdermal nicotine patch for over-the-counter sales at a dose of 15 mg for use as part of a comprehensive behavioral program of smoking cessation, although the FDA's proscription does not provide a clear statement of the constituents of such a program. Since that time, all varieties of nicotine patches have become available over the counter, some as "house brands."

Efficacy

Several meta-analyses of the efficacy of the nicotine patch have been published (Po 1993; Fiore et al. 1994c; Gourlay 1994; Silagy et al. 1994; Tang et al. 1994; Fiore et al. 2000). Each meta-analysis has concluded that the patch is an effective aid to smoking cessation.

Po (1993) combined data from 11 nicotine patch trials and found that persons using the nicotine patch had greater cessation success than persons using a

placebo patch. This finding held for both short-term follow-up (3–10 weeks; combined OR = 3.10 [95 percent CI, 2.65–3.62]) and long-term follow-up (6–12 months; combined OR = 2.26 [95 percent CI, 1.80–2.86]). Gourlay (1994) pooled the results of six trials and found that the nicotine patch produced greater cessation success than a placebo patch at all follow-up assessments (2–3 months, 6 months, and 12 months; all pooled ORs were between 2.2 and 2.4 [95 percent CI, 1.6–3.4]). Tang and colleagues (1994) conducted a meta-analysis of six patch trials. Overall, at long-term (12-month) follow-up, persons using nicotine patches had a 9-percent (6–13 percent) greater success at cessation than did persons using placebo patches. Nicotine patches were found to be more effective among self-referred subjects than among invited subjects and slightly more effective among smokers who were more dependent on nicotine. Silagy and colleagues (1994) combined data from nine patch trials and found that at long-term (12-month) follow-up, nicotine patches were associated with a combined OR of 2.07 (95 percent CI, 1.64–2.62) when compared with control conditions (placebo patches or no patch). Secondary analyses indicated that the patch's relative efficacy was not affected by the intensity of adjuvant support. Fiore and colleagues (1994c) examined 17 nicotine patch trials and found a combined OR of 2.6 (95 percent CI, 2.2–3.0) at the end of the treatment and 3.0 (95 percent CI, 2.4–3.7) at 12-month follow-up. More intensive adjuvant support was found to produce higher abstinence rates at six months (26.5 vs. 19.5 percent for low-intensity interventions) but did not increase the relative advantage of nicotine patches over placebo patches. The 16- and 24-hour patches were found to be equally effective. Neither weaning nor extending treatment beyond eight weeks was found to improve outcome. A recent meta-analysis (Fiore et al. 2000) of 27 studies reported that transdermal nicotine increased long-term cessation by 90 percent (Table 4.3). A meta-analysis of three studies reported that over-the-counter nicotine patch use increased successful long-term cessation by 80 percent (Fiore et al. 2000).

These meta-analyses strongly indicate that the nicotine patch is an effective aid to smoking cessation. This conclusion is buttressed by the findings of a continuing, regularly updated review of the existing research literature on transdermal nicotine (Silagy et al. 1999). In the most recent release of this evolving meta-analysis, Silagy and colleagues (1999) found a pooled patch-to-control OR of 1.84 (95 percent CI, 1.60–2.10). The data continue to suggest that 16- and 24-hour patches are equivalent in efficacy, that there is no advantage associated with weaning or tapering of patch dose, and that the relative efficacy of the patch is fairly independent of the intensity of adjuvant therapy. Nicotine patches have been consistently found to outperform placebo patches regardless of dosing regimen and in a variety of investigational settings. For example, a study of "real-world" use of the patch—based on a follow-back of older persons who had filled patch prescriptions—produced a self-reported cessation proportion of 29 percent at six months (Orleans et al. 1994). The patch is more effective than placebo treatment when paired with only brief support, and it is associated with the higher long-term success when paired with more intensive counseling or behavioral interventions (Fiore et al. 1994b). Though the nicotine patch does increase success rates when used with minimal formal counseling, many nicotine patch clinical trials involve frequent follow-up assessments. Such contacts might boost success rates obtained with the patch. In support of this possibility, Jorenby and colleagues (1995b) found that the combination of nicotine patch treatment plus frequent assessments produced follow-up outcomes equivalent to the nicotine patch plus intensive behavioral therapy. Further assessment of this issue is important, as frequent follow-up contact does not usually accompany nicotine patch use outside of clinical trials (Cummings et al. 1994; Swartz et al. 1995). A meta-analysis of three studies of over-the-counter nicotine patches, however, indicated that patch therapy was superior to placebo (Fiore et al. 2000).

Effects on Discomfort of Nicotine Withdrawal

Some evidence suggests that the nicotine patch reduces overall measures of nicotine withdrawal discomfort (Daughton et al. 1991; Transdermal Nicotine Study Group 1991; Jorenby et al. 1996), but this finding has not been consistent (Abelin et al. 1989; Tønnesen et al. 1991; Merz et al. 1993). Use of the nicotine patch has been repeatedly found to reduce the craving for cigarettes (Abelin et al. 1989; Rose et al. 1990; Tønnesen et al. 1991; Transdermal Nicotine Study Group 1991; Merz et al. 1993; Sachs et al. 1993; Westman et al. 1993; Fiore et al. 1994b; Levin et al. 1994; Jorenby et al. 1996), but other symptoms of nicotine withdrawal are affected less reliably (Palmer et al. 1992). In a study designed to clarify the impact the patch has on withdrawal symptoms, the patch reliably reduced craving, anxiety, and irritability but did not alleviate depressed mood, restlessness, or sleep disruption (Jorenby et al. 1996). The authors noted that with or without the patch, most withdrawal symptoms disappeared within three to four weeks.

Effect on Postcessation Change in Body Weight

Nicotine patches can attenuate postcessation weight gain while they are in use (Abelin et al. 1989; Sachs et al. 1993; Jorenby et al. 1995a; Dale et al. 1998), but this short-term effect has not always been observed (Rose et al. 1990; Tønnesen et al. 1991; Transdermal Nicotine Study Group 1991; Fiore et al. 1994b). Moreover, studies that follow up effects after treatment has ended have not found that persons who used the nicotine patch gained less weight than those who used a placebo patch (Tønnesen et al. 1991).

Side Effects and Likelihood of Inappropriate Use

Most side effects of nicotine patch use are relatively mild; less than 5 percent of patients need to discontinue patch therapy because of side effects (Hughes and Glaser 1993). Minor skin irritation at the patch site is reported by 30–50 percent of patch users and can be relieved by moving the patch to another site. Insomnia is reported by 1–23 percent of patch users (AMA 1993). Comparatively rare side effects include headache, dizziness, fatigue, gastrointestinal distress, sweating, limb pain, and palpitations (Palmer et al. 1992). Studies have found little evidence that people will inappropriately use transdermal nicotine systems (Palmer et al. 1992; Hughes 1993; Jorenby et al. 1995b).

The risks associated with using the nicotine patch during pregnancy are largely unknown. Nicotine itself poses risks to the fetus, including neurotoxicity (Slotkin 1998), and pregnant women should first be encouraged to quit without pharmacotherapy. Because exposure to nicotine through maternal use of the patch probably poses less danger to the fetus than does continued maternal smoking (Hackman et al. 1999), however, nicotine replacement therapy may be indicated for pregnant women who are unable to quit smoking (Benowitz 1991; Lewis and Fiore 1994). However, if a decision is made to use nicotine replacement therapy during pregnancy, the physician should consider monitoring blood nicotine levels, using doses at the low end of the effective range, and choosing intermittent delivery systems (such as nicotine gum) (Fiore et al. 2000). The issue is under active investigation.

Continued smoking while using the patch may be a significant problem. In an observational study of self-reported patch use, almost one-half the respondents stated that they smoked while using the patch; 20 percent of the respondents did so every day (Orleans et al. 1994). A small number of adverse cardiovascular events were reported in patients who continued to smoke while using the patch. When these events received much attention from the popular press, several analyses, including one by an FDA advisory committee, have documented no association between nicotine replacement therapy and cardiovascular events even in patients who continue to smoke intermittently (Working Group for the Study of Transdermal Nicotine in Patients with Coronary Artery Disease 1994; Joseph et al. 1996; Benowitz and Gourlay 1997; Mahmarian et al. 1997). Caution should be used, however, for patients with acute cardiovascular disease (immediately post-myocardial infarction or in the presence of serious arrhythmias or serious or accelerating angina pectoris).

Relevant Process Measures

Like nicotine gum, the nicotine patch is intended to reduce tobacco withdrawal symptoms (Palmer et al. 1992; Glover 1993b; Hughes and Glaser 1993). Although the nicotine patch appears to reduce withdrawal severity, particularly craving for cigarettes, withdrawal suppression may or may not be responsible for the patch's efficacy (Hughes 1993). For example, one trial failed to reveal reliable differences in withdrawal severity between persons using nicotine patches and those using placebo patches (Merz et al. 1993); the trial nevertheless found that participants who used the nicotine patch were nearly twice as likely to quit smoking. Another trial employing two doses of transdermal nicotine found that the higher-dose patch produced significantly greater cessation success than the lower-dose patch, even though both doses provided about the same amount of relief from withdrawal symptoms (Transdermal Nicotine Study Group 1991; Hughes 1993). Clearly, other potential mechanisms of the patch's action, as well as the action of nicotine replacement therapy in general, need to be explored.

Nicotine Nasal Spray

Nicotine nasal spray was approved for prescription use in the United States in March 1996. The spray consists of a pocket-sized bottle and pump assembly, which is fitted to a nozzle designed for insertion into the nose. Each metered spray delivers 0.5 mg of nicotine to the nasal mucosa. The recommended dose is 1 mg, or one 0.5-mg spray per nostril, as needed (Sutherland et al. 1992).

Efficacy

A number of clinical trials have assessed the efficacy of the nicotine nasal spray as an aid to smoking cessation. Sutherland and colleagues (1992) found that

26 percent of participants given nicotine nasal spray were abstinent after one year, compared with only 10 percent of participants given placebo. Hjalmarson and colleagues (1994) found similar results in a placebo-controlled trial; at one-year follow-up, abstinence rates were 27 percent and 15 percent, respectively, for participants given active spray or placebo. Schneider and colleagues (1995) again replicated this effect, finding continuous abstinence rates of 18 percent and 8 percent among participants given active or placebo spray. Another study (Blöndal et al. 1997) did not find a significant difference in abstinence rates between active spray and placebo groups at one year (25 vs. 17 percent); active spray was associated with higher abstinence rates at six months and earlier in this trial.

Recently, Blöndal and colleagues (1999) provided all participants in a second trial with active nicotine patches, then studied the incremental efficacy of adding nasal spray therapy to the patch regimen in a double-blind, placebo-controlled fashion. Results showed that participants given the active spray were more likely to be abstinent after one year than participants given placebo (27 vs. 11 percent). Participants given active spray had a higher rate of abstinence than participants given placebo a full six years after the start of treatment (16 vs. 9 percent), but this effect was only marginally significant. Taken together, the results of these studies suggest that nicotine nasal spray is an aid to smoking cessation. A meta-analysis by Silagy and colleagues (1999) reported a pooled spray-to-control OR of 2.27, and a recent meta-analysis (Fiore et al. 2000) reported an OR of 2.7 (30.5 percent long-term abstinence rate) (Table 4.3).

Effect on Discomfort of Nicotine Withdrawal

Evidence regarding the nicotine nasal spray's effects on nicotine withdrawal discomfort is sparse. The results of two studies suggest that the spray may be useful for coping with craving, but may not be effective in alleviating other withdrawal symptoms. One study (Sutherland et al. 1992) found that, compared with participants using placebo spray, participants treated with nicotine spray reported having less total withdrawal discomfort during the 48 hours immediately after smoking cessation and reported less craving for cigarettes during this period. After 48 hours, however, the two groups reported equivalent levels of withdrawal discomfort and craving. When craving did arise, the nicotine spray was consistently rated more effective than the placebo spray.

The other study (Hjalmarson et al. 1994) found that during the first 48 hours of smoking cessation, users of nicotine spray reported somewhat less severe withdrawal discomfort than placebo users, but this effect was not statistically significant. The severity of craving was found to be similar across both groups, but the nicotine spray was more helpful in quelling craving than the placebo spray was. Other clinical trials have not reported comparisons between active and placebo spray groups with regard to withdrawal measures (e.g., Schneider et al. 1995; Blöndal et al. 1999).

Effect on Postcessation Change in Body Weight

The limited evidence available suggests that the nicotine nasal spray may be capable of delaying, but not preventing, postcessation weight gain. In one of the trials (Sutherland et al. 1992), participants were allowed to use the spray they were assigned for as long as one year. Weight effects in that study differed as a function of duration of spray use: abstinent subjects who had continued to use the nicotine spray for the entire year of the study had gained significantly less weight than subjects still using the placebo spray. However, change in body weight was equivalent for abstinent patients who had stopped using either type of spray during the year.

Another study (Hjalmarson et al. 1994) failed to find any statistically significant differences in weight gain between participants using nicotine spray and those using placebo spray. The authors observed, however, that participants still using nicotine spray at the 12-month follow-up tended to gain less weight than both participants continuing to use a placebo spray and participants who had stopped using the nicotine spray before that time.

Side Effects and Likelihood of Inappropriate Use

Unpleasant side effects are common with the nasal spray. Between 75 and 100 percent of nasal spray users reported experiencing irritant effects, such as runny nose, sneezing, throat irritation, nasal irritation, watering eyes, and coughing (Sutherland et al. 1992; Hjalmarson et al. 1994; Schneider et al. 1995). Some authors have reported that these sensory irritation effects are actually viewed as desirable by many smokers and have suggested that they may help bridge the gap between cigarette smoking and nicotine replacement (Glover 1993a; Schneider 1993). Less common side effects, present in 15–25 percent of users, include nausea, sweating, headache, dizziness, and cold hands and feet.

Because the spray rapidly delivers nicotine to the user, the potential for inappropriate use (e.g., using more often or at a higher dose than recommended) is

high. The results of both clinical trials lend some credence to these speculations. Sutherland and colleagues (1992) found that 43 percent of abstinent study participants who had been given the nicotine spray chose to continue using it for the entire year of the study; moreover, mean plasma nicotine concentrations increased over the follow-up period among participants who continued to use the spray. Participants in the trial conducted by Hjalmarson and colleagues (1994) were explicitly encouraged to begin weaning themselves from the spray (whether nicotine or placebo) after three months. Nonetheless, 30 percent of abstinent participants who had been given the nicotine spray continued to use it after one year. Schneider and colleagues (1995) required that participants in their trial use the spray daily for six weeks, then allowed participants to use spray for up to six months postcessation as needed. Thirty-two percent of participants given active spray continued using it daily for six months, compared with 13 percent of participants given placebo. The authors also reported that some continuous abstainers assigned to active spray reported being concerned that they were dependent upon the spray at six months postcessation. However, a substantial proportion of these individuals remained abstinent many months after drug weaning.

Relevant Process Measures

Nicotine nasal spray, like other nicotine replacement products, is intended to aid smoking cessation by relieving withdrawal symptoms. Although the spray has been found effective in promoting cessation, its circumscribed impact on total withdrawal severity suggests that withdrawal relief is not itself responsible for the spray's usefulness. The spray's documented ability to alleviate craving may be what makes it an effective smoking cessation treatment. More research is needed to advance definitive conclusions about the spray's mechanism of action.

Nicotine Inhaler

In May 1997, the FDA approved the nicotine inhaler for prescription use. The inhaler consists of a plastic tube, about the size of a cigarette, that contains a plug impregnated with nicotine. Menthol is added to the plug to reduce throat irritation. Smokers are instructed to puff on the inhaler as they would on a cigarette. An average puff delivers approximately 13 μg of nicotine (about 1/80th the amount of nicotine contained in an average cigarette puff), which is absorbed primarily by the buccal route (Glover 1993a; Tønnesen et al. 1993). Each inhaler contains enough nicotine for approximately 300 puffs. Smokers are instructed to use between 6 and 16 inhalers per day.

Efficacy

A handful of published trials have examined the efficacy of the nicotine inhaler as an aid to smoking cessation. Tønnesen and colleagues (1993) found that 17 percent of participants randomized to active inhalers had quit smoking at six months, compared with 8 percent of participants given placebo. Corresponding rates at one year were 15 vs. 5 percent. Schneider and colleagues (1996) found active-placebo abstinence rates of 17 vs. 9 percent and 13 vs. 8 percent at six months and one year, respectively. These differences were not significant in the Schneider trial, although active inhalers were superior to placebo at all follow-ups through three months postcessation. Hjalmarson and colleagues (1997) found continuous abstinence rates of 35 percent and 28 percent for active inhaler users at 6 and 12 months, compared with 19 percent and 18 percent, respectively, among placebo users. Active-placebo comparisons were statistically significant at all follow-ups in this trial. The most recent edition of a regularly updated meta-analysis of nicotine replacement products (Silagy et al. 1999) found an inhaler-to-control pooled OR of 2.08, and another recent meta-analysis of four studies (Fiore et al. 2000) reported a pooled OR of 2.5 (Table 4.3).

Taken together, the results suggest that the nicotine inhaler is an effective aid to smoking cessation. However, the findings of Schneider and colleagues (1996) suggest that the inhaler may be most useful for producing initial abstinence and that additional interventions may be needed to prevent relapse among users of the inhaler.

Effects on Discomfort of Nicotine Withdrawal

Limited information is available regarding the effects of the nicotine inhaler on nicotine withdrawal symptoms. Two studies (Schneider et al. 1996; Hjalmarson et al. 1997) showed that active inhaler use was associated with decreased craving during the first several days of the quit attempt but not thereafter. Hjalmarson and colleagues (1997) assessed a wide array of withdrawal symptoms across the cessation attempt, but did not find any effects of active inhalers on these other than the fleeting effects on craving. However, this may have been influenced by a floor effect, as mean withdrawal scores were very low in both groups across all assessments.

Side Effects and Likelihood of Inappropriate Use

The most common side effects associated with inhaler use are throat irritation and coughing. These are reported by between 20 to 50 percent of active inhaler users and are less common among placebo inhaler users (Tønnesen et al. 1993; Schneider et al. 1996; Hjalmarson et al. 1997). Other less common side effects include nausea, bad taste in the mouth, dizziness, gastrointestinal disturbances, and oral burning or smarting. Few (0–9 percent) active inhaler users have withdrawn from clinical trials or stopped using the inhaler because of side effects. The potential for inappropriate use appears to be fairly low, with between 2 to 16 percent of active inhaler users continuing to use the device at six months postcessation in clinical trials allowing unrestricted inhaler use (Tønnesen et al. 1993; Schneider et al. 1996; Hjalmarson et al. 1997).

Effect on Postcessation Change in Body Weight

Two placebo-controlled inhaler trials have examined postcessation weight gain (Tønnesen et al. 1993; Hjalmarson et al. 1997). Neither study found evidence that active inhaler use prevented or reduced weight gain among successful quitters.

Relevant Process Measures

The nicotine inhaler is thought to act by relieving withdrawal symptoms (Glover 1993a; Leischow 1994), but little published evidence to date supports this contention. It is often suggested that the inhaler may be effective because it more closely resembles smoking than other pharmacotherapies do, replacing some of the orosensory and behavioral aspects of smoking (Glover 1993a; Tønnesen et al. 1993; Leischow 1994; Schneider et al. 1996; Hjalmarson et al. 1997).

Schneider and colleagues (1996) asked participants to rate their assigned inhalers relative to their usual brand of cigarettes in terms of sensory effects, preference, and satisfaction. Results showed that participants given the active inhaler rated their devices more highly than did participants given placebo. However, the absolute magnitude of the ratings revealed that the inhalers did not compare very favorably to cigarettes in either group. The mechanism of action of the nicotine inhaler would seem to require further scrutiny.

Bupropion

Bupropion is an atypical antidepressant that is believed to work by blocking neurotransmitter reuptake in noradrenergic and dopaminergic sites in the central nervous system (Ascher et al. 1995). Anecdotal reports of spontaneous smoking cessation in patients prescribed bupropion for depression, coupled with a growing appreciation of the importance of negative affect and clinical depression in smoking maintenance (Hall et al. 1994; Piasecki et al. 1997) have recently stimulated clinical investigations of a sustained-release bupropion preparation as an aid to smoking cessation. These investigations led to the approval of a smoking cessation indication for bupropion by the FDA in 1997. The typical dosing regimen for smoking cessation consists of 150 mg sustained-release bupropion per day for three days, followed by 150 mg twice a day thereafter. Therapy is initiated one to two weeks before the target quit date and is generally continued for three months.

Efficacy

Two large-scale clinical trials of bupropion's efficacy as a smoking cessation aid have been published to date. Hurt and colleagues (1997) compared three doses of bupropion (100 mg, 150 mg, and 300 mg) with placebo. Abstinence rates in the 150-mg and 300-mg groups were significantly higher than those of the placebo group at 12 months. All active treatment groups were found to have higher abstinence rates than the placebo group at earlier end points. Jorenby and colleagues (1999) studied active and placebo patches and active and placebo bupropion in a 2 x 2 factorial design. Abstinence rates after one year showed no difference between patch-only and placebo groups (16 percent and 15 percent, respectively). Both placebo and patch treatments were associated with higher abstinence rates when given with bupropion. Thirty percent of the bupropion-only group (150 mg twice a day) were abstinent at 12 months, whereas 36 percent of participants given active patches and bupropion were counted as abstinent.

A recent meta-analysis (Fiore et al. 2000) of two studies reported a pooled OR of 2.1 and an estimated abstinence rate of 30.5 percent (Table 4.3). Thus, the available evidence suggests that bupropion is an effective aid to smoking cessation, and that it may improve quit rates over those observed with conventional nicotine replacement therapies, although further studies will be needed to demonstrate such efficacy.

Effect on Discomfort of Nicotine Withdrawal

The evidence concerning bupropion's ability to suppress withdrawal symptoms is somewhat mixed. Hurt and colleagues (1997) found that their groups using 150 mg and 300 mg reported withdrawal

symptoms that were equivalent to those reported by placebo participants. Individuals assigned to the 100-mg group, however, reported withdrawal that was significantly worse than that among either the placebo group or the other bupropion groups. The authors suggested that this effect may have arisen because the 100-mg dose produced side effects similar to withdrawal symptoms but was not strong enough to reduce true withdrawal symptoms. Jorenby and colleagues (1999) found that all three groups receiving active treatments compared with the placebo group reported reduced withdrawal. The group given both active patches and active bupropion reported the most consistent withdrawal relief. Further research is needed to characterize the reliability and magnitude of bupropion effects on withdrawal symptoms.

Relevant Process Measures

Although nicotine replacement therapies are strongly predicated on the assumption that nicotine will relieve withdrawal symptoms, withdrawal relief represents only one of several rationales for using bupropion as a smoking cessation aid. One hypothesis is that bupropion may selectively reduce depressive symptoms after cessation. However, both trials mentioned previously excluded individuals with current major depression. Both clinical trials (Hurt et al. 1997; Jorenby et al. 1999) also included multiple assessments of postcessation depressive symptomatology, and neither found any differences among treatment groups on these measures. These findings suggest that bupropion does not work through its antidepressant effects per se in relatively healthy clinical trial participants.

Bupropion moderates dopaminergic activity in the central nervous system, and dopaminergic circuits are known to play a role in drug reinforcement (Nutt 1997). This raises the possibility that bupropion may exert its effects by replacing positive reinforcement associated with smoking (Hurt et al. 1997). To date, there is no evidence directly bearing on this hypothesis, and it is clear that this process is not easily studied in clinical trials. Laboratory-based pharmacokinetic and neuroimaging studies should be performed to explore this hypothesis.

Effects of Postcessation Change in Body Weight

Hurt and colleagues (1997) found evidence for a dose-response effect among continuous abstainers, suggesting that participants given the highest doses gained less weight after quitting. Moreover, the disparities between treatment groups in terms of weight gain increased across time while medication was dispensed. At six-month follow-up, 17 weeks after participants went off the assigned medication, no differences in weight gain were observed. These comparisons were limited to a small subsample of continuous abstainers. In the Jorenby and colleagues (1999) trial, members of all active treatment groups tended to gain less weight than did placebo participants over the first seven weeks of cessation. Weight gain suppression was greatest for the combined patch-bupropion group. However, none of the groups differed in weight gain after seven weeks after quitting. Together, the results of these trials suggest that bupropion treatment may delay, but not prevent, postcessation weight gain.

Side Effects

In both clinical trials, two side effects were reported more commonly among participants given bupropion than among those given placebo. Dry mouth was reported by 10 to 15 percent of bupropion users, and insomnia was reported by about 30 to 40 percent of bupropion users. Bupropion may increase the risk of seizure and is thus contraindicated for individuals who are seizure prone, such as individuals with a history of alcoholism or alcohol abuse, eating disorder, seizure disorder, or using MAO inhibitors. No seizures were reported in either clinical trial, but participants with risk factors for seizure were excluded from each before enrollment.

Clonidine

Clonidine is a centrally acting α_2-adrenergic agonist that dampens sympathetic nervous system activity. Clonidine is most commonly used in the management of hypertension; it has not been approved by the FDA as an aid to smoking cessation. Clonidine is available for prescription in oral and transdermal forms; both of these preparations have been investigated in smoking cessation trials. Smokers using clonidine as an aid to smoking cessation are generally started on the drug several days before quitting and are maintained on a fixed daily dose for several weeks.

Efficacy

Covey and Glassman (1991) conducted a meta-analysis of nine early trials of clonidine for smoking cessation. They found that persons given clonidine were more successful at quitting than those given a placebo (OR = 2.36). Five of the nine trials assessed outcome after the therapy was discontinued; only one

(Glassman et al. 1988) showed a significant overall advantage for clonidine. Clonidine trials using adjunctive behavioral therapy were associated with greater relative success (OR = 4.2) than were trials in which treatment essentially consisted of dispensing the drug (OR = 1.7). Trials using transdermal clonidine produced somewhat greater relative success (OR = 3.2) than did trials using oral clonidine (OR = 2.2). The two trials that analyzed efficacy according to sex found clonidine to be much more effective, relative to placebo, among women (OR = 11.0) than among men (OR = 0.9). There is no obvious explanation for this finding.

Since the Covey and Glassman (1991) meta-analysis, several large-scale clonidine trials have appeared (Prochazka et al. 1992; Glassman et al. 1993; Hilleman et al. 1993; Niaura et al. 1996). These studies indicated a therapeutic effect for clonidine, with some evidence suggesting that clonidine was more effective among women (Glassman et al. 1993; Hilleman et al. 1993) and among those most dependent on nicotine (Glassman et al. 1993).

A recent meta-analysis (Fiore et al. 2000) of five clinical trials reported a pooled OR for long-term effectiveness of 2.1 (25.6 percent abstinence rate) (Table 4.3). In these studies, the clonidine dose ranged from 0.1 mg to 0.75 mg per day and was delivered either orally or transdermally. Because of the side effects, the lack of a specific dosing regimen, the problems with abrupt discontinuation of the drug, and the lack of FDA approval, clonidine has been recommended as a second-line agent for smoking cessation (Fiore et al. 2000).

Effect on Discomfort of Nicotine Withdrawal

An early report (Glassman et al. 1984) that clonidine could reduce tobacco withdrawal symptoms, especially craving, spurred the initial investigations of clonidine's usefulness in smoking cessation. Since that report, evidence for this effect has been mixed. Clonidine- and placebo-treated patients have had equivalent levels of withdrawal severity (Wei and Young 1988; Franks et al. 1989; Gourlay et al. 1994). Studies have fairly consistently found that clonidine diminishes the specific symptom of craving (Glassman et al. 1984; Ornish et al. 1988; Prochazka et al. 1992; Gourlay et al. 1994), and some studies have found some effects on withdrawal symptoms, such as anxiety and irritability (Ornish et al. 1988; Prochazka et al. 1992).

Side Effects

Unpleasant side effects are commonly associated with clonidine use (Gourlay et al. 1994), and as many as 25 percent of patients may discontinue clonidine therapy because of them (Covey and Glassman 1991). The most frequently observed symptoms are dry mouth, fatigue, and dizziness. Local skin irritation is common with transdermal clonidine therapy. The incidence of side effects appears to be dose dependent (Gourlay et al. 1994). Care must also be taken to discontinue clonidine gradually to prevent rebound hypertension. No published clinical trials have assessed the effect of clonidine on postcessation weight gain.

Relevant Process Measures

Clonidine is presumed to exert its effects by ameliorating withdrawal discomfort (Glassman et al. 1984; Franks et al. 1989). Although a few studies have found that clonidine reduces withdrawal discomfort, findings from a well-designed, large-scale multicenter trial (Prochazka et al. 1992) have suggested that this effect does not necessarily lead to greater abstinence.

Nortriptyline

Nortriptyline is a tricyclic antidepressant that blocks reuptake of norepinephrine and serotonin. As with clonidine, smoking cessation is not an FDA-approved indication for nortriptyline; its primary indication is for the treatment of depressive symptoms. It is a prescription medication and is available in generic form. In smoking cessation studies conducted to date, treatment was initiated 2–4 weeks before the target quit date with gradual titration of dose.

Efficacy

Two studies have assessed the efficacy of nortriptyline for smoking cessation. Hall and colleagues (1998) conducted a 2 (nortriptyline vs. placebo) x 2 (history vs. no history of major depression) x 2 (cognitive behavioral vs. health education therapy) trial that produced a 24-percent sustained abstinence rate in nortriptyline users compared with 12 percent in the placebo group. There was no difference in cessation rates as a function of previous history of major depression. In a straight comparison of nortriptyline to placebo, Prochazka and colleagues (1998) found cessation rates at six months of 14 percent in participants given nortriptyline and 3 percent in participants given placebo. A meta-analysis (Fiore et al. 2000) of these two studies reported a pooled OR of 3.2 and a 30.1-percent abstinence rate (Table 4.3). Both studies provide clear evidence of nortriptyline's therapeutic effect.

Effect on Discomfort of Nicotine Withdrawal

The Hall and colleagues (1998) study assessed both nicotine withdrawal symptoms and negative affect in the first eight days following the target quit date. There were no significant differences between the drug therapy groups on nicotine withdrawal severity, suggesting that as with many of the other smoking cessation pharmacotherapies, withdrawal relief may not be the primary mechanism of action. The negative affect measure, however, increased in the first three days in the placebo group and declined in the nortriptyline group. This suggests that a negative affect assessment may be more sensitive to some of nortriptyline's therapeutic effects than a conventional nicotine withdrawal symptom scale.

Side Effects

Tricyclic antidepressants are known to produce a number of side effects, including sedation and various anticholinergic effects. In the smoking cessation studies, commonly reported side effects included dry mouth (64–74 percent), lightheadedness (49 percent), shaky hands (23 percent), and blurry vision (16 percent) (Hall et al. 1998; Prochazka et al. 1998).

Other Antidepressants and Anxiolytics

Investigators have begun to explore the potential use of other antidepressants and anxiolytics as pharmacologic aids to smoking cessation, because population-based epidemiologic samples have found that depression and anxiety are associated with cigarette smoking (Breslau et al. 1991; Kendler et al. 1993). Research has also shown that smokers with a history of depression are more likely to experience depressive symptoms (Covey et al. 1990) and to relapse after quitting (Glassman et al. 1988; Anda et al. 1990) than are smokers without such a history. Some anxiolytics (Glassman et al. 1984; Hilleman et al. 1992) have been shown to ameliorate symptoms of tobacco withdrawal, and preliminary smoking cessation trials using antidepressants (Edwards et al. 1989) and anxiolytics (Hilleman et al. 1994) have yielded encouraging results. Among the drugs that have been studied or hypothesized to be useful for smoking cessation are buspirone hydrochloride, doxepin hydrochloride, and fluoxetine hydrochloride. Although promising, this avenue of research is not yet developed enough to permit the multipart discussion given to other pharmacologic agents in this chapter.

Summary of Pharmacologic Interventions

Abundant evidence confirms that both nicotine gum and the nicotine patch are effective aids to smoking cessation. The efficacy of nicotine gum may depend on the amount of behavioral counseling with which it is paired. The 4-mg dose may be the better pharmacologic treatment for heavy smokers or for those highly dependent on nicotine. The nicotine patch appears to exert an effect independent of behavioral support, but absolute abstinence rates increase as more counseling is added to patch therapy. Nicotine nasal spray and nicotine inhalers are effective aids for smoking cessation, although their mechanisms of action are not entirely clear. All nicotine replacement therapies produce side effects, but these are rarely severe enough that patients must discontinue use. Nicotine nasal spray appears to have greater potential for inappropriate use than other nicotine replacement therapies. Nicotine replacement therapies, especially the gum and the patch, have been shown to delay but not prevent weight gain. All nicotine replacement therapies are thought to work in part by reducing withdrawal severity. The available evidence suggests that they do ameliorate some elements of withdrawal, but the relationship between withdrawal suppression and clinical outcome is inconsistent.

Bupropion is the first nonnicotine pharmacotherapy for smoking cessation to be studied in large-scale clinical trials. Results suggest that bupropion is an effective aid to smoking cessation. In addition, bupropion has been demonstrated to be safe when used jointly with nicotine replacement therapy. In the only direct comparison with a nicotine replacement product, bupropion achieved quit rates about double those achieved with the nicotine patch. Bupropion appears to delay but not prevent postcessation weight gain. The available literature contains inconsistent evidence regarding bupropion-mediated withdrawal relief. Bupropion does not appear to work by reducing postcessation depressive symptomatology, but its mechanism of action in smoking cessation remains unknown. Further research is needed to characterize bupropion's central nervous system effects, particularly to assess whether the drug partially replaces smoking-related positive reinforcement.

Evidence suggested that clonidine is capable of improving smoking cessation rates. Clonidine is hypothesized to work by alleviating withdrawal symptoms. Although clonidine may reduce craving for cigarettes after cessation, it does not consistently ameliorate other withdrawal symptoms, and its effects on weight gain are unknown. Unpleasant side effects are common with clonidine use.

Antidepressants and anxiolytics are potentially useful agents for smoking cessation. At present, only nortriptyline appears to have consistent empirical evidence of smoking cessation efficacy. However, tricyclic antidepressants produce a number of side effects, including sedation and various anticholinergic effects.

Large-Scale Public Health Programs

The shift in recent years from a clinical to a public health perspective in smoking cessation research has led to an increased emphasis on developing and evaluating cost-effective strategies that can be widely disseminated (Lichtenstein and Glasgow 1992). This emphasis is reflected in the proliferation of research on self-help manuals (see "Self-Help Manuals," earlier in this chapter and "Community Programs," later in this chapter) and on media- and community-based interventions (Flay 1987; Gruman and Lynn 1993).

As is true for self-help strategies, media-, worksite-, and community-based programs have promise because they can potentially reach many smokers who may try to quit without formal, face-to-face assistance (Fiore et al. 1990). Moreover, some evidence suggests that less educated smokers profit from media campaigns at least as much as more highly educated smokers do (Macaskill et al. 1992). (Other large-scale interventions—educational [Chapter 3] and social [Chapter 7]—are discussed separately.)

Investigators have evaluated an array of such programs, but methodological variations across the individual trials have hampered comparisons among studies (Flay 1987; Schwartz 1992). Moreover, methodological challenges compromise how research on these programs may be interpreted. For instance, ongoing coverage of smoking and its health consequences in the general media may alter the effect of research-based media information. Similarly, secular trends and events that could individually affect large populations of smokers (e.g., the introduction of a new nicotine replacement product) may alter the impact—and complicate the assessment—of media campaigns conducted around the time of such events. Such challenges may account for the inconsistencies seen in this area of research.

Media-Based Programs

Media used to transmit smoking cessation messages have included television (Brannon et al. 1989; Korhonen et al. 1992; Mudde and De Vries 1999), radio (Farquhar et al. 1990; COMMIT Research Group 1991), the telephone (Ossip-Klein et al. 1991; Pierce et al. 1992), newspapers (Cummings et al. 1987), and the mail (Gritz et al. 1992; McFall et al. 1993).

The intensity of media-based programs has varied greatly, and these variations may be related to program success. For example, one study (Gritz et al. 1992) evaluated a minimal mail-based intervention. The investigators mailed self-help smoking materials to a sample of nonvolunteer women who smoked and who belonged to a health maintenance organization. The intervention had no impact; at no point during the 18-month follow-up period were women who had received the materials more likely to quit smoking or report changes in their motivation to quit than women who had not. In contrast, a more intense media campaign evaluated in another study (Orleans et al. 1991) yielded encouraging findings, albeit among treatment volunteers. The investigators tested the impact of adding telephone calls from a smoking cessation counselor to an intervention that mailed self-help manuals to the volunteers. After 16 months, abstinence from smoking was reported by 23.0 percent of the volunteers who had received adjuvant telephone counseling and by 15.2 percent of those receiving the self-help materials alone.

Mass media campaigns of intermediate intensity, such as televised programs (Flay et al. 1989), generally produce modest increases in abstinence—increases that fall short of the moderate effect of telephone counseling found among volunteers (Orleans et al. 1991). The influence of intermediate-intensity interventions is difficult to determine precisely, because the results of individual trials may be affected by the peculiarities of the specific communities in which they are tested and (as previously discussed) by concurrent changes in secular attitudes toward smoking behavior. These problems are compounded by the designs of communitywide and mass media programs frequently failing to include matched control communities for comparison. Although more intensive interventions appear to increase cessation over time (Flay 1987), the absence of well-controlled experimental media trials limit any conclusions about a dose-response relationship for media-based programs.

The content of various media-based programs can be divided into three categories: (1) programs that present information about the negative health effects of smoking and exposure to secondhand smoke and attempt to motivate smokers to quit; (2) programs that promote the performance of simple cessation-related activities, such as calling a hot line, requesting self-help materials, or enrolling in a smoking cessation contest; and (3) programs that mimic intensive clinical interventions (Flay 1987). In general, informational

or motivational campaigns can be effective in changing smokers' attitudes, but the effect of such campaigns on behavior is not clear, in part because of the paucity of well-controlled trials that yield a consistent pattern of findings. Research suggests that other types of campaigns have greater potential than informational programs to influence smoking behavior, especially if the campaign has multiple components and intense exposure (Flay 1987; CDC 1996, 1999b; Pierce et al. 1998).

Worksite Programs

For many years, advocates for tobacco control have been enthusiastic about worksite-based programs, because worksites appear to furnish an ideal setting: a contained audience, an opportunity for smoker participation, an environment in which to convey coherent and consistent messages, and an opportunity to tie individual smoking cessation to overarching institutional policy. Much of the early work in this area provided some justification for the enthusiasm (USDHHS 1986; Glasgow 1987; Fielding and Piserchia 1989), but more recent data, described later in this section (Glasgow et al. 1995; Sorensen et al. 1996), give pause.

The main components of smoking cessation efforts in the workplace are nonsmoking policies and specific assistance for cessation attempts (Gruman and Lynn 1993). The evolution of worksite smoking policies, intimately tied to concerns about the health effects of environmental tobacco smoke (ETS) (Eriksen 1986; USDHHS 1986), is described in some detail in Chapter 5. Although early assessment suggested that restrictive policies had little effect on smoking outside of work (Glasgow 1987; Rigotti 1989; Tager 1989), most recent studies have demonstrated either reductions in daily consumption of cigarettes (Stillman et al. 1990; Borland et al. 1991; Jeffery et al. 1994) or increases in smoking cessation (Stave and Jackson 1991; Patten et al. 1995; Longo et al. 1996). As described in Chapter 5 (see "Clean Indoor Air Regulation"), there is persistent movement toward increasing restrictions in public workplaces.

The strategies for smoking cessation within workplaces are largely those discussed earlier in this chapter: self-help, physician's advice, and formal treatment (Gruman and Lynn 1993). As of 1989, about one-half of worksites that sponsored cessation activities offered self-help materials (Fielding and Piserchia 1989). Although initial dropout rates were high, 20–26 percent of participants had quit smoking by 6–12 months after the worksite programs had begun (Orleans and Shipley 1982; Glasgow 1987). Such proportions compare favorably with those observed in general populations. Physician's advice to quit smoking was a component of only about 15 percent of the company programs, but in a number of studies, this modality seemed to exert an effect similar to that observed in general populations: 15–30 percent of participants had quit smoking at the one-year follow-up (Gruman and Lynn 1993). The programs offering formal treatment appeared to produce results at the worksite that were similar to those found for such programs outside the workplace.

A special feature of worksite cessation programs is the opportunity to provide incentives, such as competitions. Several studies have documented some efficacy in this approach. For example, in one study, 33 percent of participating workers and 25 percent of all workers remained abstinent at work (Glasgow 1987). In a second study, the use of a competition was associated with significantly greater success at quitting than was reported for persons not participating in the competition (Klesges et al. 1988). In a review of incentive programs, from 15 to 60 percent of participants quit smoking; the average was around 40 percent (Gruman and Lynn 1993). Some disadvantages of incentives are that (1) determining the award may be difficult, (2) employees may falsely claim cessation, and (3) nonsmokers may feel slighted (Fiore et al. 1996). On a population basis, incentives have not been found to be effective. In these settings, incentives may be most attractive to smokers who were going to attempt quitting in any case (Chapman et al. 1993).

In contrast, a trial of the Take Heart program, which involved 26 heterogeneous worksites, a low-cost intervention, random assignment, and use of worker and management steering committees, failed to produce short-term improvements in smoking cessation that exceeded the secular trend (Glasgow et al. 1995). These results were particularly disheartening in view of the methodological strengths of the study and the diversity of the workplace settings. The authors offer a number of potential reasons for the lack of impact: the cessation activities may have been inappropriate; the behaviors may have been more resistant to change than previously assumed; workers may have had insufficient "ownership" of the project; secular trends may have been so strong that they canceled out a modest effect; the variability among worksites may have been too great; and, in general, worksite programs may not work.

Similar negative findings were observed by Sorensen and colleagues (1996) in an even larger trial of 111 worksites randomized to sites receiving or not receiving the cessation program. The Working Well Trial involved more than 28,000 workers in 16 states and compared seven-day abstinence, six-month

abstinence, and changes in smoking prevalence for both types of worksites. Changes occurred in the direction hypothesized, but they were small and nonsignificant; for example, the six-month abstinence rate was only 1.5 percent higher in the program group. Similarly, the program sites showed a nonsignificant trend toward greater adoption of smoking bans. The authors observed that the overall cessation proportions at both types of sites compared favorably with those in other worksite programs. The lack of difference may have resulted from the higher than expected cessation at control sites, which is a phenomenon reflecting a general increase in antismoking awareness.

These studies postdate recent reviews of worksite cessation efforts. Several early reviews expressed optimism about the value of worksite programs but did not provide a quantitative assessment (Hallett 1986; Bibeau et al. 1988). In a detailed meta-analysis of 20 worksite programs involving 34 comparisons, Fisher and colleagues (1990) found that the mean weighted effect size was significantly positive and that an average of 13 percent of participants had quit smoking after treatment. Although modest, these effects provide some quantitative basis for the enthusiasm for worksite programs. The addition of the two recent large projects (Glasgow et al. 1995; Sorensen et al. 1996) may well alter the meta-analytic balance.

Although the worksite setting has aforementioned features favorable to large-scale programs (including the importance of adding to a generalized reduction in exposure to ETS), the strategy cannot be recommended without qualification. Nonetheless, the role of such activities, perhaps enlightened by further targeted research, may be important in multicomponent efforts at smoking cessation.

Community Programs

Results from a number of long-term trials of communitywide programs have recently appeared. (See Chapter 7 for a more detailed discussion of these projects in the context of approaches used in the 1990s.) These trials typically incorporate mass media strategies into larger health education programs. Some, such as the Stanford Five-City Project (Farquhar et al. 1990), the Minnesota Heart Health Program (Perry et al. 1992; Luepker et al. 1994), and the Pawtucket Heart Health Program (Elder et al. 1986; Carleton et al. 1995), have been aimed at modifying smoking, as well as other risk factors for cardiovascular disease. Final reports suggest that these trials have met with little success in promoting smoking cessation.

The Stanford Five-City Project (Farquhar et al. 1990; Fortmann et al. 1993) tested an intensive multimedia approach, including television, radio, newspaper, and mass-distributed printed materials. All materials contained information about modifiable risk factors for cardiovascular disease. The average resident of a community receiving the program was exposed to more than 500 educational episodes over the course of the five-year program. By the end of this period, smoking prevalence—the only risk factor on which an impact could be demonstrated—had declined 13 percent more in the program communities than in the control ones. The Minnesota Heart Health Program failed to demonstrate an appreciable impact (Lando et al. 1995). The Pawtucket Heart Health Program had little impact on smoking behavior; its first attempt at a smoking cessation program prompted only 11 smokers to quit (Elder et al. 1986, 1987). The final results confirmed the lack of impact (Carleton et al. 1995).

One ambitious community project—COMMIT (Community Intervention Trial for Smoking Cessation)—focused on smoking cessation and on policy strategies to reduce prevalence (COMMIT Research Group 1991; Gruman and Lynn 1993). In 1986, the NCI began COMMIT, the largest randomized smoking intervention trial in the world. The design of COMMIT included 11 pairs of matched communities—10 from across the United States and 1 in Canada. One community from each pair was randomly selected to be the site in which volunteers and local agencies carried out COMMIT's 58 mandated program activities. Designed to augment existing community-based efforts to reduce smoking, these activities occurred between 1988 and 1992.

The primary end point for COMMIT was smoking cessation among heavy smokers. Main goals included increasing the priority of smoking as a public health issue, increasing the community's ability to influence smoking behavior, strengthening the community's existing economic and policy factors designed to discourage smoking, and fortifying social norms and values that stressed nonsmoking (Gruman and Lynn 1993). Main strategies included training health care providers to routinely assess and manage nicotine dependence, working with community institutions and private organizations to create smoke-free environments, increasing the availability and visibility of smoking cessation services, and using the mass media and schools to educate communities about the dangers of tobacco use.

Results of COMMIT indicate that even intensive community-based programs may not have a demonstrable impact on smoking behavior (COMMIT