SMOKELESS TOBACCO CESSATION WITH NICOTINE REPLACEMENT: A RANDOMIZED CLINICAL TRIAL

by

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This study was a randomized placebo-controlled cessation trial involving adult smokeless tobacco users. The 100 subjects involved were recruited through local media and all but one used moist snuff. Subjects were randomly and blindly assigned to receive either nicotine gum (2 mg) or placebo gum (0 mg) while abstaining from smokeless tobacco use and attending weekly group meetings that focused on behavioral skills training.

At the end of the six week intervention 45 subjects were biochemically confirmed abstinent from tobacco; of these subjects, 20 were from the placebo condition. The quit rate for subjects receiving active gum compared to subjects receiving placebo gum was not significantly different. Pretreatment measures revealed no difference between groups except for salivary cotinine (a nicotine metabolite) which was significantly higher in subjects who received nicotine gum. After adjusting for the level of cotinine, those who received nicotine gum reported less withdrawal symptomatology: They felt less anxious and had fewer feelings of anger compared to the subjects who received placebo gum.

Successful quitters were older ($p = .02$), scored higher on tobacco addiction items ($p = .04$), and reported less craving for tobacco during each week of the study. This

profile of quitters suggests older smokeless tobacco users are ready to quit in spite of their pattern of use and addiction. This research sets the stage for future cessation efforts and highlights the need for intervention services tailored to the needs of smokeless tobacco users. A group therapy format with some form of oral substitute appear to be key elements of a successful cessation program.

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DEDICATION

Dedicated to my spouse, Susan. Above all else, I was sustained through her interest and love.

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CHAPTER I

INTRODUCTION

During the decade of the 1970s, the pattern of tobacco use in the United States shifted dramatically. For the first time since the 1800s smokeless tobacco products gained in popularity as cigarette use began to decline (Christen & Glover, 1987). The rising awareness of the health consequences of smoking contributed, to both the decline in cigarette use, and focused attention on smokeless tobacco.

Although literature from the smokeless tobacco industry portrays smokeless products as safe alternatives to cigarette smoking and as substitutes in worksites where smoking is banned (American Lung Association, 1983), the proliferation of recent research articles conclude that smokeless tobacco is not a safe alternative to cigarettes (United States Department of Health and Human Services, 1986).

While research in the last ten years has made tremendous contributions to the tobacco knowledge base, smokeless tobacco use and cessation has only begun to be addressed. The development and testing of effective smokeless tobacco treatment programs are needed.

Purpose of the Study

The purpose of this study is to test the efficacy of nicotine replacement in assisting adults cease their use of wet snuff or chew. This study represents one of the first empirical, controlled studies of the efficacy of nicotine replacement in smokeless tobacco cessation.

Need for the Study

The need for this study is based on the following four premises:

1. Sales of smokeless tobacco have continued to grow and these sales reflect increased use by young people.

2. Young males of college age are initiating and becoming regular users of smokeless tobacco.

3. Use of smokeless tobacco is associated with personal and societal health consequences.

4. Tobacco addiction is primarily a behavioral and physiologic dependence on nicotine (Henningfield & Jasinski, 1988), and as such the compulsive use of smokeless tobacco is difficult to stop.

Increasing Sales and Use

In sharp contrast to its popularity of the 19th century, for most of this century chewing tobacco and oral snuff have been socially unacceptable--it was believed that the tuberculosis bacterium was spread by dust particles from contaminated tobacco juices spat onto the ground (Christen & Glover, 1987). Today, companies manufacturing smokeless tobacco are often applauded within the marketing sector for transforming an unsanitary, and in some places unlawful, behavior into a desirable image of adulthood. Their marketing campaigns include instructions for proper use; smokeless mock products; starter kits of lower strength for younger users; testimonials from sports stars; and sponsorship of athletic and recreation activities. Several researchers (American Lung Association, 1983; Christen & Glover, 1987; Olds, 1987;) attribute the resurgence of smokeless tobacco to clever advertising campaigns that focused attention on low unit cost, flavor, and feelings of satisfaction.

By the early 1980s, several estimates of increasing use were measures of the success of this smokeless promotional campaign. Between 1974 and 1981, smokeless use increased an average of 11% each year (Christen & Glover, 1987). Early prevalence reports were in disagreement, Harper (1980) suggested that as many as 22 million Americans were using smokeless tobacco, while Smight (1981) estimated 6 million. The 1986 Surgeon General's Report on Smokeless Tobacco provided a more balanced estimate of the number of smokeless tobacco users at 12 million, and half of these were regular users (USDHHS, 1986). Miller (1980), writing in a smokeless tobacco trade publication, highlighted smokeless tobacco as one of the few tobacco product lines he expected to experience growth in the 1980s.

In the same time period, smokeless tobacco production increased 40% between 1970 and 1986, from 95.2 million to 132.8 million pounds (U. S. Dept. of Agriculture, 1987). Similarly, sales of smokeless tobacco increased 52% between 1978 and 1984 (Connolly, 1985). The upward trend in sales, however, has slowed since 1984 (Maxwell, 1986). Indeed, the United States Department of Agriculture (USDA) reported a decline in the consumption of snuff during 1986 and 1987 before sales rebounded in 1988 (USDA, 1988).

Manufacturing output of snuff increased in the first quarter of 1988 while chewing tobacco production continued a four year downward trend (USDA, 1988). By September 1989 chewing tobacco production had stabilized as snuff output continued to increase (USDA, 1989). Reports from June 1991 suggested manufacturing production was highest for moist snuff and loose-leaf chewing tobacco, while plug tobacco and dry snuff production fell (USDA, 1991).

Age of Initiation

Recent research has suggested that early adulthood, as a time of active change, may be a critical time for the initiation of regular use of smokeless tobacco. In the 1986 Adult Use of Tobacco Survey (AUTS), a nationally representative sample of males aged 17 and older reported beginning both snuff and chewing tobacco at the median age of 19 (Novotny, Pierce, Fiore & Davis, 1989). Schroeder, Iaderosa, Chen, Glover, and Edmundson (1987) reported 18 as a high risk age of initiation for a non-rural, college-educated cohort of males. This finding was corroborated in a survey of university athletes, over half of whom started using smokeless after the age of 15 (Levenson-Gingiss, Morrow & Dratt, 1989).

In studying college athletes, Anderson and McKeag (1985) reported that 31% of athletes surveyed started using smokeless tobacco during college. Glover, Lafin, Flannery, and Albrilton (1989), in a national sample of college students, reported more than half of smokeless tobacco users began after the age of 16 and two thirds planned to continue using. From a sample of blue-collar gas pipeline workers, Gottlieb and fellow researchers (1992) reported a mean age of smokeless tobacco initiation as 21.8 years (SD= 9.7). In contrast to the prevalence rates and psychosocial predictors that have been the focus of most smokeless tobacco research, the cessation of smokeless tobacco is an area of research which has received little attention.

Difficulty Quitting

In addition to the resurgence of popularity in smokeless products and subsequent increases in health problems (DHHS, 1986), recent reports suggest smokeless tobacco is difficult to quit. Patterns of use and reports of cravings provide evidence of this difficulty in quitting. Conducting in-depth interviews with adolescent smokeless tobacco users, Ary, Lichtenstein, Severson, Weissman, and Seeley (1989) highlighted daily users

reporting use immediately following waking (25%) and cravings and use right after meals (73%).

Biglan, LaChance, and Benowitz (1991) also found withdrawal and craving from smokeless tobacco deprivation. Specifically, they reported an increased use of smokeless tobacco whenever cigarettes were withdrawn for subjects who used both substances. The researchers concluded that, based on subjects' self-monitoring of cravings, smokeless tobacco produced dependence. Novotny, Pierce, Fiore, and Davis (1989) reported from the Adult Use of Tobacco Surveys (AUTS) that 50% of the men in that national sample experienced difficulty quitting smokeless tobacco. In addition, these researchers reported that between 6 and 7% of smokers used smokeless tobacco to help them quit smoking. Gottlieb, Weinstein, Baun, and Bernacki (1992), found only half of the smokeless users, from a survey of gas pipeline workers, stating they were *certain* they could quit smokeless tobacco permanently.

Cognitive and Social Factors in Tobacco Cessation

The cessation of tobacco represents a distinct period in the life of a tobacco user, and as such it is correlated with a number of different influences that affect continued abstinence or resumption of tobacco use. The natural history of smoking (Lichtenstein, 1982) suggests that psychosocial factors are involved in all stages of smoking, from initiation through relapse. These influences, when viewed from the perspective of social-learning theory, interact in a reciprocal manner and affect the cessation process. Numerous researchers have attempted to measure these influences in hopes of understanding and improving cessation success. Research examining tobacco cessation has identified cognitive and social factors that appear to play a role in abstinence.

Cognitive factors related to tobacco abstinence include perceptions about the consequences of quitting, outcome attributions , and self-efficacy. Perceived self-

efficacy has been examined as a function of quitting (Condiotte & Lichtenstein, 1981) and as a part of a relapse model (Marlatt & Gordon, 1980). Strecher, DeVellis, Becker, and Rosenstock (1986) summarized the self-efficacy construct involving smoking and concluded that self-efficacy ratings distinguished active quitters from continued smokers, joiners from non-joiners, and successful quitters from unsuccessful quitters. Baer and Lichtenstein (1988) concluded that self-efficacy scores were more predictive of smoking during follow-ups than of initial cessation success.

Social factors involved in tobacco cessation include: social support, smoking cues, and stress. Stress has been examined from both a life events approach and a perceived stress method. Cohen and colleagues (1983) developed the Perceived Stress Scale to measure perceived stress without reference to the source of the stress. The scale has been tested specifically with smokers and its brevity (14-items) has been an advantage when used in smoking cessation studies. It remains unclear if cognitive and social predictors of tobacco abstinence have utility in smokeless tobacco cessation.

Research Questions

This study will address the following questions relative to adults' quitting smokeless tobacco.

1. Does the replacement of nicotine for smokeless tobacco improve rates of quitting when comparing nicotine gum to placebo gum?

2. Is the degree of dependence related to cessation success of the two groups?

3. Is quitting confidence related to cessation success?

4. Is level of perceived stress a factor in cessation success?

5. Does the use of nicotine gum affect the frequency and severity of tobacco withdrawal symptoms during smokeless tobacco cessation?

6. Does the number of pieces of gum used daily affect cessation outcome?

Limitations

The past 20 years resulted in a proliferation of research both describing and testing models of tobacco cessation. These research efforts focused predominantly on smoking and a large body of literature exists on smoking cessation. Only in recent years has research attention included smokeless cessation (Glover, 1986; DiLorenzo, Kern, & Pieper, 1991). Given the paucity of smokeless cessation research, the present study assumes that the smoking cessation therapy guidelines are applicable to cessation involving smokeless tobacco. With respect to external validity, the randomized double blind nature of this study reduces the possible interaction of extraneous variables.

Delimitations

This study tests the efficacy of nicotine replacement among adults ages 18-65 who wish to cease their use of smokeless tobacco. For this study, a user is defined as someone who uses smokeless tobacco daily and has done so for at least the past six months. Persons who also smoked tobacco had to be willing to quit all tobacco.

Three specific exclusion categories included medical contraindication, such as worsening angina pectoris, high blood pressure or active temporomandibular joint disease; history of psychiatric disorder; and previous use of Nicorette® gum. A complete list of inclusion and exclusion criteria are listed in Appendix A.

CHAPTER II

LITERATURE REVIEW

Historical Context

The genus *Nicotiana,* recognized as the wild descendent of tobacco-producing plants, has species spread throughout the world. The largest concentrations, however, are found in the Americas where the cultivation of tobacco began (Wilbert, 1987). The anthropological evidence suggests tobacco has historical origins within a number of diverse cultures. One of the earliest recorded reports of tobacco chewing is from South America in 1499 (Christen & Glover, 1987). Following Spanish exploration to the New World, tobacco use spread northward in Europe before eventually returning to the American continent (Christen, Swanson, Glover & Henderson, 1982). Several researchers have detailed the rich and extensive history of smokeless tobacco and are presented here as comprehensive sources: Christen & Glover, 1987; Christen et al., 1982).

The nasal inhalation of dry tobacco or snuff was a popular and fashionable practice in many parts of Europe. In the United States, however, tobacco chewing has remained a more popular choice, indeed, the oral chewing of tobacco is a tradition unique to the United States (Christen & Glover, 1987).

Description of the Product

Smokeless tobacco can be classified into two major types: oral snuff and chewing tobacco. Oral snuff is available in three varieties; dry, moist, and fine cut tobacco. Moist snuff, made from air-cured leaves and stems, is by far the most popular type (Olds, 1987).

Dry snuff ingested orally or nasally is a rarity in the United States. Oral moist snuff is synonymous with the practice of "dipping snuff." A user places a "dip" or pinch of snuff between the lower lip or cheek and gum. The user will keep the dip in this gingival buccal area for an average of 20 minutes or as long as an hour before putting in a fresh pinch.

Chewing tobacco is a coarser product found in three common forms; twist, plug, and loose-leaf. Twist or roll chewing tobacco is made by twisting the cured and flavored leaves into rolls. Plug tobacco may be either moist or firm, the former has a moisture content of more than 15% (Olds, 1987). The plug is formed by wrapping fine tobacco in leaf fragments and pressing into shape. Loose-leaf tobacco dominates chewing tobacco sales and consists of shredded tobacco leaves heavily treated with sugar and flavorings.

Users of chewing tobacco put a chew, often called a *quid* or *wad*, of tobacco in the cheek pouch toward the back of the mouth and actually chew or suck the tobacco to mix it with saliva and produce a juice. Most users of chew spit the juice out and frequently keep a wad in their mouths for 30 minutes or longer.

Prevalence of Smokeless Tobacco Use

The accumulated evidence beginning in the 1970s suggests that the use of smokeless tobacco in the United States has been increasing (DHHS, 1986). During the first half of the 1970s, smokeless tobacco use was restricted to nonsmoking residents of Southern states, where loose-leaf tobacco chewing was a male custom (Rouse, 1989). Evidence from the Bogalusa Heart study in Louisiana indicated oral snuff use tripled between 1976 and 1981 among young white males under 17 years old (Hunter et al., 1986). Other regional surveys have reported between 5 and 36% of male middle school, high school, and college students as regular users of smokeless tobacco (Boyle, 1989;

Wolfe, 1987). Between 1970 and 1985, national data suggest oral snuff use increased tenfold among 17 to 19 year-old males (USDHHS, 1989).

The variation in use prevalence is best explained by regional differences. Marcus, Crane, Shopland, and Lynn (1989) found more adult users in states with larger rural populations Rouse (1989) reported male use as over 4 times higher in non-metropolitan compared to metropolitan areas. Orlandi and Boyd (1989) concluded that smokeless use is more common in rural communities, smaller communities, and where the practice is traditional.

Since 1980, increases in smokeless tobacco sales have been due predominantly to the increasing popularity of moist snuff. Chewing tobacco production declined each year between 1984 and 1988, in sharp contrast, moist snuff sales increased in 1988 after 2 years of decline (USDA, 1988). Most recently, the Wall Street Journal reported (May 3, 1990) a 4.6% increase in moist snuff sales in 1989.

The growth trend in moist snuff has been fueled by both a growing consumer base that includes all socioeconomic backgrounds and regions of the country, and by the introduction of several new products designed to appeal to a broader audience (Ernster, 1989). Other possible reasons for increased snuff use include: high employment in industries where workers typically use smokeless tobacco; growing number of restrictions on smoking; and, a waning of the impact of publicity against smokeless tobacco use (USDA, 1988).

Perhaps most significantly, the shift in smokeless tobacco in the 1980s has resulted in a steady increase in young male users, whereas prevalence among older adults has diminished or remained constant. Generally, blacks and Asians are less likely to use smokeless tobacco than are whites and Hispanics (Boyd and Associates, 1987). Rates of use consistently are higher among males; while females do report trying smokeless tobacco very few can be categorized as regular users. Almost the only exception to this

gender difference has been observed among Native Americans and women living in the Southern United States. Hall and Dexter (1988), surveying public school adolescents in the Northwest, reported user rates of 4 and 24% for non-Native and Native American females respectively. In a report of Washington state Native American youth, it was reported that almost one-third of Native American females had used smokeless tobacco on more than 20 occasions (Schinke, Schilling, Gilchrist, Ashby & Kitajima, 1989). Winn, Blot, Shy, Pickle, Toledo, and Fraumeni (1981) reported long term snuff use and increased risk of cancer among Southern white women.

National Surveys

The findings from national surveys suggest prevalence rates for oral snuff are highest among adolescent and young adult males (Orlandi & Boyd, 1989; Marcus et al., 1989). The 1988 National Institute on Drug Abuse (NIDA) national household survey on drug abuse included questions about smokeless tobacco. Over 12% of males between 18 and 25 years reported using smokeless tobacco in the past month (DHHS, 1989). The national rate for the same age group (including both genders) was 6.3%. This figure is comparable to other national surveys reporting current use of smokeless tobacco (Orlandi and Boyd, 1989).

Health Consequences of Smokeless Tobacco

The Surgeon General's Report, *The Health Consequences of Using Smokeless Tobacco* was released in 1986. In addition to highlighting the plethora of dental and medical studies examining smokeless tobacco, this volume substantiated there is no safe level of tobacco use in humans Indeed, the continued growth of the smokeless tobacco industry has alarmed public health officials who fear a comparable rise in health problems associated with smokeless use as was seen with cigarettes.

Causal links between smokeless tobacco and illness can be found in medical case reports originating in Germany, Britain, India, and the United States (Friedell & Rosenthal, 1941). The early clinical evidence implicated leukoplakia and cancer in the oral and nasal cavities with smokeless tobacco use (Bloodgood, 1921). These early case studies mentioned the cancer risk as greatest in the mouth areas holding the tobacco for the longest time.

Winn and fellow researchers (1981) provided the first methodologically sound study linking smokeless tobacco and cancer. Studying subjects from rural North Carolina, these authors substantiated the earlier reports and assessed the cancer risk for female nonsmokers who used snuff. The risk for these userswas found to be 4.2 times greater than the risk of nonusers, and after more than fifty years of snuff use the risk was almost fifty times greater.

While there are differences between dipping snuff and chewing tobacco, because of mouth movement and increased salivation, the epidemiological evidence is heavily weighted against all tobacco ingestion. Only recently have researchers begun to differentiate between types of smokeless tobacco. The implications against smokeless tobacco are broad and cross many cultures. Smokeless tobacco is related to tooth abrasions and gingival inflammation (Greer & Poulson, 1983); esophageal cancer (Schroeder, 1989); oral cancer (Winn et al., 1981); lower post-natal weights of infants (Krishna, 1978); high blood cholesterol (Tucker, 1989); and high blood pressure (Schroeder & Chen, 1985). In addition there are both systemic and synergistic concerns associated with smokeless tobacco. Smokeless use is implicated in cancers of the esophagus, larynx, and stomach. The potential for synergistic interactions exist in population groups who engage in multiple oral cancer risk factors, such as drinking alcohol, smoking cigarettes, and chewing tobacco (Mattson & Winn, 1989).

The carcinogenic potential of smokeless tobacco is most closely related to the high levels of nitrosamines. The highest amounts of tobacco-specific nitrosamines (TSNA) are formed during the processing of tobacco, where nicotine and nitrate are the major TSNA precursors. The nitrosamine level in smokeless tobacco is highly correlated with the precursor concentration (Hoffman, Rivenson, Chung, & Hecht, 1991). This is best demonstrated by the significantly higher concentration of TSNA levels in snuff in comparison to chewing tobacco or cigarette tobacco. In the latter, TSNA is elevated as a consequence of both a high nitrate concentration and the fermentation and aging processes (Hecht & Hoffman, 1989). The presence of nitrosamines is of particular concern to smokeless tobacco users because the reported levels are at least 100 times higher than allowed in food (Mattson & Winn, 1989).

Treatment of Nicotine Dependence

Use of tobacco is a multidimensional behavior that is maintained by psychosocial and pharmacological factors. Intervention approaches targeting psychosocial determinants have been researched and implemented over the last 30 years. Most cessation efforts have been clinical in nature, that is, targeted at individual users who attend cessation clinics. These organized programs involve a wide variety of treatment techniques, but can be generally categorized as either self-management strategies or aversion procedures. Self-management strategies include: contingency contracting, coping skills training, stimulus control, self-monitoring, identifying and modifying cues to smoke, and altering the social and psychological smoking reinforcers. A second group of procedures aim to reduce the reinforcement from smoking by pairing it with aversive stimuli. The three most common aversive stimuli paired with smoking include electric shock, cigarette smoke, and covert sensitization (an imagery technique).

The research involving behavioral strategies includes many variations on aversion therapy and self-management, especially as clinicians search for effective programs that produce long-term quit rates. In recent years, effective programs have involved multiple components and have demonstrated high levels of success (Schwartz, 1987). Indeed, the last report of the U. S. Surgeon General (1988) concluded that behavioral interventions to treat nicotine dependence were most effective when they included multiple components.

The same report suggested that pharmacologic treatment strategies have potential application in the treatment of nicotine dependence, especially as these strategies enhance behavioral treatment. The interest in pharmacologically based interventions emerged from the growing consensus that tobacco use is maintained by the reinforcement of nicotine. Two tobacco cessation strategies are nicotine based: nicotine fading and nicotine replacement. Nicotine fading involves a planned decrease in nicotine intake, thus making initial abstinence easier. Nicotine replacement strategies, on the other hand, are modeled after earlier drug treatments for heroin and opiates (Henningfield and Jasinski, 1988), and represent potentially effective nontobacco-based nicotine delivery systems. Gum containing nicotine has been available in the United States since 1984, and has been widely researched in both minimal supportive treatment and as an adjunct to behavioral treatment.

Nicotine Replacement

A recently published volume (1988) in the Progress in Clinical and Biological Research series was entitled, *Nicotine Replacement: A Critical Evaluation.* This volume provides a comprehensive review of the efficacy of nicotine replacement.

Substance replacement as a treatment strategy for tobacco cessation has been generally accepted as useful by clinical researchers. Ove Ferno and colleagues at the University of Lund in Sweden initiated the nicotine replacement research in the 1960s

with a nicotine aerosol but settled on the delivery of nicotine as an ion-exchange resin (nicotine polacrilex) in a gum base (Ferno, Lichneckert, & Lundgren, 1973). The earliest studies of this strategy with cigarette smokers involved the use of a placebo gum that did not contain the active drug (Ferno, 1973; Brantmark, Ohlin, & Westling, 1973). The A. B. Leo company developed the nicotine replacement as Nicorette® and introduced it into Switzerland in 1978 and Sweden in 1981 (Pomerleau & Pomerleau, 1988). Schneider, Popek, Jarvik, and Gritz (1977) reported some of the first case studies in the U. S. involving Nicorette® medication. Today, Nicorette® is a widely used prescription drug that has proved successful as an adjunct to smoking cessation programs in clinical situations

The theoretical basis for nicotine replacement suggests that the physiological dependence on nicotine can be transferred to a nontobacco based modality, and that this dependency can be weaned over time. Replacement strategies for drug dependence provide the patient with a safer form of the drug that assists in alleviating withdrawal symptoms present during cessation. Nicotine replacement delivered orally as nicotine gum appears to be modestly effective in providing relief from nicotine withdrawal. This rationale suggests that by tempering withdrawal symptoms smokers are better able to focus their efforts on altering their social and psychological reinforcers.

The available evidence suggests that nicotine gum is efficacious and, when combined with behavioral treatment programs, enhances cessation success with cigarette smokers. More than sixty clinical trials involving nicotine gum have been conducted in twenty countries (Fagerstrom, 1988). Of these cessation studies, at least fifteen utilized a control group with a placebo (see Table 1).

The most effective results were obtained from studies conducted in smoking cessation clinics with trained psychologists as cessation therapists (Fagerstrom, 1982; Jarvis, Raw, Russell, & Feyerabend, 1982; Schneider, Jarvik, Forsythe, Read, Elliott, &

Schweiger, 1983; Hjalmarson 1984; Hall, Tunstall, Ginsberg, Benowitz, & Jones, 1987). Killen, Fortmann, Newman, & Varady (1990) found ad lib gum use ineffective compared to a fixed gum schedule. The fixed schedule versus placebo comparison was significant at 2 and 6-month assessments.

Brief interventions through medical practices were used in several studies (British Thoracic Society, 1983; Campbell, Lyon, & Prescott, 1987; Hughes, Gust, Keenan, Fenwick, & Healey, 1989). The negative results found by the British Thoracic Society may be due to an intervention that was provided by physicians inexperienced in the use of nicotine medication. A similar situation occurred in the study by Campbell et al., where personal advice on how to quit was not given. Hughes et al. concluded that the pharmacologic effects of nicotine gum with a brief intervention in a general medical practice were very small.

Table 1. Long-Term (6 or 12-month) Success Rates of Placebo-Controlled Studies

Study	Nicotine Gum	Placebo Gum	Relative Difference (%)	P
1. Puska, et al. (1979)	35	28	25	ns
2. Malcolm et al. (1980)	23	5	360	<.05
3. Fee & Stewart (1982)	13	9	44	<.05
4. Fagerstrom (1982)	49	37	32	ns
5. Jarvis et al. (1982)	47	21	123	<.01
6. British Thor. Society (1983)	10	14	-40	ns
7. Schneider et al. (1983)	30	20	50	ns
8. Hjalmarson (1984)	29	16	81	<.05
9. Jamrozik et al. (1984)	10	8	25	ns
10. Hughes et al. (1986)	21	10	110	<.05
11. Campbell et al. (1987)	3	2	50	ns
12. Tonneson et al. (1988)	43	22	95	<.05
13. Hall et al. (1987)	44	21	109	<.01
14. Killen et al. (1990)	19	18	5	ns
15. Hughes et al. (1989)	21	19	5	ns

Source for studies 1-13: Fagerstrom, K. O. (1988, p. 110). Efficacy of nicotine chewing gum: A review. *Progress in Clinical and Biological Research, 261*, 109-128.

Taken as a whole, these studies demonstrate that when nicotine gum is compared to placebo gum with an appropriate intervention, the short term results are impressive, and, when considering long-term cessation, the active gum demonstrates a higher, though generally not statistically significant, success rate.

Several researchers have tested (Fletcher, 1977) and discussed (Kozlowski, 1984) the use of smokeless tobacco as a nonprescription source of nicotine. The basis for this observation is the similarity in pharmacokinetics between smokeless tobacco and nicotine gum. Besides cost, taste, and use, smokeless tobacco has been suggested as a cigarette substitute because it eliminates the fire hazard (Kozlowski, 1984). The debate of the early 1980s concerning the use of smokeless tobacco to treat smoking (Blum, 1980; Russell, Jarvis, & Feyerabend, 1980; Kirkland, 1980) has lost considerable favor as the health consequences of smokeless tobacco have become apparent.

Use of Nicotine Gum

Almost 15 years of clinical work has established nicotine medication as a valuable asset in smoking cessation. Russell, Raw, and Jarvis (1980) provided the first explicit, general advice on the clinical use of nicotine gum. Two recent publications (Schneider, 1987; Schneider, 1988) highlight both the comprehensive and practical use of Nicorette® in smoking cessation.

The collective information on Nicorette® suggests that nicotine is released gradually over time, peaking between 20 and 30 minutes after use. The rate of release is dependent on the style and vigor of chewing. Although absorption occurs through the buccal mucosa, much of the nicotine remains in the gum or is lost through swallowing (Russell, 1988). The bioavailability of nicotine in gum is controlled also by salivary pH. Drinking fluids while using the medication alters the salivary pH and substantially

reduces the availability of nicotine through the mouth (Henningfield, Radzius, Cooper, & Clayton, 1990), as well as increasing the amount of nicotine swallowed.

The slow and indeterminate absorption of nicotine from the gum affects the blood nicotine concentrations. Figure 1 represents the blood nicotine concentration achieved from nicotine gum, cigarette, and oral snuff use in four men. The figure suggests that snuff contained in a teabag like sachet produces blood nicotine increases similar to nicotine gum. These sachets, however, are generally recognized as lower in nicotine and are marketed as part of a step or graduation process toward using stronger brands (Ernster, 1989). In addition, Russell (1988) suggested that the sachet may impair mixing with saliva and, when combined with a lower pH level of the tobacco contained in the sachet, results in less bioavailable nicotine.

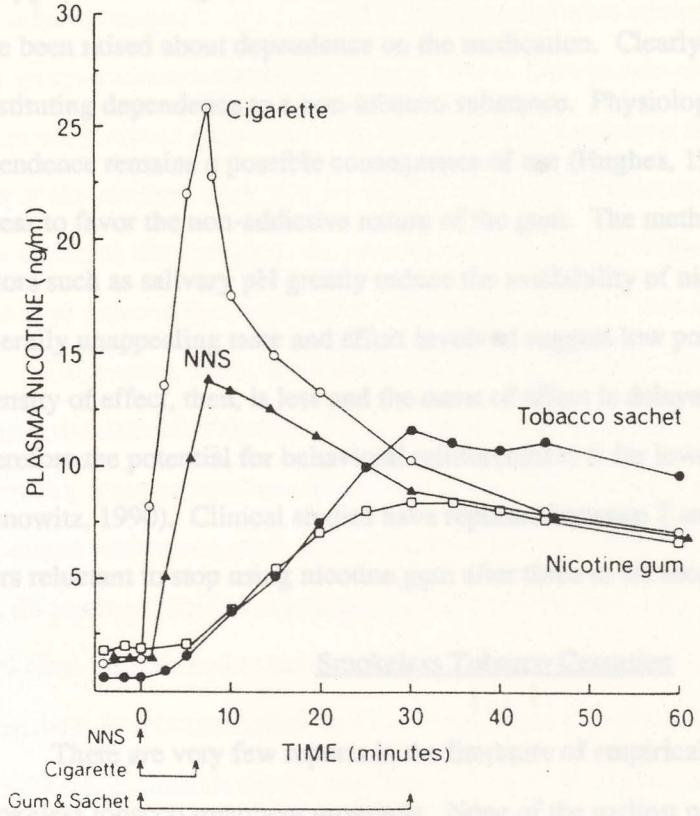

Figure 1. Average Plasma Nicotine Concentrations

Average plasma nicotine concentrations in three men produced by sucking one tobacco sachet for 30 min., and in three subjects who smoked one middle-tar cigarette (1.4 mg nicotine yield) and chewed one piece of nicotine gum (Nicorette®, 2 mg).

Source: Russell, M. A., Jarvis, M. J., West, R. J., & Feyerabend, C. (1985). Buccal absorption of nicotine from smokeless tobacco sachets. *Lancet*, *2*, 1370.

Dependence on Nicotine Gum

Since the introduction of nicotine gum into the United States in 1984, the medication has been controversial (Blum, 1984) but generally, accepted. Very few safety concerns related to gum use have been raised, and while side effects are present they do not appear to be dangerous (Christen & McDonald, 1988). At the same time, concerns have been raised about dependence on the medication. Clearly, some gum users are substituting dependence to a non-tobacco substance. Physiological and behavioral dependence remains a possible consequence of use (Hughes, 1986). Several factors appear to favor the non-addictive nature of the gum. The method of use and mediating factors such as salivary pH greatly reduce the availability of nicotine, in addition, the generally unappealing taste and effort involved suggest low potential for abuse. The intensity of effect, then, is less and the onset of effect is delayed from the onset of dosing. Therefore the potential for behavioral reinforcement is far lower than oral tobacco use (Benowitz, 1990). Clinical studies have reported between 7 and 10% of nicotine gum users reluctant to stop using nicotine gum after three to six months (Hughes, 1986).

Smokeless Tobacco Cessation

There are very few reports in the literature of empirical studies investigating smokeless tobacco treatment programs. None of the earliest published studies recruited sufficient number of subjects to permit random assignment within an experimental design. Two recent studies employed sufficient sample sizes but were designed as minimal interventions

In one of the earliest studies, Glover (1986) reported a six month abstinence rate of 2.3%. Glover's study involved 41 subjects whose participation was mandatory. This initial study adopted the American Cancer Society's Fresh Start Adult Smoking Cessation

Program but did not use random assignment or biochemical verification. As involuntary subjects, their disappointing quit rate is perhaps understandable.

Two other studies involved voluntary subjects who were recruited from local communities. Eakin, Severson, and Glasgow (1989) incorporated a multi-component treatment program in a quasi-experimental design with a sample of high school students. The subjects ranged in age from 14 to 18 years and were encouraged to attend three hour-long group sessions emphasizing coping skills. Twenty-one of the 25 subjects completed treatment, however, only nine were biochemically confirmed successful in quitting. Only three of the subjects were still nonusers at six month follow-up. Although long term quit rates appeared discouraging, the authors reported that for subjects continuing to use smokeless tobacco their self-report of daily use was 45% less than baseline measures.

DiLorenzo, Kern, and Pieper (1991) report the only other published results of a formal cessation intervention. Using a treatment program of eight one-hour sessions over six weeks, these researchers utilized cue extinction, a buddy system, and relapse prevention with seven adult male smokeless tobacco users. The mean age of the subjects was 32 years and the average length of use was 9.3 years. Six subjects quit using smokeless tobacco and remained abstinent nine months after treatment. Collateral assessment was incorporated instead of biochemical verification of self-reported quitting. In this case, collaterals were close friends who were in daily contact with the subject. Telephone calls were made to these close friends to verify abstinence.

Each of these formal treatment programs adapted recognized cognitive-behavioral techniques from smoking cessation programs. The efficacy of these techniques require further study and assessment. Two recently completed studies have examined smokeless tobacco cessation from a broader public health perspective. One hundred and ten post-secondary students were assigned to either high or low individual contact with a cessation counselor while progressing through chapters of a self-help manual. The overall quit rate

was biochemically verified as 17% at the end of treatment, and the amount of individual contact with staff had no effect on quitting (Williams, 1992). This quit rate parallels previous studies of minimal contact in smoking cessation .

Little, Stevens, Severson , and Lichtenstein (1992) reported the results of a smokeless tobacco intervention delivered in an oral healthcare setting where dental hygienists provided the intervention. A total of 518 smokeless tobacco users were randomly assigned to either usual care or special intervention. After three smonths a significantly larger proportion of the intervention patients were abstinent (32% vs 21%) compared to the control group.

Nicotine Replacement with Smokeless Cessation

At this time, there are no published reports of nicotine replacement therapy being used as an adjunct to formal smokeless tobacco cessation programs. Several researchers around the country appear to be considering or testing the use of Nicorette® medication in smokeless tobacco cessation. Hatsukami, Anton, Keenan, and Callies (1992) compared nicotine gum with placebo gum in two experiments on deprivation lasting 5 and 10 days. The authors concluded that abstinence from tobacco resulted in observable symptoms, but that these symptoms were not alleviated by nicotine gum. This area of research follows previous studies with smokers and is based on the supposition that reducing withdrawal symptoms helps smokers who are trying to quit. From this perspective nicotine gum appears at least intuitively attractive as a possible contributing factor in smokeless tobacco cessation.

In addition to reducing withdrawal symptoms, several other arguments have been offered in favor of nicotine replacement in smokeless tobacco cessation. Specifically, the rate of absorption of nicotine appears similar in each case (Russell, Jarvis, West, & Feyerabend, 1985) and is dissimilar from the sharp peaks of blood nicotine seen in

smokers. Clearly the route of administration and topography of nicotine gum and smokeless tobacco are closely related. For example, nicotine ingested orally requires the presence of an alkali buffer to alter the acidic pH of the saliva--both nicotine gum and smokeless tobacco are buffered for the maximal absorption of nicotine.

Given the increasing prevalence of smokeless tobacco use and the potentially negative health consequences, there exists a real need for effective treatment investigations. In a recent paper discussing the current status of smokeless research, Hatsukami, Nelson, and Jensen (1991) highlight the need for controlled studies to assess effective regimens These authors suggest that nicotine replacement as a form of treatment appears especially useful. One potential drawback to the use of nicotine gum with smokeless tobacco users is a method verifying abstinence independent of nicotine.

Biochemical Verification of Abstinence

Four main biochemical correlates of smoking behavior are available to verify changes in smoking status: (a) Cotinine in blood, urine, and saliva; (b) thiocyanate (SCN) in blood, urine, and saliva; (c) Carbon Monoxide (CO) in blood or expired air; and (d) nicotine in blood or urine (Kozlowski & Herling, 1988).

Both nicotine and its metabolic byproduct cotinine, are specific to tobacco use, including smokeless tobacco. A large percentage of nicotine is metabolized to cotinine (Benowitz, 1983), and, with a longer half-life, cotinine is generally recommended for measurement purposes. According to Jarvis, Tupstall-Pedoe, Feyeraband, Vesey and Salooje (1987) cotinine measured from saliva, blood or urine is the best indicator of tobacco use, with a sensitivity of 97% and a specificity of 99-100%.

Jacob and Benowitz (1991), at the first International Conference on Smokeless Tobacco, reported their early research examining the tobacco alkaloids anabasine and anatabine. These biochemical markers are detectable in the urine of smokeless tobacco

users in very large amounts compared to levels found when using Nicorette® gum or smoking tobacco. Only trace amounts (< 0.5 ng/ml) of urinary anabasine were found in Nicorette® users. In contrast, levels average 39 ng/ml (range 21-92) in smokeless users. It appears that anabasine and anatabine can differentiate tobacco users from nonusers, even while subjects are exposed to nicotine from Nicorette®.

In summary, this study proposes to test the efficacy of nicotine polacrilex medication (Nicorette®) as a replacement for either oral snuff or chewing tobacco in a cognitive-behavioral treatment program with adult users of smokeless tobacco. In addition, tobacco dependence, perceived stress, and perceptions of personal efficacy will be examined as contributing factors in quitting smokeless tobacco.

CHAPTER III

METHODOLOGY

Introduction

The methodology to test the research questions are described in the four sections of this chapter. The first two sections include the study design and recruitment of subjects, procedures and a description of the study sample. The third and fourth sections elaborate the assessment procedures, measures and how the data analysis was handled.

Design of the Study

This study adopted a design similar to previous tobacco cessation interventions by providing a balanced, double-blind, parallel comparison of two treatment regimens: nicotine gum and a placebo gum containing no nicotine. Subjects were sequentially and randomly assigned to either treatment condition according to a computer-generated randomization code.

Determination of Sample Size

The following discussion is based on information discussed by Fleiss (1981, p. 270), and on several assumptions: (a) as a preliminary study of short duration, the sample size calculation only includes post-treatment abstinence rates and, (b) the quit rate among subjects using nicotine gum is expected to be slightly higher than previous studies with cigarette smokers. The sample size required to detect significant effects assumes a post-treatment abstinence rate of 30% among placebo subjects, and a doubling of this effect to 60% for active drug subjects. In addition, β, the probability of a Type II error is set at 4α,

power, then, becomes, approximately, $1-\beta=1-4\alpha$ (Cohen, 1977). A significant comparison will require 48 subjects per condition to have power of .80 ($\alpha= .05$, two tailed).

Recruitment of Subjects

Active recruitment for volunteers to participate in this study lasted 11 weeks. Advertising to solicit volunteers involved four major media: newspapers, other print (posters & flyers), television, and radio. In addition to newspaper display advertisements, a local daily paper reported the project in a comprehensive news article. Other print media included flyers placed at local worksites and dental offices. Following a press release, a local television station produced a short segment for the late afternoon news. During the final weeks of recruitment several advertising spots were purchased from two local, commercial radio stations

Telephone calls in response to advertising were received by central reception at Oregon Research Institute. A total of 675 calls were recorded during this recruitment phase (see Table 2). Of these calls, less than 20 were second calls or calls from smokers interested in quitting.

Table 2. Weekly Telephone Calls Received During Recruitment

Week	1	2	3	4	5	6	7	8	9	10	11
Calls	42	115	93	35	61	28	50	51	37	137	26
Total (cumulative)		157	250	285	346	374	424	475	512	649	675

Screening Prospective Subjects

Project staff talked to each potential subject within three days of a telephone call being received. In most cases the call was handled as it was received or later that same day. This initial contact both permitted interested callers to learn study specifics and staff to gauge interest and eligibility. Staff were required to use this occasion to verify inclusion and exclusion criteria (see Appendix A) and persons meeting study criteria were given the opportunity to ask detailed questions before committing to a medical screening. Eligible subjects must have used smokeless tobacco for at least one year and daily for the previous three months. Subjects were excluded because of medical conditions such as diabetes, use of hypertensive medication, or ulcers requiring medical treatment.

Medical Screening

Of the 675 calls received, 150 persons were scheduled to attend a medical screening. Within 10 days of the initial call, subjects attended the medical screening. This visit took place once a week, alternating between morning and afternoon times, with all prospective subjects examined by the same physician (Table 3). Eighty percent of the study participants attended the afternoon screening coinciding with the end of their work day. Several appointments were scheduled every 15 minutes. By overscheduling in anticipation of missed appointments and organizing the screening components into four stations (see Table 3), it was possible to screen eight to nine subjects an hour. After completing the informed consent form, each person moved through the collection stations Most subjects were able to pass through all four stations within 45 minutes. Of the 110 people who attended the screening 10 were ineligible to participate. High blood pressure excluded most of these people.

Table 3. Screening Visit Outline

Station	Data collected
1	Informed consent, Contact information- address, emergency contact Other demographic information
2	Medical history Medical check of body systems
3	Vital signs- blood pressure, heart rate, temperature, height, weight Biological samples- urine and saliva
4	Psycho-social measures: perceived stress, cessation confidence

Collection of Specimens

Each subject who completed medical screening provided a sample of urine and saliva, and all subjects completing treatment provided an additional urine sample. The saliva was analyzed only for cotinine, while urine was analyzed for both anabasine and anatabine. Urine specimens were collected then preserved with sodium bisulfate, so that the final pH was 2-3. The final shipping sample measured 30 ml.

Before collecting saliva, subjects were asked to rinse their mouth with water and to refrain from providing sputum. The final shipping sample measured 10 ml. Both specimens were sealed and frozen before being shipped in dry ice for analysis at the Clinical Pharmacology Laboratory at San Francisco General Hospital.

The baseline biochemical measures obtained from the present sample of smokeless users are found in Table 4. In the present study, anabasine and anatabine were highly correlated at baseline (r= .88) and at post treatment (r= .94).

Table 4. Baseline Means of Biochemical Samples (n=100)

	Mean	(SD)	Median	r (with cotinine)
Cotinine (1)	419.7	278.7	376.0	
Anabasine (2)	24.1	30.7	14.0	.54
Anatabine (2)	42.0	51.3	22.2	.53

Notes: (1) Salivary sample ng/ml
(2) Urinary sample ng/ml

To be categorized as a success in treatment a subject must have had: (a) attended all study visit meetings. Exceptions were granted for travel or sickness, (b) reported using no tobacco for the final four weeks of the study, and (c) confirmed abstinence by urinary anabasine and/or anatabine from samples collected at visit 5. The critical cutoff value to confirm abstinence was set at 2.0 ng/ml. If either anatabine or anabasine was below the cutoff, the subject was considered a nonuser. If *both* values were above 2.0 ng/ml abstinence could not be confirmed.

Study Sample

The subjects involved in this study were, by definition, daily users of smokeless tobacco who had made at least one previous attempt to quit tobacco, and had used smokeless tobacco for the last year. The vast majority of the final study sample of 100 subjects lived in the Eugene/Springfield area, however, several traveled from outlying towns including Roseburg and Corvallis.

This sample of smokeless users ranged in age from 18 to 56 (mean=32). Although this sample included three females, the data were contrasted without regard to gender. Additionally, only one subject reported using a brand categorized as chewing tobacco other subjects were users of finely ground moist snuff. They reported using smokeless tobacco for an average of 12 years (range 1-35). Before joining this quitting

program they averaged 11 dips/day (range 4-26) and only one subject reported smoking cigarettes and using smokeless tobacco. Characteristics of previous quit attempts and use of alcohol are presented in Table 5.

Table 5. Baseline Alcohol and Tobacco Use Patterns(n=100)

Question	Answers	Response %
1. How many of your 5 best friends use smokeless	0	25%
	1	22
	2	21
	3	22
	4	8
	5	2
2. Have you ever smoked tobacco regularly	y	37%
	n	63
3. Did you ever smoke while trying to quit smokeless	y	18%
	n	82
4. How many times have you made a serious attempt to quit smokeless	0	41%
	1	30
	2	19
	3	6
	4	1
	5+	3
5. In an average week, how many drinks of alcohol do you have	0	25%
	1	13
	2	13
	3	5
	4	3
	5	3
	6	10
	7	3
	8	4
	9	5
	10+	16
6. In the past month, how many times did you have 5 or more drinks on a single occasion	0	48%
	1	19
	2	11
	3	10
	4	4
	5	8

Intervention Procedure

Within seven days of completing screening, subjects returned to the clinic for their first session. A total of 16 groups of 4-10 subjects completed the treatment program between February and May 1992. Each group was led by two cessation counselors, while large groups were supported by two additional staff members. Supportive group contact ranging from 20 to 60 minutes was provided at visits 1, 2, 3 and 4.

Supportive Group Contact

In addition to the collection and dispensing of medication and daily diary, each clinic visit included supportive group therapy. The group therapy was based on a cognitive-behavioral approach (Pechacek & Danaher, 1979) that guided subjects to view the connections between cognition, affect, and behavior. The treatment technique involved four overlapping phases: education, self-monitoring, coping skills training, and group social support. There were four goals of the education phase: (a) presenting the treatment as credible, (b) increasing subjects' knowledge of smokeless tobacco, (c) providing opportunities for subjects to assess their beliefs, attributions, and coping repertoires, and (d) teaching subjects the best use of the nicotine medication.

Self-monitoring enabled subjects to identify the events that surrounded their use of tobacco, including environmental cues, and the support that existed in their environment for quitting. The coping skills training followed a specific behavioral procedure that involved counselors leading subjects to anticipate potential problem situations and to plan coping strategies for these situations. Specifically, subjects were encouraged to plan for high risk chewing situations by avoiding the situation, altering the situation, choosing alternatives, and/or becoming more physically active. Group sessions centered around active discussion in a fairly structured atmosphere. This format was designed to enhance the support potential of each group. In addition to the group

meetings, subjects were provided with a cessation manual entitled *Enough Snuff* that was specifically written for smokeless tobacco cessation (Severson, 1992).

The structure for meetings followed a consistent format for all groups in the intervention and is summarized in Table 6. For the purposes of evaluation and data management, a three-ring notebook was maintained for every subject who attended a screening visit. All study data were recorded in this notebook.

Table 6. Outline of the Intervention

Screening	Admission criteria, medical history, schedule, consent.
Visit 1 (one day before quit day)	Medication dispensed, use of Nicorette® reviewed
Call 1 (during week 1)	Telephone call within the first 3 days to assess progress.
Visit 2 (end of week 1)	Supportive therapy, medication collected/dispensed.
Call 2 (prior to visit 3)	Reminder call
Visit 3 (end of week 2)	Supportive therapy, medication collected/dispensed
Call 3 (prior to visit 4)	Reminder call
Visit 4 (end of week 4)	Supportive therapy, medication collected/dispensed
Call 4 (prior to visit 5)	Reminder call
Visit 5 (end of week 6)	Collect medication, self-reported quitters biochemical verified Exit interviews and final evaluations

Telephone Contact

Cessation counselors contacted subjects by telephone within three days of their tobacco quit date. The subjects' quit date was to occur on the day following their first treatment visit. Subjects were also contacted prior to each treatment visit to remind them of the time and date of the visit. These calls were made by temporary employees or by cessation counselors.

Dispensing Medication

This study was designed to evaluate the efficacy of Nicorette® (2 mg nicotine) when compared to a placebo for Nicorette® (0 mg nicotine). The medication was provided by the U. S. distributor of Nicorette®, Marion Merill Dow Pharmaceuticals Inc.. Both study formulations were identical in appearance, packaging, and taste. Subjects received a box of medication each week of the study, each box was similar with the exception of a medication number and contained 120 pieces of gum. This was enough medication for eight days using 15 pieces each day. This allowed for any week to have an additional day in case of scheduling conflicts.

Dosing Instructions

All subjects were instructed to use the gum on an continuous basis throughout the day. Based on previous studies with smokers and FDA recommendations, the most relief is experienced by people using between 9 and 15 pieces each day. Subjects in the present study were instructed to follow FDA recommendations and use a target daily dose of 12 pieces, thus allowing for easy and hard days. The schedule of visits and dispensing of medication is outlined in Figure 2.

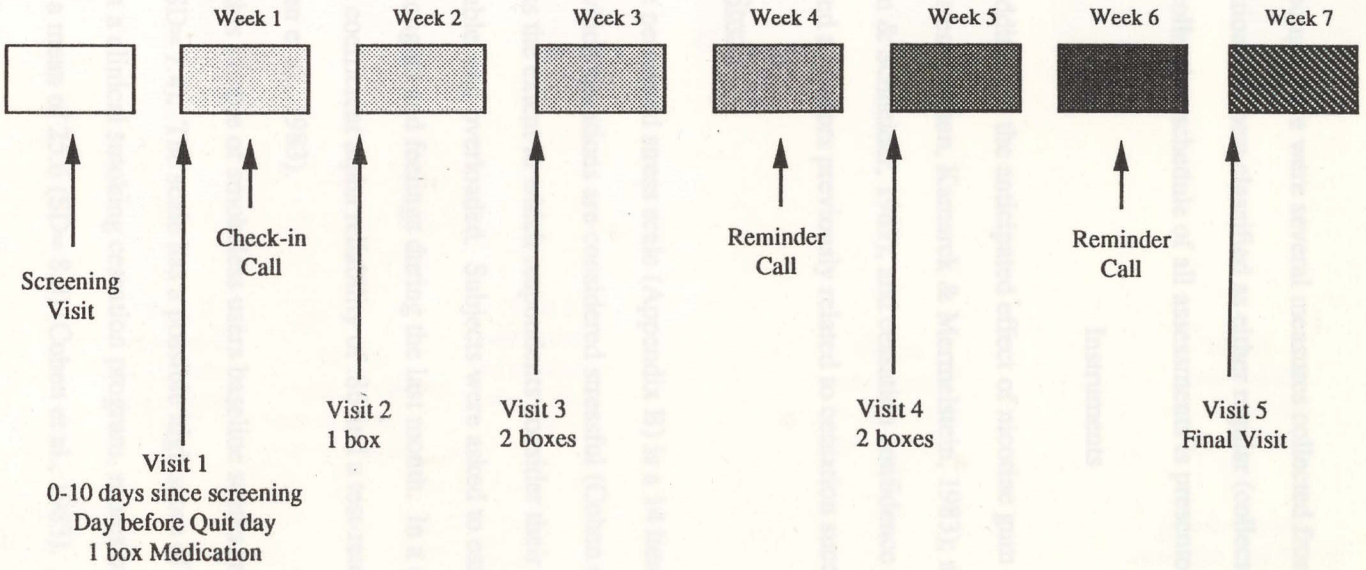

Figure 2. Schedule of Clinic Visits and Dispensing of Medication

Measures

Although there were several measures collected from each subject in this study, the information was best classified as either regular (collected daily or weekly) or pre and post. The collection schedule of all assessments is presented in Figure 3.

Instruments

In addition to the anticipated effect of nicotine gum on treatment outcome, perceived stress (Cohen, Kamarck & Mermelstein, 1983); nicotine dependence (Fagerstrom & Schneider, 1989); and cessation confidence (Baer & Lichtenstein, 1988) were selected as factors previously related to cessation success with samples of smokers.

Perceived Stress

The perceived stress scale (Appendix B) is a 14 item tool designed to measure the degree to which situations are considered stressful (Cohen et al., 1983). Specifically, the items assess the extent to which respondents consider their lives unpredictable, uncontrollable, and overloaded. Subjects were asked to estimate the frequency of stressful thoughts and feelings during the last month. In a college student population, the scale has a coefficient alpha reliability of .86 and a test-retest correlation of .85 after two days (Cohen et al., 1983).

In this sample of smokeless users baseline scores ranged from 2 to 39 with a mean of 20.31 (SD= 7.4). The scale has a possible high score of 56. In a sample of clients involved in a clinical smoking cessation program, scores on the same scale ranged from 7 to 47 with a mean of 25.6 (SD= 8.0) (Cohen et al., 1983).

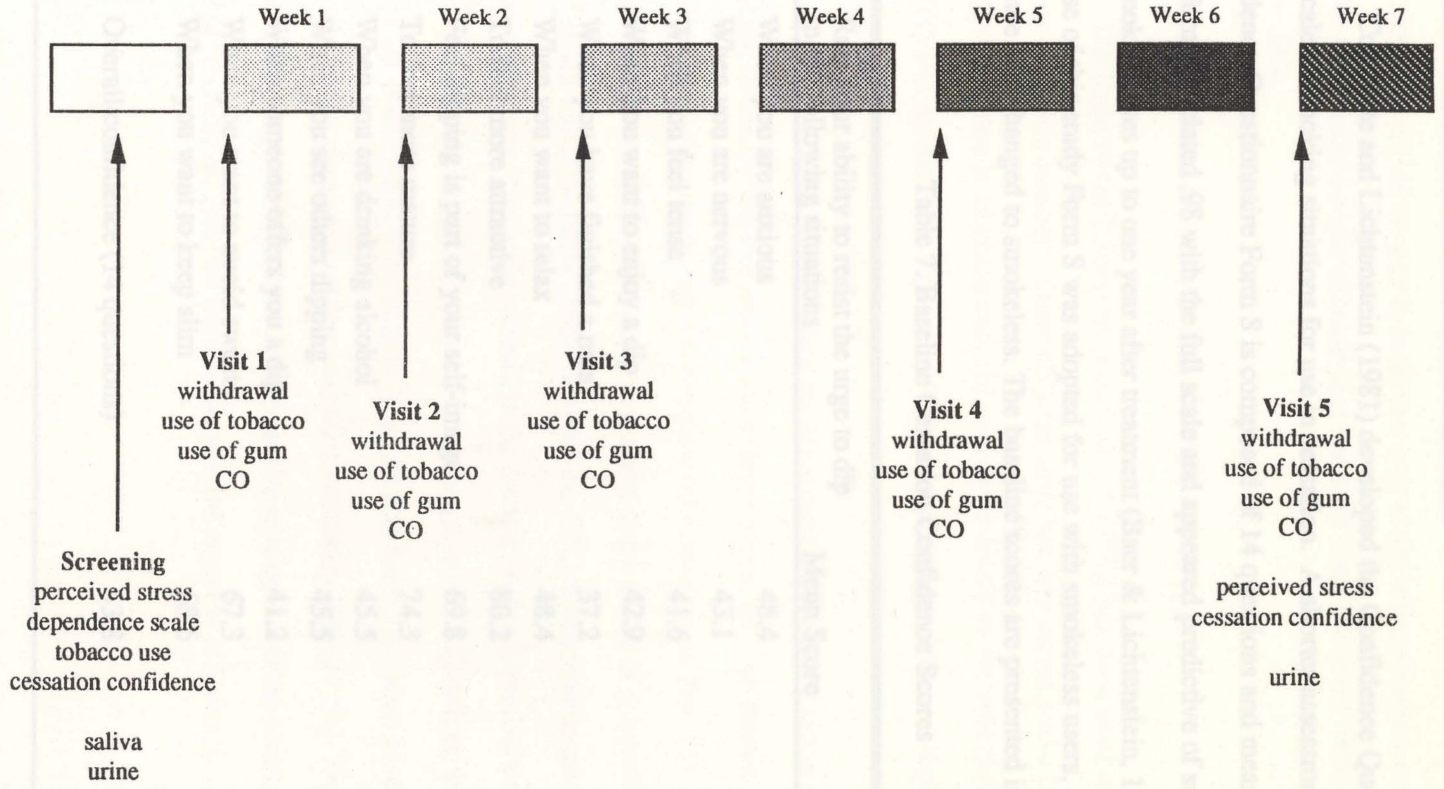

Figure 3. Schedule of Administration of Assessments

Smokeless Tobacco Cessation Self-Efficacy Scale

Condiotte and Lichtenstein (1981) developed the Confidence Questionnaire, a 46-item scale of smoking situations for use in cessation. A shorter assessment tool, the Confidence Questionnaire Form S is composed of 14 questions and mean scores from the short form correlated .98 with the full scale and appeared predictive of smoking status and smoking rates up to one year after treatment (Baer & Lichtenstein, 1988). For the purpose of this study Form S was adopted for use with smokeless users, and the frame of reference was changed to smokeless. The baseline scores are presented in Table 7.

Table 7. Baseline Cessation Confidence Scores

Rate your ability to resist the urge to dip in the following situations	Mean Score	SD
When you are anxious	48.4	27.9
When you are nervous	43.1	29.9
When you feel tense	41.6	29.4
When you want to enjoy a dip	42.9	34.6
When you have finished a meal	37.2	30.2
When you want to relax	48.4	31.1
To feel more attractive	80.2	32.6
Feel dipping is part of your self-image	69.8	34.1
To feel more mature	74.3	35.8
When you are drinking alcohol	45.5	36.3
When you see others dipping	45.5	28.9
When someone offers you a dip	41.2	32.5
When you want to avoid sweets	67.3	35.3
When you want to keep slim	68.6	36.7
Overall confidence (14 questions)	53.8	19.3

The questionnaire asked subjects to rate on a scale from 0% to 100% the probability they would be able to resist the urge to dip if the situation arose (Appendix D). For the present sample of smokeless users the scale has good internal consistency (alpha= .86).

Smokeless Tobacco Dependence Questionnaire

The Fagerstrom Tolerance Questionnaire (FTQ) has been used world-wide in smoking cessation research. Ostensibly the scale has two broad goals: (a) To elucidate the role of nicotine in smoking and, (b) to provide direction for treatment approaches. The FTQ was scored from eight questions A higher score indicated higher nicotine dependence.

Smokeless tobacco users face the same dependency on nicotine as smokers but the pattern of use differences among smokeless users is not well known. Highly dependent smokeless users may behave quite differently from less dependent users and this information could be particularly important at the outset of a cessation effort.

Eakin and colleagues (1989) adopted the FTQ for use with a smokeless tobacco treatment program. The scale utilized in the present study represents a second iteration of Eakin and colleagues original adaptation and consists of 10 questions with a possible high score of 19. With the present sample of smokeless users, the mean score was 6.75 (SD= 1.76). Although the scale had low internal consistency (alpha= .52), the value was similar to the original Fagerstrom questionnaire average reported reliability of .51. The response frequencies from the present sample are reported in Table 8.

Table 8. Items and Scoring for Smokeless Tobacco Dependence Scale

Questions	Answers	Points	Response %
1. After a normal sleeping period, do you use smokeless within 30 minutes of waking	Yes	1	68
	No	0	32
2. Is it difficult for you not to use smokeless where its use would be unsuitable or restricted	Yes	1	53
	No	0	47
3. Do you use smokeless when you are sick or have mouth sores	Yes	1	63
	No	0	37
4. What brand of smokeless do you use*	H	3	56
	M	2	40
	L	1	4
5. How many days does a tin/can last you	<3	3	68
	3-5	2	21
	6-7	1	11
6. On average how many minutes do you keep a fresh dip or chew in your mouth	10-20	3	22
	20-30	2	27
	>30	1	51
7. Do you intentionally swallow tobacco juices	Never	0	33
	Sometimes	1	47
	Always	2	20
8. Do you keep a dip or chew in your mouth almost all the time	Yes	1	61
	No	0	39
9. Do you experience strong cravings for a dip/chew when you go for more than 2 hour without one	Yes	1	91
	No	0	9
10. On average, how many dips/chews do you take each day	1-9	1	39
	10-15	2	46
	15+	3	15

*Note. Scoring for brand question is based on nicotine content. For example: A high (H) brand is Copenhagen, a medium (M) brand is Skoal, and a low (L) brand is Kodiak/Skoal Bandits.

Smokeless Tobacco Symptoms of Withdrawal Scale

Withdrawal effects resulting from smokeless tobacco deprivation have only recently been the focus of research. Keenan, Hatsukami, and Anton (1989) concluded from their work that a syndrome of withdrawal symptoms could be reliably measured when regular users of smokeless tobacco abstain. In addition these signs and symptoms appeared comparable to those observed in samples of cigarette smokers who abstained.

In a most recent study, Hatsukami's research team (1992) confirmed their earlier findings of consistent abstinence effects among regular users of smokeless tobacco. The work from their clinic was based on multiple measures intended to elucidate the extent of an abstinence effect.

For the purposes of the present research, a single scale was developed based on the Diagnostic and Statistical Manual Of Mental Disorders (3rd edition, revised) classification of tobacco withdrawal. Each subject evaluated the following symptoms daily using a 100 millimeter visual analog scale: craving for tobacco, irritability, frustration, anger, anxiety, difficulty concentrating, and restlessness.

No baseline symptoms of tobacco withdrawal were examined, rather symptoms of self-reported severity were recorded daily beginning with the first quit day. The analysis of withdrawal included only those subjects who completed treatment (n=77). Weekly means of the withdrawal symptoms were calculated for the nicotine gum and the placebo gum conditions, in addition a total withdrawal score was calculated by summing the daily scores for each symptom. Weekly means were utilized in an attempt to adjust for daily fluctuations in individual responses.

Tobacco Use Status

All one hundred subjects who attended the first visit and received medication were included in the outcome analysis. Use of tobacco was recorded daily by each subject, and the self-report non-use of smoking tobacco was verified by a concentration of carbon monoxide (CO) of 10 ppm or less in expired air. Abstinence success was defined as no use of any tobacco on visits 4 and 5, that is, the final four weeks of the six week study. Self-reported smokeless tobacco abstinence at the completion of the intervention was verified by a concentration of urinary anabasine or anatabine of less than 2.00 ng/ml.

Data Analysis

For the purposes of testing this study design and answering the research questions, the data analyses included descriptive statistics, as well as primary and secondary analyses of cessation outcome.

Descriptive Statistics

The purpose of the descriptive statistics was to compare the active gum group and placebo gum group on the following pretest measures: age, perceived stress, years of smokeless tobacco use, age of first smokeless tobacco use, number of best friends who use, use of other tobacco, use of alcohol, previous quit attempts, tobacco dependence, and quitting confidence.

Primary Analysis

The primary objective of this study was to compare the two treatment groups on four week abstinence rates. Continuous measures were analyzed using analysis of variance (ANOVA), while categorical measures were analyzed using Chi-square statistic. The primary analysis focuses on the leading research question:

1. Does the replacement of nicotine for smokeless tobacco improve rates of abstinence? The variable measured was use of tobacco categorized as user/nonuser, and the variable of interest was treatment condition--placebo gum or nicotine gum. Subjects who dropped out of the study were counted as users.

Secondary Analysis

The intention of the secondary analysis was to answer the additional research questions:

2. Is the degree of dependence related to cessation success?

Baseline values of cotinine and the dependence scale were analyzed in a logistic regression model that included the treatment group assignment.

3. Is quitting confidence related to cessation success?

4. Is level of perceived stress a factor in cessation success?

The total scores from the perceived stress scale and the self-efficacy scale at baseline were compared. Logistic regression SAS LOGISTIC was used to analyze a set of psychosocial predictors on cessation outcome. In addition to stress and confidence, age, and years of use were included in this backward elimination model.

5. Does nicotine replacement affect tobacco withdrawal symptoms?

The weekly mean for each symptom was computed and used in an analysis of covariance procedure, SAS GLM, with the gum condition and subject within gum condition entered as dependent variables and cotinine at baseline entered as a covariate.

6. Does the number of pieces of gum used daily affect cessation outcome?

A General Linear Models procedure through SAS GLM compared the mean number of pieces of gum used weekly by each treatment condition.

CHAPTER IV

RESULTS

In this chapter the results of the randomized intervention are reported. In the first section the treatment groups are compared at baseline and an attrition analysis is conducted. Each of the research questions are then considered with the presentation of analysis and results.

Treatment Groups Compared at Baseline

A total of 100 subjects were assigned to either a nicotine gum or placebo gum condition. Prior to beginning the intervention, the subjects in the two treatment conditions were essentially similar on all baseline measures (Table 9) with the exception of their pretreatment cotinine levels. Subjects in the nicotine gum condition had mean cotinine levels 124 ng/ml higher than the placebo condition, t=2.27, p=0.025.

The cotinine values in the placebo group ranged from 42 to 1010 ng/ml with a mean of 357 ng/ml. The range for subjects receiving nicotine gum was 73 to 1450 ng/ml and a mean of 481 ng/ml. Based on the median cotinine scores of 415 for nicotine gum and 316 for placebo gum, both distributions appear positively skewed. However, as a group, subjects receiving nicotine gum had generally higher levels of cotinine before beginning the study. Allowing for differences in individual rates of elimination, and assuming that cotinine reflects exposure to nicotine in the previous 48 to 72 hours (Benowitz & Jacob, 1984), these subjects appear to have been exposed to more tobacco than subjects in the placebo group. A significant difference of this magnitude raises practical comparison issues and necessitates controlling for the baseline cotinine levels.

Table 9. Mean (SD) of Pretreatment Characteristics

Characteristic	Treatment Condition Nicotine Gum	Placebo Gum
Age	32.2 (10.0)	32.2 (11.0)
Cotinine (ng/ml)	481.8 (310.5)	357.7 (229.7) *
Addiction Scale	12.7 (2.13)	12.9 (2.7)
Smokeless use (years)	12.2 (7.6)	12.1 (6.8)
Dips/ day	11.2 (5.2)	11.4 (5.4)
How long a can lasts (days)	2.6 (1.9)	2.5 (1.6)
Alcohol/ week (drinks)	4.1 (4.0)	3.9 (3.5)
Quit Attempts	1.2 (1.2)	0.9 (1.1)
Best friends who use	1.8 (1.3)	1.7 (1.4)

* $p < .05$

Attrition Analysis

Twenty three subjects did not complete treatment; of these 13 were from the nicotine gum condition. Subjects who dropped out of the study were categorized into four groups. Two subjects left the study because of adverse events related to gum use; there was no common complaint, headaches bothered one subject and gastrointestinal distress affected the other. Another two left specifically to quit on their own, while four dropped out because of family or personal reasons The remaining subjects (n=15) lost contact with research staff; about half of this group were students. Based on this analysis, no differential attrition within or between groups was detected. For the purposes of calculating quit rates, subjects who dropped out were not considered abstinent.

Descriptive analyses were conducted involving all study variables obtained at baseline to compare subjects who completed treatment (n=77) with subjects who did not finish treatment (n=23). Subjects who dropped out were on average five years younger and scored higher on the smokeless tobacco addiction scale, in particular they

experienced difficulty not using tobacco when (a) its use was unsuitable (e.g. religious service) and, (b) when sores were present in their mouth (Table 10). Although subjects who dropped out scored higher on the addiction scale, their mean cotinine level was not significantly higher.

Table 10. Significant Mean (SD) Differences Between Subjects Who Dropped Out and Subjects Who Completed Treatment

		Status			
	Variable	Dropped Out	Completed Tx	*T*	*P*
	Age	27.0 (9.8)	33.0 (10.4)	-2.38	0.02
*	Mouth sores	0.82 (0.4)	0.57 (0.5)	2.25	0.02
*	Use unsuitable	0.74 (0.5)	0.47 (0.5)	2.32	0.02
	Addiction Score	13.7 (2.6)	12.5 (2.3)	2.02	0.05

* Score of 1= difficult not to use tobacco

Primary Analysis

The primary analysis involved the planned comparison of between-group quit rates and included the one hundred subjects who entered the study.

Research Question 1

Does the replacement of nicotine for smokeless tobacco improve rates of quitting when comparing nicotine gum to placebo gum?

At the end of the six week intervention there was no significant difference between treatment conditions Fifty percent (25/50) of the subjects in the nicotine gum condition were verified abstinent and 40 percent (20/50) of the subjects receiving placebo gum were verified abstinent (Table 11).

Table 11. Effects of Treatment on Abstinence (n=100)

Condition	Study Status at Six weeks (%) Abstainer	User
Nicotine Gum	25	25
Placebo Gum	20	30
	45%	55%

Chi-Square (1) = 1.01, p= .315

Secondary Analyses

Research Question 2

Is the degree of dependence related to cessation success? Dependence on tobacco was assessed by two measures--baseline cotinine and the smokeless tobacco dependence scale (Appendix C). Mean scores from the addiction scale correlated .26 with cotinine levels. Both of these measures were entered into a model in an attempt to predict tobacco abstinence. A Logistic regression analysis was conducted with the treatment condition (active gum or placebo) included in the analysis. Prior dependence on tobacco was not a factor in abstinence at the end of the 6 week cessation program: neither baseline cotinine levels nor the dependence scale scores were significant predictors of abstinence (Table 12). Although the effect of treatment was not significant, the resulting odds ratio (.51) suggests an effect in favor of the active gum condition.

An additional analysis was conducted to determine if individual items from the dependence scale could predict successful quitters from non-quitters. A backward elimination logistic regression was used (these variables are described in Appendix F). This analysis yielded only one significant predictor, Chi-square (1) = 4.93, p = .03,

subjects who quit were more likely to intentionally swallow the tobacco juices (Mean=1.04, SD=0.80) than subjects still using tobacco (Mean=0.65, SD=0.6).

Table 12. Predicting Abstinence From Baseline Dependence (n=75)

Analysis of Maximum Likelihood Estimates					
Variable	DF	Parameter Estimate	Wald Chi-Square	p	Odds Ratio
Cotinine	1	-0.0005	0.44	0.50	0.99
Tx Group	1	-0.67	2.00	0.15	0.51
Addiction scale	1	-0.04	0.18	0.67	0.95

Coding: 0= abstinent 1= non abstinent

Research Questions 3 and 4

Is quitting confidence related to cessation success? Is level of perceived stress a factor in cessation success? Research questions three and four were considered together as part of a model examining quitting success.

In an attempt to predict cessation status, a group of psychosocial variables were analyzed. Based on the bivariate analysis (Table 13), age was highly correlated with years of smokeless tobacco use, this was not a particularly surprising finding. No other significant correlations were found.

The regression model included age, years of use, baseline confidence and stress. Again, backward elimination was the method chosen and treatment assignment--placebo or nicotine gum was included in the model. Age was the only statistically significant predictor of successful cessation, Chi-square (1)= 6.16, $p < .01$. That is, the mean age of subjects who quit smokeless tobacco was 36 years compared to 30 years for subjects still using tobacco.

Table 13. Correlation Matrix of Psychosocial Predictors

	Years of Use	Perceived Stress Scale	Quitting Confidence
Age	.66 *	-.024	-.15
Years		-.15	.066
PSS			-.12

* $p < .0001$

Research Question 5

Does the use of gum containing nicotine affect the frequency and severity of tobacco withdrawal symptoms during smokeless tobacco cessation?

Symptoms of withdrawal were analyzed individually and adjusted for the baseline differences in cotinine. The weekly means for all withdrawal symptoms are listed in Appendix E. There were significant effects ($p < 0.05$) for the gum condition on two items: anxiety and anger. Post hoc analysis revealed significant group differences only at week four for both of these symptoms. Figures 4 and 5 illustrate the pattern of change over time, with the placebo group scores starting higher on both instances and remaining higher for the duration of the study. One other item, total withdrawal score showed a tendency toward significance ($p < 0.08$). For this item the presence of anger and anxiety influenced the effect.

An additional analysis was conducted to determine if tobacco quitters experienced less withdrawal symptoms. The weekly means of each withdrawal item were analyzed with the outcome variable: use of tobacco. A significant effect for abstinence was found for one symptom, craving. This item separated quitters from non-quitters during each week of treatment. Subjects who remained abstinent from tobacco had significantly less craving during each week of the study.

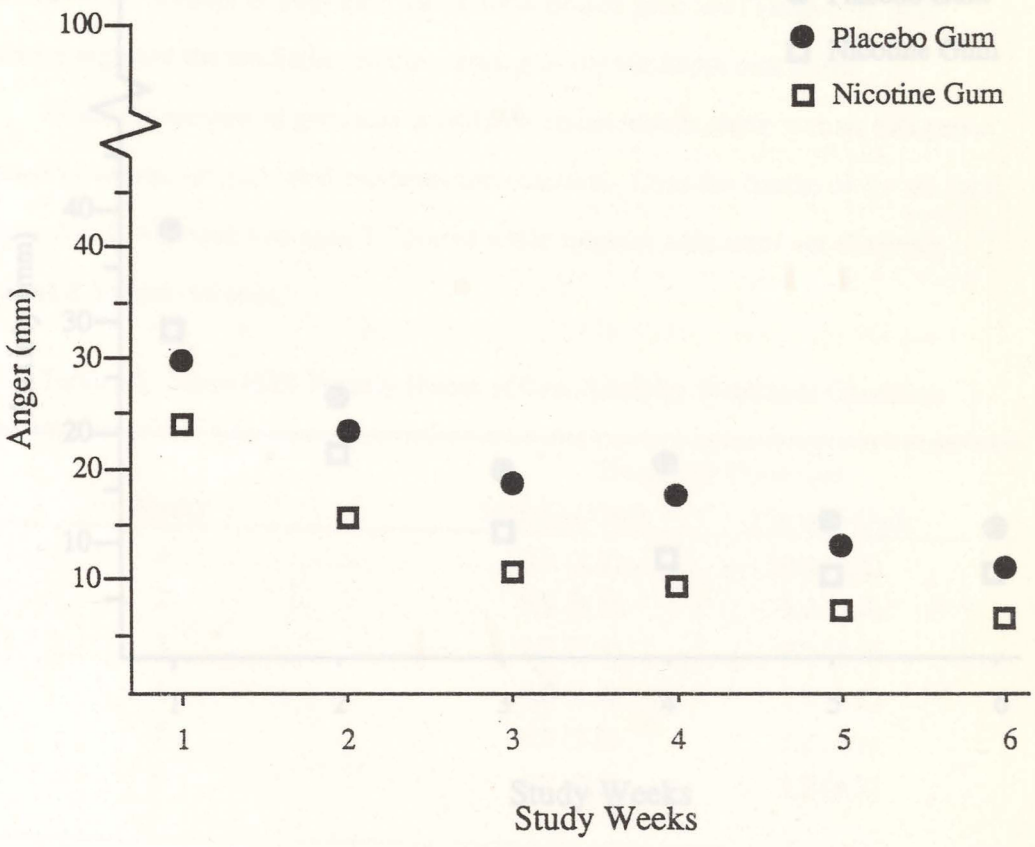

Figure 4. Mean Weekly Anger Scores For Nicotine and Placebo Gum

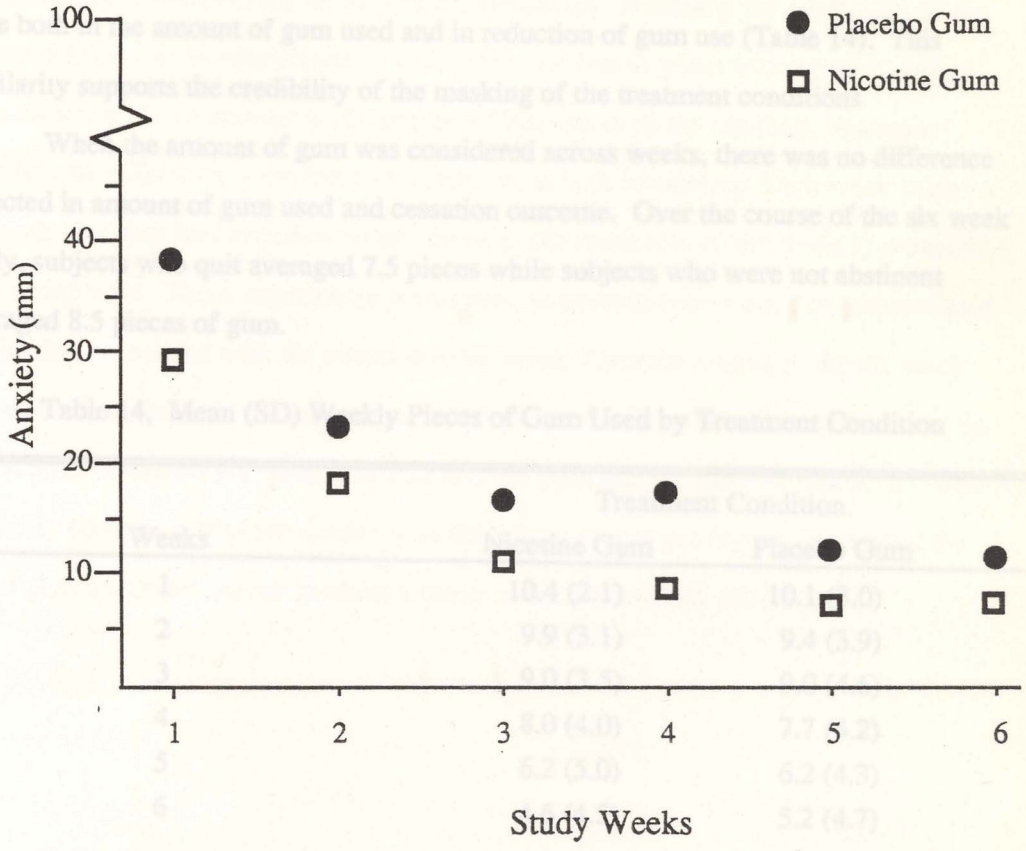

Figure 5. Mean Weekly Anxiety Scores For Nicotine and Placebo Gum

Research Question 6

Does the number of pieces of gum used affect cessation outcome? The anticipation was that gum use would be related to success in quitting either as a function of the presence of nicotine or as a consequence of experiencing less withdrawal.

The subjects in each treatment condition reported a surprisingly similar trend over time both in the amount of gum used and in reduction of gum use (Table 14). This similarity supports the credibility of the masking of the treatment conditions

When the amount of gum was considered across weeks, there was no difference detected in amount of gum used and cessation outcome. Over the course of the six week study, subjects who quit averaged 7.5 pieces while subjects who were not abstinent averaged 8.5 pieces of gum.

Table 14. Mean (SD) Weekly Pieces of Gum Used by Treatment Condition

	Treatment Condition	
Weeks	Nicotine Gum	Placebo Gum
1	10.4 (2.1)	10.1 (3.0)
2	9.9 (3.1)	9.4 (3.9)
3	9.0 (3.5)	9.0 (4.6)
4	8.0 (4.0)	7.7 (4.2)
5	6.2 (5.0)	6.2 (4.3)
6	4.6 (4.5)	5.2 (4.7)

Given the significant differences in baseline cotinine levels, an additional analysis was conducted to determine if cotinine levels played a role in gum dose. Subjects were divided into those with high and low cotinine levels based on the median cotinine detected within the nicotine gum group (<415 vs ≥415 ng/ml). During weeks 1, 2, 3, & 5

the group means were significantly different (p <0.03), with the higher cotinine group using on average two additional pieces of gum.

Credibility Analysis

No formal analysis was performed to assess the influence of expectancy of gum effects on cessation outcome or withdrawal symptoms. Normally the credibility of the gum condition can be determined by asking the subjects to guess which gum they had been chewing. In an attempt to discern the effectiveness of the blinding, treatment-specific side-effects were compared for subjects in both conditions Each week subjects were asked if they had experienced any unusual circumstances in the week(s) proceeding their group visit. These experiences were noted as adverse events and any concomitant medication associated with the events was recorded. Over the course of the six week intervention, subjects in each condition reported a similar number of adverse events; in the nicotine condition the mean was 3.22 and the mean for the placebo was 3.18 . This similarity combined with the similarity in dose (gum pieces per day) suggests that the active gum treatment did not produce a threat to the randomized blinding.

CHAPTER V

DISCUSSION AND CONCLUSION

Introduction

The intent of this final chapter is to summarize the findings of the study, discuss these findings with respect to the wider body of knowledge dealing with tobacco cessation, and to place this study in the context of the public health perspective. Of particular interest is the role cessation should play in the long term view of improving health through tobacco abatement.

Lack of Nicotine Gum Effect

This research study represented one of the first well-controlled interventions of smokeless tobacco cessation with nicotine replacement. One hundred motivated, long-term daily users of smokeless tobacco were involved in a cognitive behavioral cessation program with an oral substitute. Subjects were asked to replace their smokeless tobacco (99% used moist snuff) using active or placebo nicotine gum as an oral medication. Of the 45 subjects who were verified abstinent at the end of the six week intervention, 20 received a placebo (0.0 mg) nicotine gum and the other 25 subjects received active nicotine gum (2.0 mg).

Placebo-controlled studies with smoking cessation have shown a trend toward a nicotine gum effect, although the effect was large enough to be statistically significant in only half of these studies (Fagerstrom, 1988). Overall, the presence of nicotine gum has increased long-term (6 or 12-month) success rates by an average of 70% in smoking cessation studies.

The end of treatment quit rates are quite modest when compared to previous placebo controlled treatment studies with cigarette smokers that included behavioral counseling. Each of the studies in Table 15 verified abstinence at the end of treatment and included behavioral counseling in a cessation clinic. While the end of treatment abstinence rate among subjects receiving placebo gum was comparable, abstinence among subjects receiving nicotine gum was considerably lower.

Table 15. End of Treatment Quit Rates (%) in Placebo-Controlled Smoking Cessation Studies

Study	Nicotine Gum	Placebo Gum
Fagerstrom (1982)	90	60
Schneider et al. (1983)	73	50
Hjalmarson (1984)	77	52
Hall et al. (1987)	74	68

In the present study of smokeless tobacco cessation, the relative difference for success of active gum over placebo gum following six weeks of treatment was 25%. This difference is considerably less than the anticipated effect. Indeed, the sample size calculation was based on a doubling of the gum effect. Unfortunately the sample size calculation made no provision for attrition and nearly a quarter of the sample (23%) did not finish the program. Of the subjects who completed treatment, 58% were verified abstinent. The subjects who completed treatment were older (5 years on average), experienced less difficulty not using tobacco under certain circumstances, e.g. when sores were present in their mouth, or in situations where smokeless use was unsuitable (e.g. a religious service), and scored lower on the smokeless tobacco addiction questionnaire.

Knowledge of the differences between completers and subjects who drop out is potentially useful for future planning.

The two best predictors of abstinence at the end of treatment were addiction, as measured by one item on the dependence scale, and age. Subjects who quit were older and reported swallowing tobacco juices more often than subjects who could not quit after six weeks. Abstinence was not related to measures of perceived stress or confidence in being able to quit as measured with a self-efficacy scale. The lack of an association between efficacy measured prior to treatment and treatment success was not surprising in light of previous research examining smokers (Condiotte & Lichtenstein, 1981; McIntyre, Lichtenstein, & Mermelstein, 1983). End of treatment efficacy ratings were significantly higher for subjects who were abstinent. Of particular importance is the extent to which these ratings contribute to the prediction of future behavior (tobacco use status) as has been demonstrated previously (Condiotte & Lichtenstein, 1981; Coelho, 1984). A contrasting view has been presented by Borovec (1978). He suggested that ratings of confidence were merely a reflection of behavioral attainment. Baer, Holt, and Lichtenstein (1986), however, have demonstrated that ratings of confidence retain a unique position in behavior prediction, at least when percent of baseline smoking rate was the measure of performance. The utility of end of treatment confidence will be appraised by follow-up research with subjects in this study.

Nicotine gum as an oral and pharmacological substitute was expected to act as a powerful contributor to tobacco abstinence for users of smokeless tobacco. There are three possible reasons why nicotine gum did not help more of the smokeless users quit.

Subjects May Not Have Used Enough Gum

Smokers average 8 to 10 pieces of 2 mg nicotine gum per day while attempting to quit tobacco (Russell, 1988). At this dose, blood nicotine concentrations average a

quarter or less of levels found during smoking. The inability of nicotine gum to replicate the bolus effect of nicotine delivered by cigarettes is offered as one explanation for the low gum use by cigarette smokers.

During the first week of this study, subjects in both conditions averaged 10 pieces of gum per day with a range of 5 to 16 pieces. By the end of the second week amounts varied by only one half of a piece. An average of 10 pieces suggests a potentially effective concentration range, that is, people using this amount of active 2 mg gum could be expected to experience some relief from nicotine withdrawal. It was somewhat surprising that the chewers in this study did not use more of the gum. Given the similarity in absorption pattern between smokeless tobacco and nicotine gum, greater dosing, beyond what smokers have been known to use, was anticipated. However, although nicotine gum tends to mimic the gradual rise in blood nicotine levels observed in smokeless tobacco users, the gum does not match the peak blood nicotine levels of either chewers or dippers (Benowitz, Porchet, Sheiner, & Jacob, 1988; Russell et al., 1985). In addition, while peak blood levels of nicotine are similar between smokeless tobacco and cigarettes, the amount of nicotine absorbed is twice as great from smokeless tobacco compared to cigarettes (Benowitz et al., 1988). The average of 10 pieces during the first two weeks taken by the nicotine gum group would appear, then, to have been inadequate given their high baseline cotinine levels.

Subjects May Have Used the Gum Incorrectly

The study was double blinded and none of the investigators or staff had access to the codification of subjects. In essence, all subjects were treated in a similar manner for the duration of the study. During the first treatment visit, priority was given to the discussion of best use of the gum. In addition to written and verbal instructions, subjects practiced with a piece of gum from their first box. Instructions for use of the gum were

also printed on the inside cover of the diary booklet. All staff involved with subjects were trained and observed the group process prior to becoming involved. A part of each group visit involved individual and group discussion about the gum and its use. Yet, as most of this study took place with the subject using the medication on their own, there was little or no control over proper use of the medication. This is to be expected as the product is intended for personal use by prescription. Since both groups used an identical product (except for the presence of active medication) incorrect use of the gum does not appear to have played a role in the modest quit rate among nicotine gum subjects.

Nicotine Gum May Not Have Relieved the Urge For Tobacco

One expected outcome of smokeless abstinence was an increased use of other tobacco products as sources of nicotine. Anecdotal information from this study suggests that only subjects with a previous history of using cigarettes began smoking tobacco again in response to stopping smokeless. All subjects who quit were verified abstinent from smoking with weekly carbon monoxide monitoring.

The more interesting observation is that the subjects in the placebo condition did not need the nicotine in the gum. This scenario is accurate if there is a placebo effect. This study followed a traditional double-blind placebo design, wherein a subject received medication without information on its content, and instructions on use were given as if all medication contained nicotine. The placebo effect is a strong possibility given the earlier discussion surrounding the peak blood nicotine experienced by smokeless users and the significantly less cotinine levels present in subjects receiving placebo gum. In essence, 2 mg nicotine gum may not have been enough of a dose to compensate for reduced nicotine experienced during abstinence.

Smokeless Tobacco Withdrawal Effects

The use of nicotine gum to alleviate tobacco withdrawal syndrome followed earlier work (Hatsukami, Hughes, Pickens, & Svikis, 1984; Shiffman & Jarvik, 1976) that identified the presence of withdrawal symptoms following tobacco abstinence. Numerous consistent findings have since generally supported the role of nicotine gum in suppressing withdrawal symptoms. The presence of similar withdrawal symptoms following smokeless tobacco abstinence has only recently been the focus of intense research.

In the late 1970s, at a time in which increased use of smokeless tobacco products was beginning to be documented initial research reports indicated that physical dependence was a consequence of smokeless tobacco use. Morse, Norvich, and Graf (1977) described the case history of a male patient at the Mayo Clinic who requested help for his compulsive use of chewing tobacco. The most striking aspects of his tobacco use were the symptoms he experienced when trying to quit--these included sleeplessness, anxiety, nausea, and headaches. His use of tobacco was reinforced negatively, such that he structured his life to avoid all likelihood of experiencing tobacco withdrawal symptoms.

Some ten years later a team of researchers led by Dorothy Hatsukami conducted a study looking specifically at the existence of smokeless tobacco withdrawal symptoms. The chewers in this study could best be categorized as light to moderate users, using an average of two tins of smokeless tobacco each week. The researchers concluded that while smokeless tobacco withdrawal existed, it was less severe than the symptoms experienced in a parallel group withdrawing from cigarettes (Hatsukami, Gust, & Keenan, 1987).

Deprivation from smokeless tobacco was examined with respect to performance in the same research laboratory (Keenan, Hatsukami, & Anton, 1989). Again the subjects

in this study were light to moderate users who had chewed for an average of four and a half years. From this study the changes associated with deprivation included increased craving, reaction time, and self-rated withdrawal. These were similar to results reported by Hatsukami et al. (1987), and the signs and symptoms appear comparable to those found with cigarette deprivation.

In a more recent paper, Hatsukami and colleagues (1992) report on the effects of nicotine gum on smokeless tobacco abstinence effects. In the first of two experiments, several withdrawal symptoms were identified during abstinence from smokeless tobacco, these included--craving, difficulty concentrating, restlessness, excessive hunger, increased eating and increased total withdrawal score. In the second experiment comparing nicotine gum effects on symptoms of abstinence, nicotine gum appeared only to have an effect on craving for smokeless tobacco among users with high cotinine levels when compared to users with low cotinine levels. The results from this second experiment suggested that nicotine gum was not able to significantly reduce short term smokeless tobacco withdrawal symptoms, however, the authors noted the potential for nicotine gum to play a role in cessation and suggested that future research should assess nicotine gum effects on smokeless cessation.

In the present study, nicotine gum containing 2 mg of nicotine was compared to a placebo gum containing 0 mg of nicotine. After adjusting for baseline cotinine, subjects receiving nicotine gum reported less withdrawal symptomatology--they felt less anxious and reported fewer feelings of anger than did subjects receiving placebo gum. This significant difference occurred only during week four of the six week intervention. While Hatsukami et al., (1992) reported less craving for smokeless tobacco among subjects with high cotinine using nicotine gum, in the present study craving was not significantly lower in subjects using nicotine gum.

There were no other between-group differences for the other items (frustration, difficulty concentrating, restlessness, and irritability) measured as a part of this study. The pattern of changes over time, however, were stable: item scores declined weekly for each symptom under both conditions Although not significant and arguably less meaningful, scores for the placebo condition were consistently higher for each symptom and remained higher throughout the intervention.

It is interesting to note that subjects in the two conditions averaged a similar number of pieces of gum during each week of the study, suggesting the placebo gum was being used as an oral substitute when one might have expected less use among the placebo group. The top three symptoms of abstinence during the first week of the present study were craving, restlessness and irritability, this finding parallels the work of Hatsukami and colleagues (1992). Unfortunately, there was no similarity in symptom measurement to permit a comparison of magnitude.

Keenan et al. (1989), however, did use a similarly scaled (100 mm) line to measure craving during a 24 hour abstinence study. They reported a mean for craving of 72 mm with no oral substitute, in comparison, subjects in this study receiving placebo gum reported a mean of 69 mm for craving for the first day. Subjects receiving nicotine gum reported a mean of 61 mm for craving during the first day.

General Observations From This Study

Although no significant effect was found in favor of gum containing nicotine, there were several interesting observations that have immediate implication for smokeless tobacco cessation: Smokeless tobacco users are interested in quitting, and they appear interested in using nicotine gum, but although they appear willing to remain within the protocol guidelines, they may not use large amounts of the gum.

Strong evidence exists from this study that smokeless tobacco users appear to have a desire to quit. Almost 700 telephone calls were received in response to recruitment efforts, and while not all callers were eligible to participate, at least 90% were adult smokeless tobacco users with varying degrees of readiness to change--somewhere between contemplation and action. The sheer number of calls in response to modest advertising efforts reflects either well placed ads. or a heightened interest in stopping use of smokeless tobacco.

People who called in response to the study were interested both in quitting and in using nicotine gum. All subject recruitment notices provided information about the study involving nicotine replacement and very few callers were disappointed to learn they would be replacing their tobacco with gum based medication--time commitments, motivational deposit, and medical contraindications were more commonly cited. Based on the average amount of gum used over six weeks (nicotine gum 48 pieces vs 47.5 pieces for the placebo) smokeless users appear willing to substitute their tobacco for gum based medication, but they will not use large amounts. One possible research extension based on this finding is a comparison of a fixed schedule of gum use compared to the ad lib protocol followed here.

Perhaps one of the most interesting observations from this intervention was the influence of counseling on the quit rates. Although the design did not permit an analysis of the effect of counseling, the attention participants received appeared to be a factor in the cessation process. The study protocol included individual, small group, and large group interactions between counselors and participants during each study meeting. Within this format, participants also had opportunities to interact with each other. Indeed the large group meeting was designed to promote discussion. Many of the participants commented on the uniqueness of this situation--a group cessation program for chewers. The group meetings were highly interactive, and many subjects commented on the

similarity of their experiences. The counseling effect, then, was the net result of both a specific behavioral procedure and the opportunity for subjects to hear and exchange information about smokeless tobacco, addiction, and the quitting process. This experience, or something similar, is recognized as a necessary component of cessation with nicotine replacement.

Further Research Based On This Study

Beyond the immediate observations from this research, there are some considerations that should guide future research in the area of smokeless tobacco cessation. The most immediate concern involves the necessity of conducting follow-up assessments with the sample of smokeless tobacco users involved in this study. This would provide a more complete assessment of changes over time. An additional study is currently underway with follow-up assessments at 3, 6, and 12 months post treatment. The outcome variables are to be reported as point-prevalence--verified abstinence during the past week, and continuous abstinence since treatment termination. Although all of the intervention strategies were aimed at initial quitting, an examination of relapse episodes will be included to provide useful information about the situations most associated with relapse in smokeless tobacco users as well as information relating to the relapse curve. This study will add substantial information to the knowledge base of the long-term effects of nicotine replacement on smokeless tobacco cessation.

Another consideration based on this study is the sample size of future cessation studies. In this investigation, the failure to find a significant difference may be attributed to the small sample size and large attrition rate. Sample size is a particular concern because of the dichotomous nature of quitting: abstinence or nonabstinence. This suggests that the sample size must be large enough to detect small differences. With

differences of this magnitude only larger sample sizes could provide enough power to detect differences.

In addition to considerations of sample size, further studies should consider the relative amount of nicotine available in the 2 mg formulation. Benowitz et al. (1988) reported peak nicotine concentrations after using moist snuff to be twice that found when compared to nicotine gum. If smokeless tobacco users average eight pieces of gum per day during cessation, then relief from nicotine withdrawal could be tempered by doubling the strength of the gum. The availability and use of 4 mg gum as part of treatment could help heavy users--operationally defined by cotinine level, addiction scale score and/or use pattern. While this has appeal from a pharmacological perspective, and has support from smoking research (Tonnenson et al, 1988) the practical assessment of such an approach requires investigation.

Perhaps the most interesting question still remains, what role did the behavioral counseling play over and above the effect of the gum-based medication? The present study design did not allowing a separation of treatment effects--gum versus counseling. Future research should examine the effect of gum with low versus high counselor contact. Such a study could assess the relative role of counseling required for successful abstinence using nicotine gum.

Future Smokeless Tobacco Interventions

By many measures, reduction in tobacco use may have more to do with education, price, restrictions on promotion, and limitations on exposure to smoke than on treatment approaches. At the same time, nicotine replacement is expensive and has the potential to reach only a small proportion of eligible users. In addition it is often delivered incorrectly by health care providers, resulting in far less than optimal use. Therefore, given the results of this study and the general body of knowledge that is smokeless

tobacco, future research should follow the recent trend in smoking cessation and include all aspects of the clinical-public health continuum: from multisession clinical interventions to broad based community interventions (Lichtenstein & Glasgow, 1992). Intensive clinic interventions focusing on smokeless cessation with small groups or individuals are necessary to satisfy: (a) the needs of individuals suffering chronic oral diseases, such as premalignant and malignant neoplasms in the oral cavity; and (b) highly dependent users who are experiencing difficulty quitting.

The inherent problems with multisession interventions of a clinical nature include high cost and low participation rate. Although there were a large number of calls received as a part of recruitment for this study, a public health intervention would allow more of the smokeless tobacco users interested in quitting to receive assistance. This perspective is supported by reports indicating that most cigarette smokers are interested in quitting on their own (Fiore et al., 1990), and many who quit do so without formal assistance (Glynn, Boyd, & Gruman, 1990).

The recent study of smokeless tobacco cessation through a minimal intervention was completed as a doctoral dissertation. Williams (1992) reported a 3-month quit rate of 12.3% following completion of a self-help program that compared either two or four session contacts with smokeless users who were enrolled in post-secondary education programs. There was no difference in quit rates for subjects in either high or low contact situation. This research sets the stage for future adaptations of minimal intervention with smokeless users.

Another channel for minimal assistance interventions includes health care providers delivering tobacco quitting messages. Studies with cigarette smokers receiving advice from health care professionals have resulted in significant impacts (Glynn, Manley, & Pechacek, 1991; Vogt et al., 1989). Walters (1991) suggested there were three key areas for physician involvement in smoking abatement: (a) supporting anti-

tobacco policy initiatives, (b) personal involvement at the community level through educational outreach, and (c) sending tobacco prevention messages and offering cessation help for their patients.

In the context of smokeless tobacco, oral healthcare visits offer an opportunity for dentists and dental hygienists to provide advice on smokeless tobacco use and quitting. The oral healthcare setting affords a unique perspective for the patient who can receive detailed feedback about oral lesions. A recent study of smokeless tobacco cessation delivered through an oral healthcare setting, compared usual care with an intervention program conducted by dental hygienists. The intervention produced significantly higher quit rates after 3-months (32% vs 21%) for users of smokeless tobacco (Little, Stevens, Severson, & Lichtenstein, 1992).

In addition to the involvement of health care providers in smokeless tobacco, I believe there are several approaches from a health policy perspective that may (a) enable public health interventions targeting smokeless tobacco to be more effective, and (b) reduce the incidence of oral cancer. These strategies include--taxation, product manipulation, chemoprevention, point of purchase restrictions, use restrictions in public places, and more prominent warning labels. The various approaches outlined in the following section deserve further analysis and consideration as public health responses to the problem of smokeless tobacco, especially in light of the National Cancer Institute's goal of reducing cancer morbidity and mortality by 50% by the end of the year 2000.

Wasserman, Manning, Newhouse, and Winkler (1991) reported the impact of public smoking restrictions, specifically clean indoor air laws, on cigarette consumption. When smoking restrictions were entered in a model that included taxation, they were found to be equally as effective as taxation on reducing cigarette consumption. Specifically, if legislation was passed that increased the stringency of laws restricting smoking, overall per capita smoking would decrease by 5.9%. To achieve a similar

reduction through taxation would require a 31% increase in cigarette prices [based on a price elasticity of -0.23]. The study authors report that anti-smoking regulations appear to have a statistically significant effect on teenage smoking consumption, but regulations appear most effective in preventing teens from starting to smoke rather than encouraging teenage smokers to quit. There remains a tremendous need for use restrictions to include all tobacco products, for example, this is the case with domestic airline flights where use of smokeless tobacco products is restricted along with all other tobacco products.

Increases in excise taxation discourage tobacco use when the increase is passed onto the consumer as higher retail prices. The most dramatic evidence of this effect has been Canadian price changes. Between 1981 and 1989, per capita tobacco consumption in Canada declined at a steeper rate than per capita consumption in the U. S. Much of the decline in consumption is attributed to internal policies, most notably high taxation--taxes now represent about 75% of cigarette retail price in Canada, and to advertising bans (Kaiserman & Rogers, 1991). Federal excise taxes on smokeless tobacco are scheduled to increase in 1993, the effect of such taxation on consumption should be carefully analyzed.

The present demand for smokeless tobacco products, however, does not appear to be faltering. One of the challenges related to this demand is merchant education and enforcement of laws designed to restrict underage tobacco purchases. The rationale for restrictions suggests that making tobacco purchases inconvenient reduces adolescent use of tobacco. Recent reports have indicated that minors' attempts to purchase tobacco are successful more than 50% of the time (Altman, Rasenick-Douss, Foster, & Tye, 1991). These same authors have demonstrated long-term effects of a comprehensive merchant education program aimed at reducing tobacco sales to adolescents. Very little is known about minors' access to smokeless tobacco and the potential exists for similar educational programs to achieve a reduction in sales of smokeless tobacco to minors.

Another form of intervention involves attempts to create a safer product. One possible avenue to avert new cases of oral cancer in the future involves reducing the exogenous formation of tobacco-specific nitrosamines (TSNA) by modifying the product at various stages of manufacture. Hoffman, Rivenson, Chung, and Hecht (1991) recently highlighted several examples of TSNA reduction including: elimination of certain fungicides and pesticides, avoiding bacterial degradation of nitrate in burley ribs, and reducing nicotine content by supercritical extraction with carbon dioxide. Hoffman, Adams, Lisk, Fisenne, and Brunnemann (1987) reported dramatic reduction in levels of nitrosomorpholine (a powerful animal carcinogen) in snuff after the tobacco processors avoided contamination with morpholine.

In addition to attempts to modify the final product, another line of research involves the use of specific chemical agents as part of a stratified prevention effort. Within a chemopreventive model primary prevention goals include stopping use, while secondary and tertiary prevention efforts involve preventing the consequences of exposure and reversing pre-neoplasia with the use of carotenoids and retinoids in chemopreventive doses (Stich, Mathew, Sankaranarayanan, & Nair, 1991). The latest development from this area of research includes the isolation of phenethyl isothiocynate (PEITC) from cruciferous vegetables, this agent reduces the activity of the tobacco specific nitrosamine NNK.

By way of a summary and conclusion, the current study demonstrated a modest quit rate of 45% with long-term users of moist snuff smokeless tobacco. The subjects replaced their tobacco with gum-based medication containing either nicotine or a placebo for nicotine. A similar proportion of subjects in both conditions were able to quit all use of tobacco. Across both conditions, abstinent subjects were older. Although subjects using nicotine gum tended to report less intense symptoms of nicotine withdrawal compared to the placebo condition, only during the fourth week of the program were two

symptoms, anger and anxiety, measurably lower. While this research project is limited to a six week point prevalence quit rate, sustained quit rate of continuous abstinence for one year is the standard used to measure the success of most tobacco cessation programs. A one year follow-up of all subjects enrolled in this study is planned.

APPENDIX A

INCLUSION AND EXCLUSION CRITERIA

Criteria Form
Inclusion

Name _____ Date _____

18-65 1. How old are you _____

2. How did you hear about the study? _____newspaper ad _____which paper

_____radio _____ tv _____ friend

_____ other (describe)

3. What is (are) your usual brand(s) of smokeless tobacco? _____

1+ yrs 4. How long have you been using smokeless? _____ years

6-7days 5. Do you use smokeless tobacco every day? YES NO

3+mths 6. How long have you been using smokeless every day? _____months/years

Y/N 7. Do you currently smoke cigarettes? YES NO

Y 8. Are you willing to quit chewing and smoking? YES NO

Y 9. Have you ever seriously tried to quit your use of chew or snuff? YES NO

Exclusion

I have a few questions about your medical history:

Initials

1. Have you ever been diagnosed with heart disease? Or YES NO
2. Any diagnosed problem with your circulation? YES NO
3. Are you diabetic? YES NO
4. Are you bothered by ulcers or have you ever had an ulcer? YES NO
5. Do you have any problem chewing gum, or problems with caps or crowns? YES NO
6. Do you take any of the following medication on a regular basis? (See list) YES NO
7. Do you think you drink more than **Ten** glasses of liquid a day? YES NO
8. Do you drink alcohol? **Y** **N** How much do you drink a week? <7 7-14 >14
9. Do you use marijuana? YES NO
10. Have you ever filled and used a prescription for Nicorette gum? YES NO
11. Are you currently involved in any other program to help you quit tobacco? YES NO

APPENDIX B

PERCEIVED STRESS SCALE

Perceived Stress Scale

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate *how often* you felt or thought a certain way. Although some of the questions are similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer each question fairly quickly. That is, don't try to count up the number of times you felt a particular way, but rather indicate the alternative that seems like a reasonable estimate.

For each question choose from the following alternatives:

0. never
1. almost never
2. sometimes
3. fairly often
4. very often

1. In the last month, how often have you been upset because of something that happened unexpectedly?
2. In the last month, how often have you felt that you were unable to control the important things in your life?
3. In the last month, how often have you felt nervous and "stressed"?
4. In the last month, how often have you dealt successfully with irritating life hassles?
5. In the last month, how often have you felt that you were effectively coping with important changes that were occurring in your life?
6. In the last month, how often have you felt confident about your ability to handle your personal problems?
7. In the last month, how often have you felt that things were going your way?
8. In the last month, how often have you found that you could not cope with all the things that you had to do?
9. In the last month, how often have you been able to control irritations in your life?
10. In the last month, how often have you felt that you were on top of things?
11. In the last month, how often have you been angered because of things that happened that were outside of your control?
12. In the last month, how often have you found yourself thinking about things that you have to accomplish?
13. In the last month, how often have you been able to control the way you spend your time?

14. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

APPENDIX C

SMOKELESS TOBACCO DEPENDENCE QUESTIONNAIRE

Question	Answers	Coding
1. After a normal sleeping period, do you use smokeless within 30 minutes of waking?	Yes No	1 0
2. Is it difficult for you not to use smokeless where its use would be unsuitable or restricted?	Yes No	1 0
3. Do you use smokeless when you are sick or have mouth sores?	Yes No	1 0
4. What brand of smokeless do you use?*	H M L	3 2 1
5. How many days does a tin/can last you?	<3 3-5 6-7	3 2 1
6. On average how many minutes do you keep a fresh dip or chew in your mouth?	10-20 20-30 >30	3 2 1
7. Do you intentionally swallow tobacco juices?	Never Sometimes Always	0 1 2
8. Do you keep a dip or chew in your mouth almost all the time?	Yes No	1 0
9. Do you experience strong cravings for a dip/chew when you go for more than 2 hours without one?	Yes No	1 0
10. On average, how many dips/chews do you take each day? _____	1-9 10-15 15+	1 2 3

*Note. Scoring for brand question is based on nicotine content. For example: A high (H) brand is Copenhagen, Skoal is medium (M), and a low (L) brand is Kodiak/Skoal Bandits.

APPENDIX D

SMOKELESS TOBACCO CESSATION

CONFIDENCE QUESTIONNAIRE

Below is a list of 14 situations in which people frequently dip tobacco. Please read each one carefully, then circle the number underneath that best describes THE PROBABILITY THAT YOU WILL BE ABLE TO RESIST THE URGE TO DIP IF THAT SITUATION ARISES. If you are absolutely certain that you will not dip in that situation, circle 100%. If you have no confidence in your ability to resist a dip in that situation, circle 0%.

1. When you feel anxious

   0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

2. When you are nervous

   0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

3. When you feel tense

   0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

4. When you want to sit back and enjoy a dip

   0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

5. When you have finished a meal or snack

   0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

6. When you want to relax

   0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

7. When you want to feel more attractive

   0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

8. When you feel dipping is part of your self-image

   0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

9. When you want to feel more mature and sophisticated

   0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

10. When you are drinking an alcoholic beverage (beer, wine, or hard liquor)

    0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

11. When you see others dipping

    0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

12. When someone offers you a dip

    0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

13. When you want to avoid eating sweets

    0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

14. When you want to keep slim

    0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

APPENDIX E

WEEKLY WITHDRAWAL SYMPTOMS BY TREATMENT CONDITION

Withdrawal Symptom	Week	Nicotine Gum M	(SD)	Placebo Gum M	(SD)
Craving	1	51	(23)	57	(18)
	2	37	(23)	43	(24)
	3	28	(21)	33	(27)
	4	22	(21)	31	(27)
	5	18	(19)	27	(26)
	6	17	(19)	23	(25)
Irritability	1	37	(26)	41	(25)
	2	22	(23)	29	(25)
	3	14	(17)	22	(24)
	4	12	(15)	20	(24)
	5	8	(11)	16	(22)
	6	8	(11)	13	(19)
Frustration	1	32	(24)	34	(24)
	2	18	(20)	25	(22)
	3	14	(15)	21	(22)
	4	11	(15)	20	(23)
	5	8	(12)	15	(20)
	6	8	(10)	12	(17)
Anger	1	24	(23)	30	(24)
	2	16	(19)	23	(24)
	3	11	(13)	19	(22)
	4	9	(12)	18	(22)
	5	7	(12)	13	(19)
	6	6	(10)	11	(15)

Anxiety	1	30 (24)	39 (22)
	2	17 (20)	23 (20)
	3	11 (13)	17 (18)
	4	8 (10)	17 (19)
	5	7 (10)	12 (15)
	6	7 (10)	11 (15)
Difficulty	1	29 (23)	36 (25)
Concentrating	2	16 (20)	22 (20)
	3	13 (17)	17 (16)
	4	10 (13)	16 (16)
	5	9 (14)	10 (12)
	6	10 (14)	10 (12)
Restlessness	1	37 (25)	41 (23)
	2	24 (22)	27 (22)
	3	18 (20)	19 (17)
	4	15 (18)	17 (18)
	5	13 (19)	11 (12)
	6	12 (17)	12 (13)
Total Score	1	239 (145)	278 (139)
	2	150 (129)	192 (143)
	3	110 (102)	146 (128)
	4	89 (90)	140 (134)
	5	70 (87)	105 (108)
	6	68 (77)	92 (99)

APPENDIX F

STATISTICAL DESCRIPTION OF TOBACCO USE VARIABLES

Question	Tobacco Abstinence M(SD) No	Yes
1. After a normal sleeping period, do you use smokeless within 30 minutes of waking?	.66 (.47)	.65 (.48)
2. Do you use smokeless when you are sick or have mouth sores?	.53 (.50)	.62 (.49)
3. How many days does a tin/can last you?	2.44 (.75)	2.65 (.60)
4. On average how many minutes do you keep a fresh dip or chew in your mouth? 10-20mins= 3 20-30mins= 2 >30mins= 1	1.68 (.84)	1.78 (.83)
5. Do you intentionally swallow tobacco juices?	1.04 (.80)	.65 (.60)
6. Is it difficult for you not to use smokeless where its use would be unsuitable or restricted?	.51 (.50)	.40 (.50)
7. On average, how many dips/chews do you take each day?	11.5 (5.7)	9.9 (3.5)
8. What brand of smokeless do you use?	2.48 (0.6)	2.30 (.50)
9. Do you keep a dip or chew in your mouth almost all the time?	.62 (.49)	.50 (.51)
10. Do you experience strong cravings for a dip/chew when you go for more than 2 hour without one?	.93 (.25)	.87 (.34)

BIBLIOGRAPHY

Altman, D. G., Rasenick-Douss, L., Foster, V., & Tye, J. B. (1991). Sustained effects of an educational program to reduce sales of cigarettes to minors. *American Journal of Public Health, 81*, 891-893.

American Lung Association. (1983). A guide to smokeless tobacco.

Anderson, W. A., & McKeag, D. B. (1985). The substance use and abuse habits of college student athletes. Mission, Kansas, National Collegiate Athletic Service.

Ary, D. V., Lichtenstein, E., Severson, H., Weissman, W., & Seeley, J. R. (1989). An in-depth analysis of male adolescent smokeless tobacco users: Interviews with users and their fathers. *Journal of Behavioral Medicine, 12*, 449-467.

Baer, J. S., Holt, C. S., & Lichtenstein, E. (1986). Self-efficacy and smoking reexamined: construct validity and clinical utility. *Journal of Consulting and Clinical Psychology, 54*, 846-852.

Baer, J. S., & Lichtenstein, E. (1988). Cognitive Assessment. In D. M. Donovan & G. A. Marlatt (Eds.), *Assessment of Addictive Behaviors* (pp. 189-213). New York: The Guilford Press.

Bandura, A. (1977). Self-Efficacy: Toward a unifying theory of behavioral change. *Psychological Review, 84*, 191-215.

Biglan, A., LaChance, P., & Benowitz, N. (1990). Experimental analyses of the effects of smokeless tobacco deprivation. Unpublished manuscript.

Bloodgood, J. C. (1921). Cancer of the tongue: A preventable disease. *Journal of The American Medical Association, 77*, 1381-1387.

Blum, A. (1980). Smokeless tobacco. *Journal of The American Medical Association, 244*, 192-193.

Blum, A. (1984). Nicotine gum and the medicalization of smoking. *Annals of Internal Medicine, 101*, 121-122.

Benowitz, N. L. (1983). The use of biologic fluid samples in assessing tobacco smoke consumption. *National Institute of Drug Abuse Monograph, 48*, 6-26.

Benowitz, N. L. (1990). Pharmacokinetic considerations in understanding nicotine dependence. *Ciba Foundation Symposium*, 152, 186-200.

Benowitz, N. L., & Jacob, P. (1984). Daily intake of nicotine during cigarette smoking. *Clinical Pharmacology and Therapeutics, 35*, 499-504.

Benowitz, N. L., Porchet, H., Sheiner, L., & Jacob, P. (1988). Nicotine absorption and cardiovascular effects with smokeless tobacco use: Comparison with cigarettes and nicotine gum. *Clinical Pharmacology and Therapeutics, 44*, 23-28.

Borkovec, T. D. (1978). Self-efficacy: Cause or reflection of behavioral change? *Advances in Behavior Research and Therapy, 1*, 163-170.

Boyd, G. & Associates. (1987). Use of smokeless tobacco among children and adolescents in the United States. *Preventive Medicine, 16*, 402-421.

Boyle, R. (1989). Adolescent knowledge of smokeless tobacco's health consequences. *Health Education, 20*, 35-38.

Brantmark, B., Ohlin, P., & Westling, H. (1973). Nicotine-containing chewing gum as an anti-smoking aid. *Psychopharmacologia, 31*, 191-200.

British Thoracic Society. (1983). Comparison of four methods of smoking withdrawal in patients with smoking related diseases. *British Medical Journal, 286*, 595-597.

Campbell, I. A., Lyons, E., & Prescott, R. J. (1987). Stopping smoking: Do nicotine chewing gum and postal encouragement add to doctor's advice. *The Practitioner, 231*, 114-117.

Christen, A. G., & Glover, E. D. (1987). History of smokeless tobacco use in the United States. *Health Education, 18*, 6-13.

Christen, A. G., & McDonald, J. L. (1988). Safety of nicotine-containing gum. *Progress in Clinical and Biological Research, 261*, 219-235.

Christen, A. G., Swanson, B. Z., Glover, E. D., & Henderson, A. H. (1982). Smokeless tobacco: The folklore and social history of snuffing, sneezing, dipping, and chewing. *Journal of the American Dental Association, 105*, 821-829.

Coelho, R. J. (1984). Self-efficacy and cessation of smoking. *Psychological Reports, 54*, 309-310.

Cohen, J. (1977). *Statistical power analysis for the behavioral sciences*. New York: Academic Press.

Cohen S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior, 24*, 385-396.

Condiotte, M. M., & Lichtenstein, E. (1981). Self-efficacy and relapse in smoking cessation programs. *Journal of Consulting and Clinical Psychology, 49*, 648-658.

Connolly, G. N. (1985). Tobacco and Snuff: Growing health threats. *The Nations Health*, April 6.

Dilorenzo, T. M., Kern, T. G., & Pieper, R. M. (1991). Treatment of smokeless tobacco use through a formalized cessation program. *Behavior Therapy, 22*, 41-46.

Eakin, E., Severson, H., & Glasgow, R. (1989). Development and evaluation of a smokeless tobacco cessation program: A pilot study. *NCI Monograph, 8*, 95-100.

Ernster, V. L. (1989). Advertising and promotion of smokeless tobacco products. *NCI Monograph, 8*, 87-94.

Fagerstrom, K-O. (1978). Measuring the degree of dependence in tobacco smoking with reference to individualization of treatment. *Addictive Behaviors, 3*, 235-241.

Fagerstrom, K-O. (1982). A comparison of psychological and pharmacological treatment in smoking cessation. *Journal of Behavioral Medicine, 5*, 343-351.

Fagerstrom, K-O. (1988). Efficacy of nicotine chewing gum: a review. *Progress in Clinical and Biological Research, 261*, 109-128.

Fagerstrom, K-O., & Schneider, N. G. (1989). Measuring nicotine dependence in tobacco smoking: A review of the Fagerstrom Tolerance Questionnaire. *Journal of Behavioral Medicine, 12*, 159-181.

Fee, W. M., & Stewart, M. J. (1982). A controlled trial of nicotine chewing gum in a smoking withdrawal clinic. *The Practitioner, 226*, 148-151.

Ferno, O. (1973). A substitute for tobacco smoking. *Psychopharmacologia, 31*, 201-204.

Ferno, O., Lichneckert, S. J. A., & Lundgren, C. E. G. (1973). A substitute for tobacco smoking. *Psychopharmacologia, 31*, 201-204.

Fiore, M. C., Novotny, T. E., Pierce, J. P., Giovino, G. A., Hatziandreu, E. J., Newcomb, P. A., Surawicz, T. S., & Davis, R. M. (1990). Methods used to quit smoking in the United States. Do cessation programs help? *Journal of The American Medical Association, 263*, 2760-2765.

Fleiss, J. L. (1981). *Statistical methods for rates and proportions* New York: Wiley & Sons

Fletcher, C. (1977). Snuff to give up smoking. *Practitioner, 218*, 338-341.

Flay, B. R. (1985). Psychosocial approaches to smoking prevention--a review of findings. *Health Psychology, 4*, 449-488.

Friedell, H. L., & Rosenthal, L. M. (1941). The etiologic role of chewing tobacco in cancer of the mouth. *Journal of The American Medical Association, 116*, 2130-2135.

Glasgow, R. E., & Lichtenstein, E. (1987). Long-term effects of behavioral smoking cessation interventions *Behavior Therapy, 18*, 297-324.

Glover, E. D., Lafin, M., Flannery, D., & Albritton, D. L. (1989). Smokeless tobacco use among American college students. *Journal of American College Health, 38*, 81-85.

Glover, E. D. (1986). Conducting smokeless tobacco cessation clinics. *American Journal of Public Health, 76*, 207.

Glynn, T. J., Boyd, G. M., & Gruman, J. C. (1990). Essential elements of self-help/minimal intervention strategies for smoking cessation. *Health Education Quarterly, 17*, 329-345.

Glynn, T. J., Manley, M. W., & Pechacek, T. F. (1991). Physician-initiated smoking cessation program: the National Cancer Institute trials. In: P. Engstrom. (Ed.) *Advances in Cancer Control* . New York: Alan Liss Inc.

Gottlieb, N., Weinstein, R., Baun, W., & Bernacki, E. (1992). A profile of health risks among blue-collar workers. *Journal of Occupational Medicine*, *34* , 61-68.

Greer, R O., & Poulson, T. C. (1983). Oral tissue alterations associated with the use of smokeless tobacco by teenagers, I. Clinical findings. *Oral Surgeon*, *56*, 275-284.

Hall, R. L., & Dexter, D. (1988). Smokeless tobacco use and attitudes toward smokeless tobacco among Native American and other adolescents in the Northwest. *American Journal of Public Health*, *78*, 1586-1588.

Hall, S. M., Tunstall, C. D., Ginsberg, B., Benowitz, N. L., & Jones, R. T. (1987). Nicotine gum and behavioral treatment: A placebo-controlled trial. *Journal of Consulting and Clinical Psychology*, *55*, 603-605.

Harper, S. (1980). In tobacco, where there's smokeless fire. *Advertising Age*, June 23, 85.

Hatsukami, D. K., Anton, D., Keenan, R., & Callies, A. (1992). Smokeless tobacco abstinence effects and nicotine gum dose. *Psychopharmacology*, *106*, 60-66.

Hatsukami, D. K., Gust, S. W., & Keenan, R. M. (1987). Physiologic and subjective changes from smokeless tobacco withdrawal. *Clinical Pharmacology and Therapeutics*, *41*, 103-7.

Hatsukami, D. K., Hughes, J. R., Pickens, R. W., & Svikis, D. (1984). Tobacco withdrawal symptoms: an experimental analysis. *Psychopharmacology*, *84*, 231-236.

Hatsukami, D. K., Nelson, R., & Jensen, J. (1991). Smokeless tobacco: current status and future directions *British Journal of Addiction*, *86*, 559-563.

Heatherton, T. F., Kozlowski, L. T., Frecker, R. C., & Fagerstrom, K-O. (1991). The Fagerstrom test for nicotine dependence: A revision of the Fagerstrom tolerance questionnaire. *British Journal of Addiction*, *86*, 1119-1127.

Hecht, S. S. & Hoffman, D. (1989). *Cancer Surveys*, *8*, 275-294.

Henningfield, J. E., & Jasinski, D. R. (1988). Pharmacologic basis for nicotine replacement. *Progress in Clinical and Biological Research*, *261*, 35-61.

Henningfield, J. E., Radzius, A., Cooper, T. M., and Clayton, R. R. (1990). Drinking coffee and carbonated beverages blocks absorption of nicotine from nicotine polacrilex gum. *Journal of The American Medical Association*, *264*, 1560-1564.

Hjalmarson, A. I. (1984). Effect of nicotine chewing gum in smoking cessation: A randomized, placebo-controlled, double-blind study. *Journal of the American Medical Association*, *252*, 2835-2838.

Hoffman, D., Adams, J. D., Lisk, D., Fisenne, I., & Brunnemann, K. D. (1987). *Journal of the National Cancer Institute, 79*, 1281-1286.

Hoffman, D., Rivenson, Chung, F-L., & Hecht, S. S. (1991). Relevance of nicotine derived N-nitrosamines in tobacco carcinogenesis. In F. Adlkofer & K. Thurau (Eds.), *Effects of nicotine on biological systems* . Berlin: Birkhauser Verlag.

Hughes, J. R. (1986). Problems of nicotine gum. In J. K. Ockene (Ed.) , *The pharmacologic treatment of tobacco dependence: Proceedings of the World Congress* (pp. 141-147). Cambridge, MA: Harvard University.

Hughes, J. R., Gust, S. W., Keenan, R. M., Fenwick, J. W., & Healey, M. L. (1989). Nicotine versus placebo gum in general medical practice. *Journal of the American Medical Association, 261*, 1300-1305.

Hughes, J. R., Gust, S. W., Keenan, R. M., Skoog, K. P., Pickens, R. W., Ranlett, D., & Healy, M. (1986). Efficacy of nicotine gum in general practice. Unpublished Manuscript

Hunter, S. M., Croft, J. B., Burke, G. L., Parker, F. C., Webber, L. S., Berenson, G. S. (1986). Longitudinal patterns of smoking and smokeless tobacco use in youth. *American Journal of Public Health, 76*, 193-195.

Jacob, P., & Benowitz, N. L. (1991). *Excretion of the alkaloids anabasine and anatabine in urine of smokeless tobacco users and cigarette smokers.* Paper presented at the first International Conference on Smokeless Tobacco: Tobacco and Health, Columbus, Ohio.

Jamrozik, K., Fowler, G., Vassey, M., & Wald, N. (1984). Placebo controlled trial of nicotine chewing gum in general practice. *British Medical Journal, 289*, 794-797.

Jarvis, M. J., Raw, M., Russell, M. A. H., & Feyeraband, C. (1982). Randomised controlled trial of nicotine chewing gum. *British Medical Journal, 285*, 537-540.

Jarvis, M. J., Tupstall-Pedoe, H., Feyerabend, C., Vesey, C., & Saloojee, Y. (1987). Comparison of tests used to distinguish smokers from nonsmokers. *American Journal of Public Health, 77*, 1435-1438.

Jasinski, D. R. & Henningfield, J. E. (1988). Conceptual basis of replacement therapies for chemical dependence. *Progress in Clinical and Biological Research, 261*, 13-34.

Kaiserman, M. J., & Rogers, B. (1991). Tobacco consumption declining faster in Canada than in the U. S. *American Journal of Public Health, 81*, 902-904.

Keenan, R. M., Hatsukami, D. K. & Anton, D. J. (1989). The effects of short-term smokeless tobacco deprivation on performance. *Psychopharmacology, 98*, 126-130.

Killen, J. D., Fortmann, S. P. Newman, B., & Varady, A. (1990). Evaluation of a treatment combining nicotine gum with self-guided behavioral treatments for smoking relapse prevention. *Journal of Consulting and Clinical psychology, 58*, 85-92.

Kirkland, L. R. (1980). The nonsmoking uses of tobacco. *New England Journal of Medicine*, *303*, 165.

Kozlowski, L. T. (1984). Pharmacological approaches to smoking modification. In J. D. Matarozzo, S M. Weiss, J. A. Herd, N. E. Miller, & S. M. Weiss (Eds.), *Behavioral Health* (pp. 713-728). New York: Wiley & Sons

Kozlowski, L. T., & Herling, S. (1988). Objective Measures. In D. M. Donovan & G. A. Marlatt (Eds.), *Assessment of addictive behaviors* (pp. 214-235). New York: The Guilford Press.

Krishna, K. (1978). Tobacco chewing in pregnancy. *British Journal of Obstetrics and Gynecology*, *85*, 726-728.

Levenson-Gingiss, P., Morrow, J. R., & Dratt, L. M. (1989). Patterns of smokeless tobacco use among university athletes. *Journal of American College Health*, *38*, 87-90.

Lichtenstein, E. (1982). The smoking problem: A behavioral perspective. *Journal of Consulting and Clinical Psychology*, *50*, 804-819.

Lichtenstein, E., & Glasgow, R. Smoking Cessation : what have we learned over the past decade? *Journal of Consulting and Clinical Psychology*, *60*, 518-527.

Lichtenstein, E., & Mermelstein, R. J. (1984). Review of approaches to smoking treatment: Behavior modification strategies. In J. D. Matarozzo, S. M. Weiss, J. A. Herd, N. E. Miller, & S. M. Weiss (Eds.), *Behavioral Health* (pp. 695-712). New York: Wiley & Sons

Malcolm, R. E., Sillett, R. W., Turner, J. A., & Ball, K. P. (1980). The use of nicotine chewing gum as an aid to stopping smoking. *Psychopharmacology*, *70*, 295-296.

Marcus, A. C., Crane, L. A., Shopland, D. R., & Lynn, W. R. (1989). Use of smokeless tobacco in the United States: Recent estimates from the current population survey. *NCI Monograph*, *8*, 17-23.

Marlatt, G. A., & Gordon, J. R. (1980). Determinants of relapse: implications for the maintenance of behavior change. In P. O. Davidson, & S. M. Davidson (Eds.), *Behavioral medicine: Changing Health Lifestyles*. (pp. 410-452). New York: Brunner/Mazel.

Mattson, M. E., & Winn, D. (1989). Smokeless tobacco: Association with increased cancer risk. *NCI Monograph*, *8*, 13-16.

Maxwell, J. C. (1986). Tobacco takes dip: smokeless sales slide 6.2%. *Advertising Age*, Dec. 1, 62-63.

McIntyre, K. O., Lichtenstein, E., & Mermelstein, R. J. (1983). Self-efficacy and relapse in smoking cessation: a replication and extension. *Journal of Consulting and Clinical Psychology*, *51*, 632-633.

Morse, R. M., Norvich, R. C., & Graf, J. A. (1977). Tobacco chewing. An unusual case of drug dependence. *Mayo Clinic Proceedings, 52*, 358-360.

Novotny, T. E., Pierce, J. P., Fiore, M. C., Davis, R. M. (1989). Smokeless tobacco use in the United States: The adult use of tobacco surveys. *NCI Monograph, 8*, 25-28.

Olds, R. S. (1987). Smokeless tobacco and teenagers: A time to act. *American Journal of Health Promotion*, Summer, 14-20.

Orlandi, M. A., & Boyd, G. M. (1989). Smokeless tobacco use among adolescents: a theoretical overview. *NCI Monograph, 8*, 5-12.

Pechacek, T. F., & Danaher, B. G. (1979). How and why people quit smoking: a cognitive-behavioral analysis. In P. C. Kendall & S. D. Hollow (Eds.), *Cognitive-behavioral interventions: Theory research and procedures*. (pp. 389-422) New York: Academic Press.

Pomerleau, O. V., & Pomerleau, C. S. (1988). Nicotine replacement: an overview. *Progress in Clinical and Biological Research, 261*, 279-295.

Puska, P., Bjorkqvist, S., & Kosela, K. (1979). Nicotine containing chewing gum in smoking cessation: A double-blind trial with half-year follow-up. *Addictive Behaviors, 4*, 141-146.

Rouse, B. A. (1989). Epidemiology of smokeless tobacco use: A national study. *NCI Monograph, 8*, 29-33.

Russell, M. A. (1988). Nicotine replacement: The role of blood nicotine levels, their rate of change, and nicotine tolerance. *Progress in Clinical and Biological Research, 261*, 63-94.

Russell, M. A., Jarvis, M. J., & Feyerabend, C. (1980). A new age for snuff? *Lancet, 1*, 474-475.

Russell, M. A., Jarvis, M. J., Feyerabend, C., & Ferno, O. (1983). Nasal nicotine solution: A potential aid to giving up smoking? *British Medical Journal, 286*, 683-684.

Russell, M. A., Jarvis, M. J., Sutherland, G., & Feyerabend, C. (1987). Nicotine replacement in smoking cessation: Absorption of nicotine vapor from smoke-free cigarettes. *Journal of The American Medical Association, 257*, 3262-3265.

Russell, M. A., Jarvis, M. J., West, R. J., & Feyerabend, C. (1985). Buccal absorption of nicotine from smokeless tobacco sachets. *Lancet, 2*, 1370.

Russell, M. A., Raw, M., & Jarvis, M. J. (1980). Clinical use of nicotine chewing gum. *British Medical Journal, 280*, 1599-1602.

Schinke, S. P., Schilling, R. F., Gilchrist, L. D., Ashby, M. R., & Kitajima, E. (1989). Native youth and smokeless tobacco: Prevalence rates, gender differences, and descriptive characteristics. *NCI Monograph, 8*, 39-42.

Schinke, S. P., Schilling, R. F., Gilchrist, L. D., Ashby, M. R., & Kitajima, E. (1989). Native youth and smokeless tobacco: Prevalence rates, gender differences, and descriptive characteristics. *NCI Monograph, 8*, 39-42.

Schneider, N. G., Jarvik, M. E., Forsythe, A. B., Read, L. L., Elliott, M. L., & Schwieger, A. (1983). Nicotine gum in smoking cessation: A placebo-controlled, double-blind trial. *Addictive Behaviors, 8*, 253-261.

Schneider, N. G., Popek, P., Jarvik, M. E., & Gritz, E. R. (1977). The use of nicotine gum during cessation of smoking. *American Journal of Psychiatry, 134*, 439-440.

Schneider, N. G. (1987). Nicotine gum in smoking cessation: rationale, efficacy, and proper use. *Comprehensive Therapy, 13*, 32-37.

Schneider, N. G. (1988). *How to use nicotine gum.* New York: Pocket Books.

Schroeder, K. L. (1989). Oral and systemic concerns with smokeless tobacco. *Clinical Dentistry, 2*(9), 1-27.

Schroeder, K. & Chen, M. (1985). Smokeless tobacco and blood pressure. *New England Journal of Medicine, 312* , 919.

Schroeder, K. L., Iaderosa, G. B., Chen, M. S., Glover, E. D., & Edmundson, E. W. (1987). Bimodal initiation of smokeless tobacco usage: Implications for cancer education. *Journal of Cancer Education, 2*, 1-7.

Severson, H. H. (1992). *Enough Snuff: A manual for quitting smokeless tobacco on your own.* Eugene, OR: Rainbow Productions

Shiffman, S. M., & Jarvik, M. E. (1976). Smoking withdrawal symptoms in two weeks of abstinence. *Psychopharmacology, 50*, 35-39.

Smight, T. (1981). On chewing tobacco. *ADA News, 8*(2), 19.

Stich, H. F., Mathew, B., Sankaranarayanan, R., & Nair, M. K. (1991). Remission of oral precancerous lesions of tobacco/areca nut chewers following administration of beta-carotene or vitamin A, and maintenance of the protective effect. *Cancer Detection and Prevention, 15*, 93-98.

Strecher, V. J., DeVellis, B. M., Becker, M. H., & Rosenstock, I. M. (1986). The role of self-efficacy in achieving health behavior change. *Health Education Quarterly, 13*, 73-91.

Suedfeld, P. (1984). Restricted environmental stimulation therapy (REST). In J. D. Matarozzo, S. M. Weiss, J. A. Herd, N. E. Miller, & S. M. Weiss (Eds.), *Behavioral Health* (pp. 755-764). New York: Wiley & Sons

Tonnesen, P., Frtd, V., Hansen, M., Helsted, J., Gunnersen, A. B., Forchhammer, H., & Stockner, M. (1988). Effect of nicotine chewing gum in combination with group counseling on the cessation of smoking. *New England Journal of Medicine, 318*, 15-18.

Tucker, L. A. (1989). Use of smokeless tobacco, cigarette smoking, and hypercholesterolemia. *American Journal of Public Health, 79*, 1048-1050.

United States Department of Agriculture. (1987). *Situation and Outlook Yearbook.: Tobacco* , September, 1987. Washington, DC: GPO (A93.25).

United States Department of Agriculture. (1988). *Situation and Outlook Yearbook.: Tobacco* , June, 1988. Washington, DC: GPO (A93.25).

United States Department of Agriculture. (1989). *Situation and Outlook Yearbook.: Tobacco* , September, 1989. Washington, DC: GPO (A93.25).

United States Department of Agriculture. (1990). *Situation and Outlook Yearbook.: Tobacco* , June, 1991. Washington, DC: GPO (A93.25).

United States Department of Health and Human Services. (1986). *The health consequences of using smokeless tobacco: A report of the advisory committee to the Surgeon General* (DHHS Pub. No. 86-2874). Washington, DC: GPO.

United States Department of Health and Human Services. (1989). *National household survey on drug abuse. 1988 population estimates* (DHHS Pub. No. ADM 89-1636).Washington, DC: U. S. GPO.

Vogt, T. M., Lichtenstein, E., Ary, D., Biglan, A., Danielson, R., Glasgow, R. E., Hollis, J. F., Hornbrook, M. C., Lando, H., Mullooly, J., Severson, H., & Stevens, V. (1989). Integrating tobacco intervention into a health maintenance organization: the TRACC program. *Health Education Research, 4*, 125-135.

Walters D. J. (1991). The gathering momentum against tobacco: Action by physicians is needed on all fronts. *Canadian Medical Association Journal, 144*, 134-136.

Wasserman, J., Manning, W. G., Newhouse, J. P., & Winkler, J. D. (1991). The effects of excise taxes and regulations on cigarette smoking. *Journal of Health Economics, 10*, 43-64.

Wilbert, J. (1987). *Tobacco and Samanism in South America.* New Haven: Yale University Press.

Williams, N. (1992). *A smokeless tobacco cessation program for post-secondary students*. Unpublished doctoral dissertation, Memphis State University, Memphis.

Winn, D. N., Blot, W. J., Shy, C. M., Pickle, L. M., Toledo, A., & Fraumeni, J. F. (1981). Snuff dipping and oral cancer among women in the Southern United States. *New England Journal of Medicine, 304*, 745-749.

Wolfe, R. (1987). Smokeless tobacco. The fatal pinch. *Multinational Monitor*, July/August, 20-21.