Available online at www.sciencedirect.com

SCIENCE DIRECT®

Addictive Behaviors 30 (2005) 61–75

ADDICTIVE BEHAVIORS

A placebo controlled randomized trial of the effects of phenylpropanolamine and nicotine gum on cessation rates and postcessation weight gain in women

Theodore V. Cooper[a,*], Robert C. Klesges[b], Margaret W. DeBon[c], Susan M. Zbikowski[d], Karen C. Johnson[c], Linda H. Clemens[e]

[a]*Department of Psychiatry and Human Behavior, G.V. (Sonny) Montgomery Veterans Affairs Medical Center, University of Mississippi Medical Center, 2500 North State Street, Jackson, MS 39216, USA*
[b]*The University of Memphis Center for Community Health, USA*
[c]*Department of Preventive Medicine, University of Tennessee Health Science Center, USA*
[d]*Group Health Center for Health Promotion, USA*
[e]*Department of Consumer Science and Education, University of Memphis, USA*

Abstract

With smoking prevalence rates beginning to decline, studies designed to promote cessation in more challenging populations, like weight-concerned smokers, warrant attention. This study assessed the efficacy of two forms of pharmacotherapy [nicotine and phenylpropanolamine (PPA) gums] in addition to a 13-week cognitive behavioral smoking cessation program targeted for women. Participants were 439 females who met rigorous screening criteria and were randomized to one of the three treatment intervention groups (PPA gum, nicotine gum, or placebo gum). All participants attended a 13-week cognitive behavioral smoking cessation program and were given specific instructions on gum chewing. At posttest (13 weeks), and 6- and 12-month follow-ups, body weight and point prevalence abstinence were assessed. Analyses to determine potential differences between treatment groups on weight change and cessation rates were performed. Results indicated that neither change in body weight nor cessation rates significantly differed between groups. Attendance to sessions did appear to consistently increase the likelihood of quitting smoking at posttest and at each of the follow-ups. These results suggest that although the pharmacological interventions had no effect on cessation rates and postcessation weight gain, the behavioral component of the intervention was effective in increasing the odds of quitting smoking in weight-concerned women. Future efforts

* Corresponding author. Tel.: +1-601-362-4471x5581; fax: +1-601-984-5857.
E-mail address: tvcooper@psychiatry.umsmed.edu (T.V. Cooper).

doi:10.1016/j.addbeh.2004.04.013

should focus on increasing adherence to behavioral program components, particularly session attendance.

Keywords: Tobacco; Tobacco cessation; Smoking; Body weight

1. Introduction

Despite the existence of effective methods for smoking cessation (US Department of Health and Human Services [DHHS], 1990), many smokers continue to smoke. One important reason why smokers may continue to smoke is for the purpose of weight control. It is established that long-term smokers weigh less than do same aged nonsmokers and those who quit smoking experience postcessation weight gain (Klesges, Benowitz, & Meyers, 1991; Klesges, Meyers, Klesges, & LaVasque, 1989; US DHHS, 1990). These weight differences appear to be most pronounced for females (Klesges et al., 1989; Williamson et al., 1991). Weight concerns are often expressed by females attempting to quit smoking (French & Jeffery, 1995; Klesges & Klesges, 1988; Weekley, Klesges, & Relyea, 1992). Furthermore, weight concerns appear to be a barrier to successful cessation (Jeffery, Hennrikus, Lando, Murray, & Liu, 2000; Meyers et al., 1997), and interventions are needed to address this issue.

1.1. Behavioral intervention for postcessation weight gain

Recent studies have shown that long-term reductions in postcessation weight gain, at least in weight-conscious smokers, can indeed be sustained, and smoking cessation can be enhanced by behavioral interventions (Danielsson, Rossner, & Westin, 1999; Marcus et al., 1999; Spring et al., 1999). However, these programs must be sufficiently intense to be efficacious, and individuals in a natural environment are more successful at tackling smoking cessation prior to turning their attention toward weight control.

1.2. Pharmacological intervention for post cessation weight gain

Common findings from nicotine replacement, serotonin-enhancing drugs, and bupropion include either promising short-term results or, in longer length studies, modest weight suppression in drug intervention groups, followed by weight rebound, so that by follow-up, weights do not differ between groups (Borelli et al., 1999; Hurt et al., 1997; Jorenby et al., 1996, 1999; Li Wan Po, 1993; Pomerleau, Pomerleau, Morrell, & Lowenbergh, 1991; Spring, Wurtman, Gleason, Wurtman, & Kessler, 1991; Spring et al., 1995; Sutherland et al., 1992; Tonnenson, Norregaard, Mikkelsen, Jorgensen, & Nilsson, 1993). However, a more recent study suggests longer term weight gain attenuation in participants treated with bupropion (Hays et al., 2001).

Despite the inconsistent impact of pharmacological agents on postcessation weight gain, two drug interventions appear to hold some promise: nicotine and phenylpropanolamine (PPA) gums. The use of nicotine gum is associated with less postcessation weight gain (3.8 lb over 10 weeks), and greater use is associated with less weight gain (Doherty, Militello, Kinnunen, & Garvey, 1996; Gross, Stitzer, & Maldonado, 1989; Killen, Fortmann, Newman & Varady, 1990; Leischow, Sachs, Bostrom, & Hansen, 1992). It may be the case that nicotine gum reduces postcessation weight gain while individuals chew the gum, but that the results are not sustained after the discontinuation of the treatment.

A second promising pharmacologic agent in reducing postcessation weight gain is PPA, an over-the-counter appetite suppressant found in a number of commercial products (e.g., Stay Trim Gum). PPA provides anorectic effects similar with moderate to high doses of caffeine without central nervous stimulation. However, PPA's promise as a method for reducing postcessation weight gain is tempered by the FDA, who recently recommended that this over-the-counter product be curtailed because it increases the prevalence of a relatively rare stroke (this study was completed before the FDA concern). Two studies of PPA indicate its relative efficacy in reducing postcessation weight gain in the short term (Klesges, Klesges, Meyers, Klem, & Isbell, 1990; Klesges et al., 1995). In the first study (Klesges et al., 1990), cessation rates were significantly higher in participants receiving PPA gum (94%) than those receiving no (70%) or placebo gum (57%), and abstinent participants receiving PPA gained significantly less weight over the 2-week period. In the second study (Klesges et al., 1995), PPA did not enhance cessation rates; however, results indicated that hunger ratings and actual weight gain in abstinent participants were significantly reduced in both men and women in the PPA group (PPA=.74 kg; placebo = 1.13 kg). Although the findings of these short-term studies are encouraging, long-term studies of PPA and postcessation weight gain do not exist, suggesting that further exploration of this relationship is needed.

1.3. Rationale for this study

Therefore, it appears that PPA and nicotine gums are methods of reducing postcessation weight gain worthy of further exploration. To date, however, no investigation has compared the relative efficacy of these two agents both in the reduction of postcessation weight gain and their resultant cessation rates, particularly in women, the group most influenced by weight concerns and most likely to experience postcessation weight gain. Thus, the aims of this study are twofold. First, the efficacy of both nicotine and PPA gums will be determined relative to a placebo in the reduction of postcessation weight gain in women throughout a 13-week cognitive–behavioral smoking cessation program, as well as at both a 6- and a 12-month follow-up. Second, it will be determined if nicotine and PPA gums increase smoking cessation relative to placebo gum in a sample of female smokers at posttest and at 6- and 12-month follow-ups.

It is hypothesized that females in both active drug groups will gain significantly less weight following smoking cessation than those in the placebo condition will. It is anticipated that the two groups (PPA and nicotine gum) will not differ in efficacy at posttest. Following the termination of these drugs, it is expected that individuals in both the PPA and nicotine

gum groups will gain weight. However, it is expected that the weight gain in the PPA group will be significantly less than the weight gain in the nicotine gum group at the 6- and 12-month follow-ups. Related to the cessation analysis, it is predicted that higher cessation rates will be observed in the PPA and nicotine gum groups, relative to the placebo gum group, at posttest and at each follow-up.

2. Method

2.1. Overview

Eligible women were randomized to either the PPA, the nicotine, or the placebo gum group and participated in a 13-week cognitive–behavioral smoking cessation program. Three cycles of the 13-week program were conducted per year for 3 years.

2.2. Participants

Participants were recruited through a variety of public media. Over 650 participants were screened for the study. Of these, 439 enrolled in the study and provided demographic information, resulting in a sample in which 86.3% of the female participants were Caucasian (12.5% African American), and the average age was 38.2 (S.D. = 10.2) years. Potential participants were prescreened by phone for eligibility: (1) normotensive women between the ages of 18 and 70 (blood pressure $<140/90$ mm Hg and heart rate <100), (2) smoked 10 or more cigarettes/day, (3) not pregnant or lactating, (4) not taking medication contraindicated for gum use, and (5) not currently taking antidepressant medication or receiving psychiatric or alcohol/drug abuse treatment. Prescreening excluded women with a history of depression still in treatment, heart disease, endocrine disorders, current ulcers, kidney or liver disease, and lung disease. In addition, women who had previously participated in a center study using nicotine and/or PPA gum were excluded from participation. Eligible women attended an orientation session within 2 weeks prior to the first session. A comprehensive medical history and blood pressure screening was conducted. Eligible participants were asked to pay a US$35 deposit and were randomized following physician approval. Participants' deposits were returned at posttest if 10 of 13 sessions were attended. Monetary incentives of US$25 were given for each follow-up session, as well as entry into a raffle for a larger monetary incentive if participants attended follow-up sessions. Nonreturned deposits were forfeited to charity. The protocol used for this study was approved by the University's IRB.

2.3. Behavioral intervention

Weekly meetings included a 1-hour group intervention session delivered by standard protocol and a brief laboratory session consisting of questionnaire assessments, measures of height and weight, expired CO, and blood pressure. Program strategies included self-

monitoring, reduction strategies, problem-solving training, social support identification, tips on how to avoid weight gain, relapse prevention, and development of cohesion among group members. During Weeks 1 through 4, participants reduced cigarette use by 25% each week, and Week 5 was designated as the quit week. Group facilitators played a critical role in helping the participants to overcome barriers to successful cessation and/or anything that might lead to nonadherence.

2.4. Pharmacological intervention

Beginning at the quit date, each participant was given a weekly supply of chewing gum, which included 16 pieces of gum per day. Each piece of nicotine gum was 2 mg, while each piece of PPA gum was 8.33 mg. The participants were instructed on a gum chewing protocol, which suggested that the participants chew their gum on an as needed basis, with the caveat that they chew 10 to 12 pieces per day and no more than one piece of gum per hour. Participants in all three conditions received the following information. (1) Place one piece of gum in your mouth and chew very slowly 15 times. (2) After the 15 chews, stop chewing and "park" the gum between the cheek and gums. (3) After a minute or so, chew again for another 15 chews. Park the gum again in a different location of the mouth. (4) Repeat Steps 2 and 3 for 20–30 min. In addition, participants were admonished against drinking coffee and carbonated beverages during or immediately before chewing gum, as both substances appear to reduce nicotine absorption (Henningfield, Radzius, Cooper, & Clayton, 1990). The participants were also asked to return chewed gum, which was collected in the laboratory and recorded to avoid relying on self-report adherence with gum chewing instructions. "Weaning" of gum chewing took place on Weeks 11 through 13 by reducing the amount of gum chewed by 33% each week.

Gum counselors were used to help participants overcome side effects, ensure adherence to treatment, and problem solve with participants when barriers emerged. All group facilitators and participants were blind to treatment conditions.

2.5. Design and measures

Based on previous research, covariates that were assessed for inclusion in both analyses included age, race, education level, number of years a smoker, attendance to sessions, nicotine dependence, chewed gum, and baseline CO. In addition, pretest weight and weight concerns were covariates in the cessation analyses. The independent variable was gum type (PPA, nicotine, or placebo). The dependent measure for the weight gain attenuation analysis was body weight change from baseline. The dependent variable for the cessation analysis was point prevalence abstinence, as this measure ensures the biochemical verification of quit status at posttest (i.e., 13 weeks and 6-month and 1-year follow-ups.

2.5.1. Demographic information

At baseline, demographic information was obtained by standardized questionnaires. Demographics included race, age, income, and level of education.

2.5.2. Smoking status and smoking history

Point prevalence abstinence at each assessment was defined by self-report of no smoking at the time of the assessment and a carbon monoxide (CO) level of <10 ppm at the current assessment. CO tests were conducted using the procedures of Hughes, Frederiksen, and Frazier (1978). In instances in which smoking status could not be verified because of absence from that intervention session, the participants were categorized as smoking, indicating intention to treat analyses. A baseline measure of CO was also taken.

Smoking history variables included the number of years as a regular smoker and the Fagerstrom Test for Nicotine Dependence (Fagerstrom, 1991).

2.5.3. Weight

Participants' weights were taken, in clothing but without shoes or heavy garments, at all sessions. Weight was recorded as absolute weight in pounds with a Detecto Electronics Scale accurate to $+2$ oz.

Weights at baseline, posttest, and both follow-ups were examined for normality, skewness, and kurtosis. Outliers on weight (higher or lower than three standard deviations from the mean) were winsorized for subsequent analyses, a process in which outliers are retained in the analyses and given the value of three standard deviations below or above the mean (Kirk, 1982). The following number of participants' weights were winsorized: baseline ($n=9$), posttest, ($n=3$), 6-month follow-up ($n=3$), and 1-year follow-up ($n=2$). Because there was a high correlation between participant's weights at Weeks 1 and 2 (r=.973; $P<.01$), in rare instances ($n=26$) to decrease missing data, participants' weights at week 2 were used as a measure of baseline weight. Weight change was also calculated from baseline to posttest and the 6-month and the 1-year follow-ups. The same process of winsorizing was performed for outliers on the three weight change variables: changes at posttest ($n=2$) and at 6-month ($n=5$) and at 1-year follow-ups ($n=4$).

2.5.4. Weight concerns

A number of strategies have been used in the literature to assess concerns about postcessation weight gain (Klesges et al., 1989; Meyers et al., 1997). Here, participants' perceptions of the relationship between different levels of postcessation weight gain and return to smoking were directly assessed. To assess tolerance for weight gain, prior to treatment, participants were asked a series of 10 questions: "If after quitting smoking, you gained 18–20 lb, would you start smoking again?" The participants were asked the same question nine subsequent times, with decreasing weight gains in 2-lb intervals, ending with a query of a gain less than 2 lb. Participants who responded affirmatively concerning return to smoking for 8 to 20 lb were classified as weight concerned, as this range appears consistent with actual weight gain reported in the literature (Klesges et al., 1989), and to increase the range from less than 2 to 20 lb resulted in a negligible increase in weight-concerned participants ($n=1$).

2.5.5. Attendance to sessions

Participants' attendance to each intervention session was recorded, and attendance remained a continuous variable that could range between 1 and 15 sessions.

2.5.6. Adherence with gum chewing instructions

Participants returned chewed gum for Weeks 6 through 13 to gauge adherence with the gum chewing protocol. Adherence with gum chewing instructions was calculated as follows. First, the number of pieces of chewed gum returned for each day was calculated. Second, the number of days that the participants returned chewed gum was calculated. The number of days that the participants returned gum was used, as a failure to return chewed gum was not sufficient to know whether gum was chewed during that day or not (e.g., chewed but not returned). Third, the average of chewed gum per day was computed by dividing the sum of pieces returned by the number of days each that participant returned chewed gum. The average gum chewed and returned per day remained a continuous variable.

2.6. Approach to analyses

2.6.1. Body weight

Because the primary purpose of the study was to evaluate the effects of nicotine and PPA gums on those participants who abstained from smoking, all body weight analyses were conducted with the resultant sample of quit smokers ($n = 89$).

The first analysis, a 3×3 repeated-measures MANCOVA, determined potential between-groups differences between nicotine, PPA, and placebo gums on weight change from baseline weight at posttest and at the 6-month and at the 12-month follow-ups. The dependent variable of the treatment (placebo, nicotine, PPA gums) by time (posttest, 6- and 12-month follow-ups) MANCOVA was body weight change from baseline. In addition, tests were performed to ensure that assumptions of MANCOVA were not violated.

2.6.2. Cessation

The cessation-related analyses determined if individuals on active drugs (PPA and nicotine gums) were more successful in quitting smoking than those on placebo gum at posttest and at each follow-up. The impact of treatment condition on cessation was investigated using a multiple logistic regression analysis. Quit status (1 = quit smoking, 0 = not quit) served as the dependent variable for the analysis, and intervention group (placebo gum served as the referent group) was used as the independent variable.

Logistic regression models were used to evaluate the odds of quitting smoking as a function of the type of gum chewed. The proposed covariates were evaluated as a set and removed if they were not significantly contributing to the improvement in fit of the model and if they were not significantly related to the outcome of quitting smoking. The most nonsignificant covariate in the model was removed first. This process continued until only covariates that significantly improved the model and significantly related to quitting smoking remained in the model.

3. Results

3.1. Participant characteristics

Table 1 contains the number of participants and the means and standard deviations, by treatment group, of the continuous covariates used in the cessation analyses (i.e., entire sample). There were no differences between groups on these variables. As shown in Table 1, the average participant was 38.2 years old (S.D. = 10.2), a long-time smoker (M = 19.1 years; S.D. = 9.8), weighed 144.5 lb (S.D. = 27.2 lb), had a baseline CO rate consistent with a moderate to heavy smoker (M = 28.9 ppm; S.D. = 13.7), at baseline, smoked, on average, just over a pack of cigarettes per day (M = 22.6; S.D. = 8.0), attended just over half of the intervention sessions (M = 8.7 sessions; S.D. = 4.2), had a Fagerstrom score just below that which is considered nicotine dependent (M = 5.7; S.D. = 2.1), and demonstrated poor adherence with gum chewing instructions (M = 4.5 pieces per day; S.D. = 3.4). In addition, the majority of participants were Caucasian (86.3% Caucasian, 12.5% African American), well educated (73.2% with some college, a college degree, or professional training), earned an average yearly income of just under US$20,000, and were weight concerned (63.6%).

Table 1
Participant characteristics

Characteristics	Placebo gum	PPA gum	Nicotine gum
Age (years)			
n	147	147	146
M (S.D.)	39.0 (10.2)	37.3 (9.6)	38.4 (10.8)
Baseline weight (lb)			
n	148	146	146
M (S.D.)	145.9 (27.5)	145.3 (27.4)	142.2 (26.7)
Number of years smoking			
n	147	146	146
M (S.D.)	19.5 (10.3)	18.4 (9.2)	19.4 (9.7)
Fagerstrom score			
n	147	147	146
M (S.D.)	5.8 (2.0)	5.7 (2.1)	5.5 (2.1)
Baseline CO (ppm)			
n	147	142	144
M (S.D.)	29.9 (14.4)	28.8 (13.9)	28.0 (12.8)
Attendance to sessions			
n	148	147	146
M (S.D.)	8.2 (4.1)	8.6 (4.1)	8.6 (4.3)
Gum chewing adherence (average pieces per day)			
n	108	105	107
M (S.D.)	4.5 (3.2)	4.3 (3.2)	4.6 (3.7)

All P values $>.05$.

3.2. Weight analyses

Of the 89 participants who quit smoking, 27 cases were rejected because of missing data, resulting in a sample of 62 women. The observed means and standard deviations and the adjusted means and standard errors of weight change by treatment group at posttest and each follow-up are displayed in Table 2. At posttest, adjusted weight changes from baseline for each group were as follows: the placebo group ($n=22$) gained, on average, 4.6 lb; the nicotine gum group ($n=24$) gained, on average, 2.6 lb; while those in the PPA gum group ($n=16$) gained, on average, 1.6 lb. At the 6-month follow-up, adjusted weight changes from baseline were the following: placebo, 9.5 lb gained; nicotine gum, 4.6 lb gained; and PPA gum, 4.2 lb gained. After 1 year, adjusted weight changes from baseline were the following: placebo, 5.0 lb gained; nicotine gum, 4.1 lb gained; and PPA gum, 2.8 lbs. gained. Despite seeming differences in weight change, there were no significant differences between groups in weight change ($F=1.07$; $df=2$; $P=.35$). In addition, there was no significant time-by-treatment effect ($F=0.58$; $df=4$; $P=.68$). There was only a significant time effect in the repeated-measures MANCOVA ($F=4.90$; $df=2$; $P=.01$). Observed power ($\alpha=.05$) to detect treatment, time-by-treatment, and time effects were .23, .19, and .80 respectively.

Given these findings, indications that attendance to intervention sessions was a strong covariate in the study (see below, inclusion in analyses, predictor of cessation at all time points), and the assumption of homogeneity of variance violation that prompted the exclusion of one covariate (number of years smoking), three other analyses were performed. First, the same analysis was performed without any covariates, yielding similar results (treatment effect: $F=0.72$, $df=2$, $P=.49$; time-by-treatment effect: $F=1.05$, $df=4$, $P=.39$; time effect: $F=5.15$, $df=2$, $P=.007$). Second, the analysis was performed using only attendance to intervention sessions as a covariate, and results again were similar (treatment effect: $F=0.70$, $df=2$, $P=.50$; time-by-treatment effect: $F=1.05$, $df=4$, $P=.39$; time effect: $F=5.15$, $df=2$, $P=.007$). Finally, the analysis was performed using only the number of years a smoker as a covariate, and results demonstrated the same trends (treatment effect: $F=0.77$, $df=2$, $P=.47$; time-by-treatment effect: $F=1.07$, $df=4$, $P=.37$; time effect: $F=5.44$, $df=2$, $P=.005$).

A series of logistic regression analyses were performed to explore the odds of being included in the weight analysis. Results indicated that for every unit increase in attendance,

Table 2
Weight change at posttest and at 6-month and 1-year follow-ups

Time of measurement	Placebo gum ($n=22$)	Nicotine gum ($n=24$)	PPA gum ($n=16$)
Posttest weight change (lbs.)			
M (S.D.)	+4.0 (4.8)	+3.3 (4.0)	+1.3 (6.7)
Adjusted mean (S.E.)	+4.6 (1.2)	+2.6 (1.2)	+1.6 (1.3)
6-month follow-up weight change (lbs.)			
M (S.D.)	+8.1 (8.4)	+6.4 (9.1)	+3.6 (14.0)
Adjusted mean (S.E.)	+9.5 (2.1)	+4.6 (2.1)	+4.2 (2.4)
1-year follow-up weight change (lbs.)			
M (S.D.)	+4.1 (10.1)	+5.6 (7.1)	+1.8 (15.7)
Adjusted mean (S.E.)	+5.0 (2.4)	+4.1 (2.4)	+2.8 (2.7)

women were 1.8 times more likely to be included in the weight analysis. No other variable, including treatment group, significantly increased the odds of inclusion in the analysis.

3.3. Cessation analyses

The significant variables resulting from the three logistic regression analyses, along with the odds ratios and the 95% confidence intervals, are presented in Table 3. The first logistic regression model explored the odds of quitting smoking among the three gum groups at posttest. There was no significant effect for treatment group in this model (P=.26).

As indicated in Table 3, for every unit increase in sessions of the program attended, smokers were 1.7 times more likely to quit than not to quit smoking at posttest (P<.001).

The second logistic regression model explored the odds of quitting smoking among the three gum groups at the 6-month follow-up. There was no significant effect for treatment group in this model (P=.56). For every unit increase in sessions of the program attended, smokers were 1.2 times more likely to quit than not to quit smoking at the 6-month follow-up (P<.001).

The final logistic regression model explored the odds of quitting smoking among the three gum groups at the 1-year follow-up. There was no significant effect for treatment group in this model (P=.49). For every unit increase in sessions of the program attended, smokers were 1.2 times more likely to quit than not to quit smoking at the 1-year follow-up (P<.001).

Although there was no significant effect for treatment group in any of the three logistic regression models, Table 4 indicates the rates of cessation of those included in the models at posttest and each follow-up by treatment group.

Logistic regressions were performed to explore the odds of inclusion in each of the cessation analyses. At posttest and both follow-ups, for every unit increase in attendance,

Table 3
Logistic regression models at posttest and at 6-month and 1-year follow-ups: Predicting the odds of not smoking vs. smoking

Time	Variables	B	Odds ratio	95% Confidence intervals		P
				Lower	Upper	
Posttest[a]	Attendance to sessions	.503	1.653	1.468	1.861	<.001
	Constant	−6.611				<.001
6-month follow-up[b]	Attendance to sessions	.217	1.243	1.141	1.353	<.001
	Constant	−4.194				.015
1-year follow-up[c]	Attendance to sessions	.1678	1.192	1.100	1.292	<.001
	Constant	−3.827				.02

[a] n=441 (89 quitters, 352 smokers). The ns were reduced because of missing values on some independent variables. Cox and Snell R^2=.280; model goodness of fit: x^2=144.778. P<.001.

[b] n=441 (55 quitters, 386 smokers). The ns were reduced because of missing values on some independent variables. Cox and Snell R^2=.071; model goodness of fit: x^2=32.276. P<.001.

[c] n=441 (54 quitters, 387 smokers). The ns were reduced because of missing values on some independent variables. Cox and Snell R^2=.048; model goodness of fit: x^2=23.027. P<.001.

Table 4
Cessation rates at posttest and at 6-month and 1-year follow-ups by treatment group

Treatment group	Posttest	6-month follow-up	1-year follow-up
Placebo ($n = 148$)			
n not smoking	29	16	15
% not smoking in group	19.6	10.8	10.1
Nicotine gum ($n = 146$)			
n not smoking	35	17	17
% not smoking in group	24.0	11.6	11.6
PPA gum ($n = 147$)			
n not smoking	25	22	22
% not smoking in group	17.0	15.0	15.0

women were 2.9 times more likely to be included in this cessation analysis. Those women lost to the analyses did not differ according to treatment group.

4. Discussion

These results do not confirm the a priori hypotheses of this study. Although there appears to be a trend toward the attenuation of postcessation weight gain in the PPA gum group, no significant differences in weight change were detected among the gum groups. In addition, those women in the nicotine and PPA gum groups did not yield higher cessation rates than those in the placebo gum group at posttest and each follow-up.

Given no significant differences in weight change among gum groups and an apparent trend toward weight gain attenuation in the PPA gum group, three considerations are noteworthy for interpretation. First, although it is tempting to point to the clinical, rather than statistical, significance of the apparent weight gain attenuation in the PPA gum group, the large variability in weight change evidenced in this group limits such an interpretation. Given such variability, it appears that PPA gum may be effective for a subset of female weight-concerned smokers but much less effective for others. Second, because of poor cessation rates and the loss of participants due to missing data, the small sample size in the weight analysis significantly diminished the power and, thus, the ability to detect group differences. Finally, it should be noted that the FDA is in the process of removing PPA from all drug products and requesting that all drug companies discontinue marketing products containing PPA. For this reason, any argument of a trend in weight gain attenuation in the PPA gum group is moot. It is clear that future studies in the area of smoking cessation and weight gain attenuation need to revisit behavioral cessation and weight gain reduction interventions or explore these behavioral interventions in combination with other potential weight suppressing agents, like sibutramine or, given the study by Hays et al. (2001), bupropion. In addition, based on these results and interpretations, such future studies should assess characteristics of responders and nonresponders to these weight-suppressing agents, as well as ensure adequate sample size to maintain sufficient power to detect a weight gain attenuation effect among intervention groups.

Cessation rates in this study were poor, regardless of gum group. Three potential explanations are noteworthy. First, adherence with gum chewing instructions was low. It is clear that women in this study failed to achieve and maintain therapeutic levels of active drugs necessary to gain typical relief from withdrawal symptoms and thus quit smoking, much less diminish weight gain. Although group facilitators instructed participants that chewing the recommended amount of gum was important and problem solved issues around adherence, perhaps, future studies of this sort should more closely monitor adherence to drug regimens and include components tailored to nonadherent participants (e.g., mid-week follow-up telephone calls). The second explanation for poor cessation rates in this study is the amount of response burden required of the women. In addition to chewing, saving, and returning gum, the participants were required to attend 15 intervention sessions in which weight and CO were measured and a multitude of questionnaires were completed during each session. This assertion is consistent with literature that suggests that meeting a threshold of adjutant behavioral intervention is important for cessation (e.g., a minimum of six contacts); however, as programs increase in complexity, cessation rates plateau and, in some instances, start deteriorating (Klesges, Ward, & DeBon, 1996; Lichtenstein & Glasgow, 1992). It is true that attendance to intervention sessions increased the odds that women in this study quit smoking; however, it is likely that shorter and less complex studies would yield similar, if not better, benefits of behavioral adherence. Future studies of combined behavioral and pharmacologic cessation programs should minimize the complexity of cessation programs without sacrificing either adequate behavioral intervention or methodological rigor (e.g., measurement of variables). Lastly, it is possible that the active drug groups did not differ from the placebo for different reasons particular to the type of pharmacotherapy. That is, it is possible that the PPA group did not differ from the placebo group because PPA is an effective tobacco cessation pharmacotherapy in the short term (i.e., 4 weeks or fewer; Klesges et al., 1990, 1995) but not in the long term, while the nicotine gum group did not differ from placebo because NRT is less effective in women than in men. This possibility is consistent with findings from other studies of nicotine gum that demonstrate no differences in outcome between nicotine gum and placebo groups in women (Killen, Fortmann, & Newman, 1990) and poorer outcomes in women relative to men (Bjornson et al., 1995), although others have found no significant differences in outcome between men and women (Killen, Fortmann, Varady, & Kraemer, 2002). Many barriers or stressors specific to women have been noted as possible reasons why some studies find a gender gap in cessation rates with NRT use, including hormonal cycles, a greater likelihood of comorbid depression, and concerns about weight gain (Gritz et al., 1996). Confirmation of this possibility would require further studies of nicotine gum and other forms of pharmacotherapy using both men and women. However, it is possible that in a group largely comprised of weight-concerned women, nicotine gum is no more effective than placebo is as an adjunct to an intensive behavioral smoking cessation intervention.

The strengths of this study are many, including vigorous recruitment and retention strategies, randomization, ample behavioral intervention, and the measurement of all variables, with no reliance on self-report. Unfortunately, it appears that the major strengths of this study also serve as its greatest limitation. That is, the length and complexity of the

behavioral components of this study were likely too cumbersome for the participants, resulting in the failure to reach therapeutic levels of nicotine or PPA sufficient enough to quit smoking and/or minimize postcessation weight gain. As mentioned earlier, future studies of combined behavioral and pharmacologic interventions for smoking cessation and post-cessation weight gain attenuation should (1) include adequate sample size representative of both genders, (2) assess the characteristics of both responders and nonresponders to potential weight suppressing agents, (3) monitor and target participant adherence, especially with pharmacologic intervention components, and (4) minimize the complexity of behavioral components of the intervention without sacrificing either adequate participant contact or solid methodology.

In sum, neither nicotine nor PPA gum in this methodologically rigorous study significantly attenuated postcessation weight gain in women. In addition, smoking cessation in the active treatment groups did not differ from placebo. However, the results of this study do support the importance of adherence to intervention.

References

Bjornson, W., Rand, C., Connett, J. E., Lindgren, P., Nides, M., Pope, F., Buist, A. S., Hoppe-Ryan, C., & O'Hara, P. (1995). Gender differences in smoking cessation after 3 years in the Lung Health Study. *American Journal of Public Health*, *85*, 223–230.

Borelli, B., Spring, B., Niaura, R., Kristeller, J., Ockene, J. K., & Keuthen, N. J. (1999). Weight suppression and weight rebound in ex-smokers treated with fluoxetine. *Journal of Consulting and Clinical Psychology*, *67*, 124–131.

Danielsson, T., Rossner, S., & Westin, A. (1999). Open randomized trial of intermittent very low energy diet together with nicotine gum for stopping smoking in women who gained weight in previous attempts to quit. *British Medical Journal*, *319*, 490–494.

Doherty, K., Militello, F. S., Kinnunen, T., & Garvey, A. J. (1996). Nicotine gum dose and weight gain after smoking cessation. *Journal of Consulting and Clinical Psychology*, *64*, 799–807.

Fagerstrom, K. O. (1991). The Fagerstrom test for nicotine dependence: A revision of the Fagerstrom Tolerance Questionnaire. *British Journal of Addiction*, *86*, 1119–1127.

French, S. A., & Jeffery, R. W. (1995). Weight concerns and smoking: A literature review. *Annals of Behavioral Medicine*, *17*, 234–244.

Gritz, E.R., Nielsen, I.R., & Brooks, L.A. (1996). Smoking cessation and gender: the influence of physiological, phychological, and behavioral factors. *Journal of the American Medical Womens Association*, *51*, 35–42.

Gross, J., Stitzer, M. L., & Maldonado, J. (1989). Nicotine replacement: Effects on post cessation weight gain. *Journal of Consulting and Clinical Psychology*, *57*, 87–92.

Hays, J. T., Hurt, R. D., Rigotti, N. A., Niaura, R., Gonzales, D., Durcan, M. J., Sachs, D. P. L., Wolter, T. D., Buist, A. S., Johnston, J. A., & White, J. D. (2001). Sustained-release bupropion for pharmacologic relapse prevention after smoking cessation: A randomized, controlled trial. *Annals of Internal Medicine*, *135*, 423–433.

Henningfield, J. E., Radzius, A., Cooper, T. M., & 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.

Hughes, J. E., Frederiksen, L. W., & Frazier, M. (1978). A carbon monoxide analyzer for measurement of smoking behavior. *Behavior Therapy*, *9*, 293–296.

Hurt, R. D., Sachs, D. P. L., Glover, E. D., Offord, K. P., Johnston, J. A., Lowell, L. C., Khayrallah, M. A., Schroeder, D. R., Glover, P. N., Sullivan, C. R., Croghan, I. T., & Sullivan, P. M. (1997). A comparison of

sustained release bupropion and placebo for smoking cessation. *New England Journal of Medicine*, *337*, 1195–1202.

Jeffery, R. W., Hennrikus, D. J., Lando, H. A., Murray, D. M., & Liu, J. W. (2000). Reconciling conflicting findings regarding postcessation weight concerns and success in smoking cessation. *Health Psychology*, *19*, 242–246.

Jorenby, D. E., Hatsukami, D. K., Smith, S. S., Fiore, M. C., Allen, S., Jensen, J., & Baker, T. B. (1996). Characterization of tobacco withdrawal symptoms: Transdermal nicotine reduces hunger and weight gain. *Psychopharmacology*, *128*, 130–138.

Jorenby, D. E., Leischow, S. J., Nides, M. A., Rennard, S. I., Johnston, J. A., Hughes, A. R., Smith, S. S., Muramoto, M. L., Daughton, D. M., Doan, K., Fiore, M. C., & Baker, T. B. (1999). A controlled trial of sustained release bupropion, a nicotine patch, or both for smoking cessation. *New England Journal of Medicine*, *340*, 685–691.

Killen, J. D., Fortmann, S. P., & Newman, B. (1990). Weight change among participants in a large-sample minimal-contact smoking relapse prevention trial. *Addictive Behaviors*, *15*, 323–332.

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

Killen, J. D., Fortmann, S. P., Varady, A., & Kraemer, H. C. (2002). Do men outperform women in smoking cessation trials? Maybe, but not by much. *Experimental and Clinical Psychopharmacology*, *10*, 295–301.

Kirk, R. E. (1982). *Experimental design: Procedures for the behavioral sciences* (2nd ed.). Belmont, CA: Brooks/Cole.

Klesges, R. C., Benowitz, N. L., & Meyers, A. W. (1991). Behavioral and biobehavioral aspects of smoking and smoking cessation: The problem of post cessation weight gain. *Behavior Therapy*, *22*, 179–199.

Klesges, R. C., & Klesges, L. M. (1988). Cigarette smoking as a dieting strategy in a university population. *International Journal of Eating Disorders*, *7*, 413–419.

Klesges, R. C., Klesges, L. M., DeBon, M., Shelton, M. L., Isbell, T. R., & Klem, M. L. (1995). Effects of phenylpropanolamine on withdrawal symptoms. *Psychopharmacology*, *119*, 85–91.

Klesges, R. C., Klesges, L. M., Meyers, A. W., Klem, M. L., & Isbell, T. (1990). The effects of phenylpropanolamine on dietary intake, physical activity, and body weight after smoking cessation. *Clinical Pharmacology and Therapeutics*, *47*, 747–754.

Klesges, R. C., Meyers, A. W., Klesges, L. M., & LaVasque, M. E. (1989). Smoking, body weight, and their effects on smoking behavior: A comprehensive review of the literature. *Psychological Bulletin*, *106*, 204–230.

Klesges, R. C., Ward, K. D., & DeBon, M. (1996). Smoking cessation: A successful behavioral/pharmacologic interface. *Clinical Psychology Review*, *16*, 479–496.

Leischow, S. J., Sachs, D. P. L., Bostrom, A. G., & Hansen, M. D. (1992). Effects of differing nicotine-replacement doses on weight gain after smoking cessation. *Archives of Family Medicine*, *1*, 233–237.

Lichtenstein, E., & Glasgow, R. E. (1992). Smoking cessation: What have we learned in the past decade? *Journal of Consulting and Clinical Psychology*, *60*, 518–527.

Li Wan Po, A. (1993). Transdermal nicotine in smoking cessation: A meta-analysis. *European Journal of Clinical Pharmacology*, *45*, 519–528.

Marcus, B. H., Albrecht, A. E., King, T. K., Parisi, A. F., Pinto, B. M., Roberts, M., Niaura, R. S., & Abrams, D. B. (1999). The efficacy of exercise as an aid for smoking cessation in women: A randomized controlled trial. *Archives of Internal Medicine*, *159*, 1229–1234.

Meyers, A. W., Klesges, R. C., Winders, S. E., Ward, K. D., Peterson, B. A., & Eck, L. H. (1997). Are weight concerns predictive of smoking cessation? A prospective analysis. *Journal of Consulting and Clinical Psychology*, *65*, 448–452.

Pomerleau, O. F., Pomerleau, C. S., Morrell, E. M., & Lowenbergh, J. M. (1991). Effects of fluoxetine on weight gain and food intake in smokers who reduce nicotine intake. *Psychoneuroendocrinology*, *16*, 433–440.

Spring, B., Pingitore, R., Johnsen, L., Pergadia, M., Richmond, M., Gunnarsdottir, D., Corsica, J., Mills, M., &

Crayton, J. (1999). Promoting smoking cessation and reducing weight gain. *Annals of Behavioral Medicine*, *21*(Supplement), S091.

Spring, B., Wurtman, J., Gleason, R., Wurtman, R., & Kessler, K. (1991). Weight gain and withdrawal symptoms after smoking cessation: A preventive intervention using D-fenfluramine. *Health Psychology*, *10*, 216–223.

Spring, B., Wurtman, J., Wurtman, R., el-Khoury, A., Goldberg, H., McDermott, J., & Pingitore, R. (1995). Efficacies of dexfenfluramine and fluoxetine in preventing weight gain after smoking cessation. *American Journal of Clinical Nutrition*, *62*, 1181–1187.

Sutherland, G., Stapleton, J. A., Russell, M. A. H., Jarvis, M. J., Hajek, P., Belcher, M., & Feyerabend, C. (1992). Randomised controlled trial of nasal nicotine spray in smoking cessation. *The Lancet*, *340*, 324–329.

Tonnenson, P., Norregaard, J., Mikkelsen, K., Jorgensen, S., & Nilsson, F. (1993). A double blind trial of a nicotine inhaler for smoking cessation. *JAMA*, *269*, 1268–1271.

U.S. Department of Health and Human Services (1990). *The health benefits of smoking cessation: A report of the Surgeon General*. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, Center for Disease Control, Center for health Promotion and Education, Office on Smoking and Health. DHHS publication no. (CDC) 90-8416.

Weekley, C. K., Klesges, R. C., & Relyea, G. (1992). Smoking as a weight control strategy and its relationship to smoking status. *Addictive Behaviors*, *17*, 259–271.

Williamson, D. F., Madans, J., Anda, R. F., Kleinman, J. C., Giovino, G. A., & Byers, T. (1991). Smoking cessation and severity of weight gain in a national cohort. *New England Journal of Medicine*, *324*, 739–745.