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Factors Associated with Discontinuation of Bupropion and Counseling among African American Light Smokers in a Randomized Clinical Trial

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Abstract

Background—African Americans are at risk for inadequate adherence to smoking cessation treatment yet little is known about what leads to treatment discontinuation.

Purpose—Examine the factors associated with discontinuation of treatment in African American light smokers (< 10 cigarettes per day).

Methods—Bupropion plasma levels and counseling attendance were measured among 540 African American light smokers in a placebo-controlled randomized trial of bupropion.

Results—By Week 3, 28.0% of subjects in the bupropion arm had discontinued bupropion and only moderate associations were found between plasma levels and self-reported bupropion use ($r_s=0.38$). By Week 16, 36.9% of all subjects had discontinued counseling. Males had greater odds of discontinuing medication (OR=2.02, 95% CI, 1.10–3.71, $p=0.02$) and older adults had lower odds of discontinuing counseling (OR=0.96, 95% CI, 0.94–0.97, $p<0.0001$).

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Conflicts of Interest Statement

Dr. Benowitz serves as a consultant to Pfizer Pharmaceuticals, Inc. and has been a paid expert witness in litigation against tobacco companies; no Pfizer funds were used in this work. Dr. Tyndale has consulted for Novartis and McNeil.

Conclusions—Bupropion and smoking cessation counseling are underutilized even when provided within the context of a randomized trial. Future research is needed to examine strategies for improving treatment utilization among African American smokers.

Keywords

Smoking cessation; discontinuation of treatment; African Americans

Cigarette smoking is the leading cause of preventable morbidity and mortality in the United States, with a disproportionately higher burden among low-income populations and in some racial and ethnic minority groups, including American Indians/Alaska Natives and African Americans (1). Nearly 75% of African American smokers use 10 or fewer cigarettes per day and, therefore, can be described as light smokers (2). Although African Americans smoke fewer cigarettes per day than the general population, they have the highest incidence rates for all cancers combined and a 43–55% higher smoking-attributable lung cancer risk compared to Whites (3). Successful treatment of African American smokers, particularly light smokers, is a clear public health priority (4).

Adherence, or the extent to which a person's behavior corresponds to recommendations from a health care provider, is a primary determinant of treatment success (5). Current *Clinical Practice Guidelines* recommend that pharmacotherapy and behaviorally-oriented smoking cessation counseling be offered to all smokers who are interested in quitting (4). Greater adherence to smoking cessation pharmacotherapy (6–8) and counseling sessions (9, 10) has been consistently associated with higher rates of smoking abstinence. Consistent predictors of adherence to *smoking cessation pharmacotherapy* in randomized clinical trials include older age, male gender, higher body mass index, early smoking abstinence, fewer baseline cigarettes per day, greater number of recent quit attempts, greater confidence in taking the medication, higher stress, higher baseline carbon monoxide (a marker of tobacco exposure), and less severe early medication side effects (6, 7, 11). Factors associated with adherence to *smoking cessation counseling* in randomized trials include older age, male gender, higher educational level, lower levels of nicotine dependence and withdrawal, smoking fewer cigarettes per day, and limited history of depression (10, 12).

However, existing studies have methodological flaws that limit their generalizability. First, nearly all rely on self-reported adherence, which tends to overestimate actual adherence (5) and wide variability has been used for defining adherence. Second, the existing studies lack a conceptual model for understanding predictors of adherence to pharmacotherapy and counseling. Third, and most notably, nearly all of the subjects are White, moderate to heavy smokers (15 cigarettes per day) who differ from African American light smokers in smoking characteristics, beliefs about treatment, and overall rates of treatment adherence and cessation (13). This study improves upon previous studies by using plasma drug levels, a biological marker of medication actually taken that is generally deemed the most accurate indicator of medication use (14), and by using an overarching conceptual model to guide the understanding of factors that may explain treatment utilization among African American smokers.

While smoking cessation pharmacotherapy adherence is an issue across all populations, population-based studies (15, 16) and randomized clinical trials (17, 18) suggest that African American smokers are at greater risk for suboptimal adherence compared to White smokers. Racial and ethnic minorities encounter unique barriers that may influence their initiation, utilization, and response to treatment (19). The Information-Motivation-Behavior Skills Model of Adherence has been widely applied to health behaviors and asserts that adherence is more likely if individuals have adequate *information/knowledge* about their condition and

the importance of treatment, positive attitudes and beliefs about the experience of treatment and its outcome (*personal motivation*), support from important others (*social motivation*), and confidence in their ability to carry out treatment as prescribed (*behavioral skills*) (20). The model also asserts that *situational* and *individual* factors such as stress, mental health, economic, family, and substance use issues influence the ability of information, motivation, and behavioral skills to be successfully applied to treatment adherence.

Several factors in the Information-Motivation-Behavior Skills Model may help to explain lower rates of smoking cessation treatment adherence in African American smokers. On average, African Americans in the United States are of lower socioeconomic status (SES) than Whites (21). Smokers of low SES encounter more stress than high SES individuals (22) and they often have less social support and resources for quitting that may adversely impact their ability to carry out treatment as prescribed (23). African Americans have less favorable attitudes toward smoking cessation pharmacotherapy compared to Whites, including stronger belief that pharmacotherapy isn't needed and concern about safety and addictive potential (24). Negative beliefs in racial/ethnic minorities are particularly pronounced for bupropion and varenicline because these medications are more likely than nicotine replacement therapies to be seen as 'medicine' that alters the mind and causes harmful side effects (25). African American men express negative views about cessation-related behavioral counseling (25), which may make adherence to behavioral counseling alone or in combination with pharmacotherapy less likely for African American men compared to women.

Variables across several domains of the Information-Motivation-Behavior Skills model were collected within the context of this study, including beliefs about the study medication and motivation to quit (*personal motivation*), social support (*social motivation*), and confidence to quit (*behavioral skills*). Situational and individual factors known to impact continuation of treatment were also collected, including previous use of pharmacotherapy, withdrawal, craving, nicotine dependence, adverse events, stress, depression, negative affect, alcohol use, and income (6, 7, 10–12), allowing for examination of how these factors explain lower rates of pharmacotherapy and counseling utilization in African American smokers. It is important to note that the study from which the current data were drawn was not designed a priori to test the Information-Motivation-Behavior Skills Model of Adherence. While this model provides a useful framework for understanding variables examined within the context of this study, the current study is not fully testing an Information-Motivation-Behavior Skills conceptual model.

Light smokers have been traditionally excluded from randomized trials because of the misconception that they are less addicted and can quit without the help of medication or counseling (13). A clear association has been established between pharmacotherapy/counseling use and smoking abstinence for Whites, but the evidence for African Americans is mixed. In one of the first randomized clinical trials, African American light smokers clearly benefited from adherence to counseling; however adherence to nicotine gum decreased the likelihood of quitting (12). A second study found low rates of abstinence among African American moderate and heavy smokers (>10 cigarettes per day) despite high rates of adherence to varenicline (86.1%) (26). These studies raise interesting questions about the benefit of treatment utilization, particularly use of pharmacotherapy, on smoking abstinence in African American smokers that warrant further attention.

The aims of this study were twofold: First, we examined the association between discontinuation of treatment and smoking cessation in African American light smokers, hypothesizing that subjects who continued bupropion and counseling would be significantly more likely to quit smoking than those who discontinued bupropion and counseling. Second,

we identified characteristics of African American light smokers most at risk for early discontinuation of smoking cessation treatment. Guided by the Information-Motivation-Behavior Skills Model, we hypothesized that subjects who discontinued bupropion and counseling would have lower motivation and confidence to quit, less social support, and less favorable attitudes about the study medication. We also hypothesized that subjects who discontinued bupropion and counseling would be younger, male, and smoke fewer cigarettes per day, be less likely to have used pharmacotherapy in their last quit attempt, have lower levels of nicotine dependence, baseline withdrawal and craving and higher levels of depression, stress, negative affect, and impulsivity, and report greater use of alcohol and study-related adverse events than subjects who continued bupropion and counseling.

Method

Study Design

Data for this study come from *Kick it at Swope III* (KIS III), a randomized, placebo-controlled trial that evaluated the efficacy of sustained release bupropion in combination with health education counseling for smoking cessation among African-American light smokers (< 10 cigarettes per day) described previously(18). Five hundred and forty African-American light smokers recruited from the Kansas City area were randomly assigned to an active bupropion and health education counseling condition (n = 270) or to a placebo and health education comparison condition (n = 270). Subjects received pharmacotherapy treatment (bupropion or placebo) for 7 weeks and health education counseling from Weeks 0–16. All procedures for the parent randomized clinical trial were approved and monitored by the University of Kansas Medical Center Human Subjects Committee.

Eligibility

Inclusion and exclusion criteria are described in detail elsewhere (18). In brief, eligible individuals self-identified as African-American, were age 18 or older, interested in stopping smoking, and smoked < 10 cigarettes per day. Subjects were excluded if they had medical contraindications for bupropion,(18) including use of medications to treat depression and anxiety; history of a cardiovascular event in the past month; history of seizures, bulimia or anorexia nervosa; alcohol/substance abuse history; current use of nicotine replacement therapy; pregnant, contemplating pregnancy, or breast feeding. Subjects were also excluded if they were planning to move from the area, or another smoker in the household was enrolled in the study.

Intervention

Bupropion SR or placebo—At baseline (Week 0), a research assistant gave each subject a 7-week supply of bupropion SR 150 mg or placebo. Because both subjects and investigators were blinded to the pharmacotherapy condition, all subjects received a one-page information sheet on bupropion (e.g., what it is, how it works, what to expect). Subjects were also instructed to take the medication according to standard dosing guidelines (i.e., one 150 mg tablet once a day from Days 1–3 followed by one 150 mg tablet twice a day from Day 4 through Week 7). A quit day was scheduled for 7 days after initiation of the medication.

Health education counseling—Health Education counseling that was consistent with the *Clinical Practice Guidelines for Treating Tobacco Dependence* provided information about the risks of continued smoking and the benefits of quitting, developed a quit plan, and discussed strategies for successful quitting, recognizing and managing withdrawal and craving, and overcoming barriers to abstinence (4). Because adherence was not a focus of the parent study, medication use was generally not discussed. Subjects were asked if they

had any questions regarding the medication during their second counseling visit (Week 1). Medication use and/or subject's experience with the medication was discussed at other counseling visits only if initiated by the subject. Counseling was provided to subjects in both arms of the study in person at Weeks 0, 1, 3, 7 and by phone at Weeks 5 and 16. Sessions were conducted by trained counselors and were audiotaped and monitored for fidelity during weekly supervision with a PhD-level psychologist. Sessions lasted 15–20 minutes.

Quit smoking guide—At baseline, all subjects received the 36-page *Kick It at Swope Stop Smoking Guide*. This guide was developed and used for African American light smokers in a previous clinical trial (17) and included information on the disproportionate effects of tobacco on African American smokers and the health consequences of tobacco use and benefits of quitting.

Measures

Smoking Status

Smoking status at weeks 3 and 26 was measured among self-reported quitters using salivary cotinine. Salivary cotinine analysis was conducted using gas chromatography (27), with the standard cut-point of 15 ng/ml used to differentiate smokers (> 15 ng/ml) from non-smokers (< 15 ng/ml) (28).

Independent Variables

All questionnaire items were read to subjects by trained research assistants at baseline.

Personal Motivation

Motivation—Motivation to quit smoking was measured using a single item that has been reliably found to predict health behavior change (29), “On a scale of 0 to 10, with 0 being ‘not at all important’ and 10 being ‘extremely important,’ how important is it to you to quit smoking completely or stay quit after your quit date.”

Beliefs about the study medication—Beliefs about the study medication were assessed at week 7 using a single item that asked subjects to rate how helpful the medication was in helping them to quit smoking on a 5-point scale ranging from ‘not at all helpful’ to ‘very helpful’ (11).

Social motivation

Social support—Social support was measured using the 12-item Interpersonal Support Evaluation List (30) This measure yields both a summary score and subscale scores across the domains of appraisal, belonging, and tangible support.

Behavioral Skills

Confidence—Subject's confidence in their ability to quit smoking was measured using a single item that has been reliably found to predict health behavior change (29), “On a scale of 0 to 10, with 0 being ‘not at all confident’ and 10 being ‘extremely confident,’ how confident are you that you could quit smoking completely or stay quit after your quit date,” with higher scores indicating greater confidence in their ability to quit.

Individual and Situational Factors

Demographic characteristics—Subjects were asked to indicate their age, gender, marital status, current number of cigarettes smoked per day, and type of cigarette smoked (menthol or non-menthol) using standardized questionnaires (31).

Alcohol use—Alcohol use in the past month was assessed using the AUDIT-C (32). Specifically, subjects were asked to consider a ‘drink’ a can or bottle of beer, a glass of wine, a wine cooler, a cocktail, or a shot of liquor and to indicate, for the days that they drank in the past 30, how many drinks they consumed on average.

Socioeconomic status—Educational attainment and monthly family income were assessed at baseline and used to indicate socioeconomic status (31).

Self-reported medication use—Self-reported use of bupropion was assessed at week 3 using the 3-Day Recall, a standardized measure that asks subjects to recall the number of pills they took yesterday, two days ago, and three days ago (33). This measure yields a percent adherence for each subject, calculated by dividing the total doses taken in the past three days by the total possible doses. Importantly, the 3-Day Recall captured adherence to bupropion over the same 3-day window detected by the plasma bupropion levels. The threshold of 5 out of 6 pills was used to differentiate self-reported continuation of bupropion (≥ 5 pills taken in past 3 days) from self-reported discontinuation of bupropion (< 5 pills taken in the past 3 days) because it is consistent with the levels of adherence (80% or greater) considered optimal for achieving maximum effects in other clinical trials (34).

Depression—The 10-item Center for Epidemiologic Studies Short Depression Scale was used at baseline to assess depressive symptoms experienced in the past week (35).

Positive and Negative Affect—The 20-item Positive and Negative Affect Scale (PANAS) was administered at baseline to measure positive (e.g., the extent to which a person feels alert, active, and enthusiastic) and negative (e.g., the extent to which a person experiences anger, anxiety, and fear) affective states during the past week (36).

Impulsivity—Impulsivity was measured at baseline using the 4-item Reward Responsiveness subscale of the Behavioral Inhibition System/Behavioral Activation Scale (37). Items measure the degree of positive response to anticipation of a reward with higher scores indicating a greater impulsivity. Impulsivity has been found to negatively impact health behaviors, including quitting smoking, and may also influence continuation of smoking cessation treatment. Specifically, individuals who are more sensitive to reward may discontinue treatment because treatment is less rewarding than continuing smoking (38).

Stress—Subject’s self-appraisal of the amount of stress they experienced in the past month was measured using the 4-item Perceived Stress Scale (39).

Withdrawal—Withdrawal from nicotine was measured using the 8-item Minnesota Nicotine Withdrawal Scale (40), which asks subjects to rate the degree to which they have experienced eight common withdrawal symptoms (e.g., craving, irritability, difficulty concentrating) in the past 24-hours.

Craving—Craving to smoke was measured using the brief version on the Questionnaire for Smoking Urges (41). The Questionnaire for Smoking Urges-Brief consists of 10 items (e.g., ‘I have a desire for a cigarette right now’) that reflect intensity of smoking-related cravings.

Nicotine dependence—Nicotine dependence was assessed using the ‘time to first cigarette of the day’ item from the Fagerström Test for Nicotine Dependence (42). This single item has been found to be a strong measure of nicotine dependence and predictor of nicotine exposure in light smokers (43). Responses are collapsed into two categories, ‘smoking within 30 minutes of waking’ or ‘smoking after 30 minutes of waking,’ with smoking within 30 minutes of waking indicating greater nicotine dependence.

Adverse events—Adverse events were assessed and graded at Weeks 1, 3, 5, 7, and 16 using standard questions from the National Cancer Institute’s Common Toxicity Criteria for Adverse Events version 3.0 (grade 1= mild Adverse Event to grade 5=death-related adverse event) (44). Because there was a relatively low prevalence of adverse events reported and very few were moderate to severe (18), the experience of adverse events was collapsed into two categories for the purpose of this study; *any* experience of an adverse event during the study or *no* experience of an adverse during the study.

Use of pharmacotherapy during last quit attempt—Subjects were asked to indicate if they had used nicotine gum, patch, nasal spray, inhaler, bupropion, nortriptyline, or varenicline during their last quit attempt. Responses were captured as a dichotomous variable: ‘used/did not use pharmacotherapy during the last quit attempt.’

Outcome Variables

Discontinuation of bupropion and discontinuation of counseling were treated as separate outcome variables because discontinuation of bupropion could only be analyzed in those randomized to the bupropion arm (n=270), while discontinuation of counseling could be analyzed in all subjects (n=540). In addition, medication use was not discussed within the context of counseling and, for subjects in the bupropion arm, there was no difference in the rate of continuation of counseling between those who continued and those who discontinued bupropion (82.5% versus 73.5%, $p=0.13$). Finally, literature suggests that the factors associated with adherence to medication are different from those associated with adherence to counseling so modeling these two outcome variables provided the opportunity to identify unique factors that place African American light smokers at risk for discontinuation of bupropion separately from discontinuation of counseling.

Discontinuation of Bupropion

Plasma was drawn at Week 3 for assessment of bupropion levels. Plasma levels represent medication actually taken and are generally deemed the most accurate measure of medication use (14). Week 3 was selected as the time point for sampling to allow adequate time for bupropion to reach steady state following the initiation of medication (45).

There are no definitive bupropion values that establish levels of adherence. Typical steady state bupropion levels in fully adherent individuals taking 150 mg bid (300 mg/day), the dose used in this study, are 61–80 ng/ml (45). However, there is much individual variability in the pharmacokinetics of bupropion (46), with factors such as age, body weight, and bupropion metabolism genotype (i.e., *CYP2B6*) all influencing plasma bupropion levels (46–48). In addition, the level of 61–80 ng/ml associated with full adherence comes from studies of predominately white smokers that cannot be applied to African Americans. The majority of Blacks (64%) versus 44% of Whites have at least one copy of a *CYP2B6* reduction-of-function allele that causes them to metabolize bupropion at a slower rate, thereby altering bupropion plasma levels (47, 49). No literature exists on expected bupropion plasma levels in a sample of fully adherent subjects where the majority - 65% in our sample (46)- were intermediate and slow metabolizers of bupropion, and there was no

way of establishing that cut-point with our data because the day/time that subjects took their last dose of bupropion was not collected.

Given these limitations, the cut-point of detectable versus undetectable plasma bupropion levels used in this study were conservative. The half-life of bupropion is 10–20 hours, meaning that in a person who had achieved steady state, after 3–5 days of not taking bupropion the level would be at or below the limit of quantitation of our assay (1 ng/ml). We sought evidence of subjects taking bupropion in that time frame, and therefore we used the limit of quantitation as a cut point for defining medication use. Discontinuation of bupropion was defined as having bupropion plasma levels below the limit of quantitation (< 1.0 ng/ml) at Week 3, while continuation of bupropion was defined as having bupropion plasma levels at or above the limit of quantitation (≥ 1.0 ng/ml). Because subjects and staff were blinded to treatment condition, plasma was collected from all subjects. Chemical analysis was performed by liquid chromatography mass-spectrometry as described elsewhere (50).

Discontinuation of Counseling

Subjects received six health education counseling sessions from Weeks 0–16 and attendance at each session was recorded. Discontinuation was defined as attending less than 5 of the 6 health education counseling sessions ($< 83\%$ of sessions), while continuation of counseling was defined as attending 5 or more health education counseling sessions ($\geq 83\%$ of sessions). This cut-point is consistent with other studies (12) and with the threshold of 80%–95% attendance that is commonly used for treatments of similar duration and intensity (34).

Data Analysis

Two separate logistic regression models were used to examine the association between continuation of bupropion/counseling and smoking cessation (study aim 1). The first model, examined only among the subjects randomized to the bupropion arm ($n=270$), provided an estimate of the likelihood of quitting in subjects with detectable compared to undetectable bupropion plasma levels. Cotinine-confirmed smoking status at Week 3 was entered as the dependent variable and bupropion use at Week 3, derived from plasma levels, was entered as the independent variable. The second model, examined among all subjects ($n=540$), provided an estimate of the likelihood of quitting in subjects who continued counseling compared to those who discontinued counseling. In this model, cotinine-confirmed smoking status at Week 26 was entered as the dependent variable, global counseling utilization from Weeks 0–16 was entered as the independent variable, and treatment group (1=bupropion; 0=placebo) was entered as a control variable.

An iterative approach was used to identify the characteristics of African American light smokers most at risk for early discontinuation of bupropion and counseling (study aim 2). First, categorical-level independent variables were compared between treatment utilization group (i.e., discontinued bupropion/counseling versus continued bupropion/counseling) using the chi-square test and continuous variables were compared using the two sample *t* tests. These analyses yielded a set of univariate predictors of discontinuation of bupropion and discontinuation of counseling. Second, separate multiple logistic regression analyses with full stepwise and best subset variable selection procedures were performed to identify a set of multiple predictors of discontinuation of bupropion and discontinuation of counseling. Since counseling utilization was evaluated across both treatment groups (i.e., those randomized to bupropion and placebo), a design effect was incorporated into each of the modeling iterations for discontinuation of counseling. Model size selection for both models was based on the evaluation of the change of the best model's chi-squared statistic relative to the corresponding change in model degrees of freedom. Univariate factors associated with discontinuation of bupropion and discontinuation of counseling at $p < 0.20$ were included in

the model selection process. All two-way interactions were then assessed for the final set of predictors. The subsets of predictors in the final models were all statistically significant ($p < 0.05$).

Results

Of the 270 subjects in the bupropion arm, 51 were lost to follow-up at week 3 and 5 did not provide blood, leaving a final sample of 214 subjects. Of these 214, 60 (28.0%) had bupropion plasma levels below the limit of quantitation (< 1.0 ng/ml) and were classified as having discontinued their medication and 154 (72%) had bupropion plasma levels at or above the limit of quantitation (≥ 1.0 ng/ml) and were classified as continuing their medication. The median bupropion plasma level among the 154 subjects still using medication was 45.8 ng/ml (range = 1.1 ng/ml – 234.0 ng/ml). Of the 540 subjects included in the counseling analysis, 199 (36.9%) attended less than 5 of 6 possible counseling sessions and were classified as having discontinued counseling and 341 (63%) attended 5 or 6 of the 6 possible counseling sessions and were classified as continuing counseling.

Association between Continuation of Bupropion/Counseling and Smoking Abstinence

Logistic regression models revealed significant associations between continuation of bupropion/counseling and cotinine-confirmed smoking abstinence. Among the subjects randomized to bupropion, those who continued bupropion (i.e., detectable Week 3 bupropion plasma levels) had 2.13 greater odds (95% CI, 1.03–4.78, $p=0.05$) of quitting smoking at Week 3 than subjects who had discontinued bupropion (i.e., undetectable bupropion plasma levels) (29.9% versus 16.7%). Similarly, controlling for treatment (bupropion versus placebo), subjects who continued counseling (i.e., attended ≥ 5 sessions) had 6.39 greater odds of (95% CI, 2.70–15.12, $p<0.0001$) quitting smoking at Week 26 than subjects who had discontinued counseling (16.7% versus 3.0%).

Factors Associated with Discontinuation of Bupropion

Univariate factors—Results of the analyses examining the association of factors to discontinuation of bupropion are presented in Table 1. Of the 23 factors examined, only gender and self-reported bupropion use were found to be significantly associated with discontinuation of bupropion. Despite the fact that men comprised only 35.6% of the sample, 50% of those who discontinued bupropion were men ($p=0.02$). Similarly, while 75.2% of the sample reported being adherent to their medication in the last 3 days (i.e., 5 or more doses taken), 49.2% were classified as discontinuing bupropion by their plasma level ($p<0.001$). Further analysis revealed only a moderate association between Week 3 bupropion plasma levels and self-reported medication use per the 3-Day Recall ($r_s=0.38$, $p<0.0001$). Four additional factors, craving ($p=0.13$), positive affect ($p=0.07$), education ($p=0.15$), and perceived helpfulness of bupropion ($p=0.19$), were under the $p<0.20$ level that was set for inclusion in the multiple logistic regression model. All other factors did not differ significantly between subjects who continued bupropion and those who did not ($p>0.05$) and did not meet criteria for inclusion in the final multiple logistic regression model ($p>0.20$).

Final multiple logistic regression model—Gender, self-reported bupropion use, craving, positive affect, education, and perceived helpfulness of bupropion were tested for inclusion in a final multiple logistic regression model of factors associated with discontinuation of bupropion. Gender was the only factor retained in the final model, with men having 2.02 greater odds of discontinuing bupropion at Week 3 than women (95% CI, 1.10–3.71, $p=0.02$).

Factors Associated with Discontinuation of Counseling

Univariate factors—Results of the analyses examining the association of factors to discontinuation of counseling are presented in Table 2. Of the 21 factors examined only age, use of menthol cigarettes, and the experience of adverse events were found to significantly differ between subjects who continued counseling and those who did not. Specifically, subjects who discontinued counseling were younger (43.3 ± 10.7 versus 48.4 ± 11.2 , $p < 0.001$), more likely to smoke menthol cigarettes (89.5% menthol use versus 80.3% menthol use, $p < 0.01$), and more likely to experience *no* adverse events during the 16 week treatment period (73.4% versus 65.1%, $p = 0.05$). Three additional factors, alcohol use ($p = 0.14$), perceived stress ($p = 0.14$), and pharmacotherapy use during the last quit attempt ($p = 0.19$), were under the $p < 0.20$ level that was set for inclusion in the multiple logistic regression model. All other factors did not differ significantly between subjects who continued counseling and those who did not ($p > 0.05$) and did not meet criteria for inclusion in the final multiple logistic regression model ($p > 0.20$).

Final multiple logistic regression model—Age, use of menthol cigarettes, adverse events, alcohol use, perceived stress, and pharmacotherapy use during the last quit attempt were tested for inclusion in a final multiple logistic regression model of factors associated with discontinuation of counseling. Treatment (bupropion versus placebo) was entered in the model because half of the subjects included in these analyses received bupropion in addition to counseling ($n = 270$) and half received placebo ($n = 270$). Over and above the effect of treatment ($OR = 0.85$, 95% CI, 0.60–1.22, $p = 0.38$) only age was retained in the final model. Specifically, for each year of age increase, subjects had lower odds of discontinuing counseling ($OR = 0.96$, 95% CI, 0.94–0.97, $p < 0.0001$). The interaction between treatment and age was not statistically significant and, therefore, was not included in the final model.

Discussion

This is one of the first studies to examine smoking cessation pharmacotherapy use measured via a biological marker of medication actually taken (i.e., plasma drug levels). As hypothesized, African American light smokers who continued bupropion were significantly more likely to quit smoking than those who discontinued bupropion. Also as hypothesized, African American light smokers who continued counseling were significantly more likely to quit smoking than those who discontinued counseling. Contrary to the misconception that light smokers can quit on their own without the help of medication and counseling, the current study suggests that continuation of both bupropion and smoking cessation counseling improves the likelihood of quitting for African American light smokers although this may be less true for men and for younger adults.

Few characteristics were associated with early discontinuation of treatment, with men having greater odds of discontinuing bupropion and older subjects having lower odds of discontinuing counseling. These findings inform clinical practice, suggesting that African American light smokers who are younger or male may benefit from more frequent follow-up, closer monitoring of treatment utilization, and strategies designed to enhance motivation and address common adherence barriers (e.g., low self-efficacy) (20). Factors such as higher educational level, fewer baseline cigarettes per day, lower levels of nicotine dependence and withdrawal, greater number of quit attempts, greater confidence in taking the medication, less stress, limited history of depression, higher baseline carbon monoxide (a marker of tobacco exposure), and less severe medication side effects have been found to predict adherence to smoking cessation pharmacotherapy and/or counseling in previous studies (6, 7, 10, 11) but these factors were not found to be significant predictors of discontinuation of bupropion or counseling in this study. In addition, factors from the Information-Motivation-

Behavior Skills Model thought to be particularly useful for explaining lower rates of smoking cessation treatment adherence in racial/ethnic minorities (e.g., beliefs about treatment) were not found to be associated with discontinuation of bupropion or counseling in the present study.

There are a number of possible reasons for the lack of associations found in this study compared to others. The parent study's focus on African American light smokers and the extensive exclusion criteria led to a relatively homogenous sample with restricted range on many of the individual (e.g., income, cigarettes per day, menthol) and situational factors (e.g., alcohol use, depression) of interest. In addition, there was limited variability on many of the motivation and behavioral factors with the sample having high motivation and confidence to quit, high levels of social support, low levels of perceived stress, limited craving, and relatively few study-related adverse events. This study also differed from those in the literature in terms of the population (i.e., White moderate to heavy smokers versus African American light smokers), who have different smoking characteristics (13) and overall rates of adherence (15, 16), and in terms of how adherence was measured and defined (i.e., self-report versus biologically confirmed).

While participants endorsed high levels of social support, motivation, and confidence to quit, the rates of discontinuation of bupropion and counseling were moderately high. Nearly 40% of subjects discontinued counseling. This is consistent with qualitative work that has documented that African American smokers, and African American men in particular, have generally negative views about participating in smoking cessation counseling and prefer group over individual counseling for cessation (25). Nearly 30% of subjects had discontinued use of bupropion by Week 3. Given the average half-life of bupropion it is likely that subjects discontinued use of bupropion at least 5 days prior to the Week 3 visit. Rates of smoking cessation pharmacotherapy use are expected to be higher in tightly controlled randomized trials (51). However, the rate of bupropion use in this study is consistent with those achieved in population-based studies where the median duration of bupropion use is 21 days and 23.9% of smokers discontinue use after 2–4 weeks (52). The most commonly cited reasons for discontinuation of pharmacotherapy are relapse to smoking, perception that pharmacotherapy is no longer needed, and medication side effects (52). Only 16.7% of subjects who discontinued bupropion in this study were successfully quit at Week 3. Similarly, 67.4% in the bupropion arm who returned at Week 3 experienced *no* adverse events. Therefore it is also unlikely that subjects discontinued bupropion because it was no longer needed (i.e., they quit) or because of treatment-related side effects.

These findings raise interesting questions about reasons for the unexpectedly high and early discontinuation of bupropion among subjects in this study. Almost 40% of subjects in the bupropion arm thought bupropion was not at all or only somewhat helpful, which is surprisingly low considering that this was a randomized clinical trial of highly motivated smokers willing to take bupropion to help them quit. Beliefs about medication are associated with treatment adherence and outcome in predominately White smokers (11, 53). Interestingly, however, this study did not find a significant association between beliefs about bupropion and the rate of discontinuation, although this may be due to our use of a single item measure to assess the perceived helpfulness of bupropion. Future studies are needed in African American smokers to include a more in-depth assessment of beliefs about smoking cessation pharmacotherapy, including beliefs about the importance of medication to quitting, the risks of medication versus the risks of continued smoking, perceptions of how smoking cessation pharmacotherapy works, its addictive potential, and the likelihood of harm (24, 54) and to examine how beliefs are associated with use of smoking cessation pharmacotherapy. Consistent with qualitative findings by Fu (25), a recent study by Lynam (55) found that African American smokers had less favorable attitudes toward pills (i.e.,

bupropion, varenicline) than nicotine replacement therapies (i.e., patch, gum, lozenge), suggesting that it may be particularly important for future studies to more closely distinguish attitudes/beliefs by medication type.

Another notable finding of this study is the incongruence between discontinuation of bupropion, as measured through bupropion plasma levels, and self-reported medication adherence. Of the nearly one-third of subjects in the bupropion arm who had discontinued use of bupropion by Week 3, half reported they had taken more than 80% of their bupropion in the last 3 days. This clear discrepancy between self-reported and biochemically-verified adherence is consistent with literature showing that patients substantially overestimate the amount of medication taken (5) and points to the importance of using objective adherence measures. For studies involving bupropion or varenicline, monitoring blood levels of medication metabolites is feasible, and is recommended when possible. For nicotine replacement therapy – i.e., nicotine patch, gum, nasal spray, inhaler, or lozenge -- therapeutic drug levels cannot be biologically confirmed because these products all use nicotine and detectable levels of nicotine/cotinine could reflect medication use or smoking. However, other biomarkers (e.g., urine anabasine, anatabine) are present in tobacco but not in nicotine replacement therapies and can be used for biochemical verification of drug use (56). When biochemical verification is not feasible, other objective measures such as electronic pill bottle caps (Medication Event Monitoring Systems) or directly observed counts of nicotine replacement therapy use have been successfully used by others, validated against blood levels, and should be considered in place of or as an adjunct to self-reported adherence (57, 58).

Limitations of this study include the lack of published literature on expected bupropion plasma levels in a sample where 65% are intermediate and slow metabolizers of bupropion. While we could say with confidence that subjects with bupropion plasma levels below the limit of quantitation were 0% adherent in the last 3–5 days, we could not draw any conclusions about the level of bupropion use among subjects with detectable levels. The median bupropion level among subjects still using medication was 45.8 ng/ml, which is somewhat lower than the 61–80 ng/ml bupropion steady state plasma levels found in other studies (45). However, our values ranged from 1.1 ng/ml to 234.0 ng/ml, representing wide variability (~ 0% to > 100% adherence) in the amount of medication taken. Bupropion plasma levels were collected at Week 3 only; therefore we cannot draw any conclusions about the trajectory of medication use or distinguish those who never took the medication from those who stopped the medication early. As research supporting the importance of adherence to smoking cessation pharmacotherapy continues to build, more studies are needed to quantify bupropion plasma levels throughout the duration of treatment. As previously mentioned, this study was not designed to fully test the Information-Motivation-Behavior Skills conceptual model. This model provides a useful framework, but connections between specific measures and the larger Information-Motivation-Behavior Skills Model are not perfect (e.g., the current study measured behavioral skills to quit smoking not skills to complete treatment) or were not assessed (e.g., information/knowledge of treatment was not collected in the current study). Thus, while the Information-Motivation-Behavior Skills Model provides a valuable way to conceptualize and explain some of our findings, a more comprehensive assessment is needed to fully test the Information-Motivation-Behavior Skills Model in African American smokers. Finally, subjects were excluded if they had medical contraindications to bupropion and, as a result, our sample was relatively healthy. While our findings generalize to other samples that are medically eligible to take bupropion to quit smoking, they may not generalize to other forms of smoking cessation pharmacotherapy (i.e., patch, lozenge, inhaler, spray, and varenicline).

In conclusion, our findings demonstrate that continuation of bupropion and health education counseling is beneficial to African American light smokers. However, rates of discontinuation of treatment were high among our motivated sample and a high degree of incongruence was found between objective and self-reported medication adherence. Given the importance of adherence to treatment outcome, future research with African American smokers should be designed to provide a more comprehensive assessment of the Information-Motivation-Behavior Skills Model. In addition, future research should assess medication adherence using objective measures, examine reasons for discontinuation of treatment, including concerns about the effectiveness, safety, and addictive potential of smoking cessation pharmacotherapy, and should identify methods to enhance continued use of treatment.

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References

1. Caraballo RS, Yee SL, Gfroerer J, Mirza SA. Adult tobacco use among racial and ethnic groups living in the United States, 2002–2005. *Prev Chronic Dis*. 2008; 5:A78. [PubMed: 18558028]
2. Trinidad DR, Perez-Stable EJ, Emery SL, et al. Intermittent and light daily smoking across racial/ethnic groups in the United States. *Nicotine Tob Res*. 2009; 11:203–210. [PubMed: 19246433]
3. Haiman CA, Stram DO, Wilkens LR, et al. Ethnic and racial differences in the smoking-related risk of lung cancer. *N Engl J Med*. 2006; 354:333–342. [PubMed: 16436765]
4. Fiore, M.; Jaen, C.; Baker, T., et al. Treating Tobacco Use and Dependence Clinical Practice Guideline: 2008 Update. Washington, DC: U.S. Department of Health and Human Services; 2008.
5. Waldroup, W.; Gifford, E.; Kalra, P. Adherence to smoking cessation treatment. In: Donohue, W.; Levensky, E., editors. *Promoting Treatment Adherence: A Practical Handbook for Health Care Providers*. Thousand Oaks, California: Sage Publications, Inc; 2006. p. 235-252.
6. Catz SL, Jack LM, McClure JB, et al. Adherence to varenicline in the COMPASS smoking cessation intervention trial. *Nicotine Tob Res*. 2011; 13:361–368. [PubMed: 21350041]
7. Hays JT, Leischow SJ, Lawrence D, Lee TC. Adherence to treatment for tobacco dependence: association with smoking abstinence and predictors of adherence. *Nicotine Tob Res*. 2010; 12:574–581. [PubMed: 20457644]
8. Shiffman S, Sweeney CT, Ferguson SG, Sembower MA, Gitchell JG. Relationship between adherence to daily nicotine patch use and treatment efficacy: secondary analysis of a 10-week randomized, double-blind, placebo-controlled clinical trial simulating over-the-counter use in adult smokers. *Clin Ther*. 2008; 30:1852–1858. [PubMed: 19014840]
9. Akkaya A, Ozturk O, Cobanoglu H, et al. Evaluation of patients followed up in a cigarette cessation clinic. *Respirology*. 2006; 11:311–316. [PubMed: 16635090]
10. Dörner TE, Trostl A, Womastek I, Groman E. Predictors of short-term success in smoking cessation in relation to attendance at a smoking cessation program. *Nicotine Tob Res*. 2011; 13:1068–1075. [PubMed: 21832273]
11. Fucito LM, Toll BA, Salovey P, O'Malley SS. Beliefs and attitudes about bupropion: implications for medication adherence and smoking cessation treatment. *Psychol Addict Behav*. 2009; 23:373–379. [PubMed: 19586156]
12. Okuyemi KS, Zheng H, Guo H, Ahluwalia JS. Predictors of adherence to nicotine gum and counseling among African-American light smokers. *J Gen Intern Med*. 2010; 25:969–976. [PubMed: 20495885]
13. Okuyemi KS, Harris KJ, Scheibmeir M, et al. Light smokers: issues and recommendations. *Nicotine Tob Res*. 2002; 4 (Suppl 2):S103–112. [PubMed: 12573172]

14. Vermeire E, Hearnshaw H, Van Royen P, Denekens J. Patient adherence to treatment: three decades of research. A comprehensive review. *Journal of Clinical Pharmacy and Therapeutics*. 2001; 26:331–342. [PubMed: 11679023]
15. Cokkinides VE, Halpern MT, Barbeau EM, Ward E, Thun MJ. Racial and ethnic disparities in smoking-cessation interventions: analysis of the 2005 National Health Interview Survey. *Am J Prev Med*. 2008; 34:404–412. [PubMed: 18407007]
16. Fu SS, Kodl MM, Joseph AM, et al. Racial/Ethnic Disparities in the Use of Nicotine Replacement Therapy and Quit Ratios in Lifetime Smokers Ages 25 to 44 Years. *Cancer Epidemiology Biomarkers & Prevention*. 2008; 17:1640–1647.
17. Ahluwalia JS, Okuyemi K, Nollen N, et al. The effects of nicotine gum and counseling among African American light smokers: a 2 × 2 factorial design. *Addiction*. 2006; 101:883–891. [PubMed: 16696632]
18. Cox LS, Nollen NL, Mayo MS, et al. Bupropion for Smoking Cessation in African American Light Smokers: A Randomized Controlled Trial. *J Natl Cancer Inst*. 2012
19. Fagan P, King G, Lawrence D, et al. Eliminating tobacco-related health disparities: directions for future research. *Am J Public Health*. 2004; 94:211–217. [PubMed: 14759929]
20. Fisher JD, Fisher WA, Amico KR, Harman JJ. An information-motivation-behavioral skills model of adherence to antiretroviral therapy. *Health Psychol*. 2006; 25:462–473. [PubMed: 16846321]
21. De-Navas-Walt, C.; Proctor, B.; Smith, J. US Census Bureau, Current Population Reports, P60–236, Income, poverty, and health insurance coverage in the United States 2007. Washington, D.C: U.S. Government Printing Office; 2008.
22. Gallo LC, Matthews KA. Understanding the association between socioeconomic status and physical health: do negative emotions play a role? *Psychol Bull*. 2003; 129:10–51. [PubMed: 12555793]
23. Adler NE, Ostrove JM. Socioeconomic status and health: what we know and what we don't. *Ann N Y Acad Sci*. 1999; 896:3–15. [PubMed: 10681884]
24. Ryan KK, Garrett-Mayer E, Alberg AJ, Cartmell KB, Carpenter MJ. Predictors of Cessation Pharmacotherapy Use Among Black and Non-Hispanic White Smokers. *Nicotine & Tobacco Research*. 2011
25. Fu SS, Burgess D, van Ryn M, et al. Views on smoking cessation methods in ethnic minority communities: a qualitative investigation. *Prev Med*. 2007; 44:235–240. [PubMed: 17175016]
26. Nollen NL, Cox LS, Nazir N, et al. A pilot clinical trial of varenicline for smoking cessation in black smokers. *Nicotine Tob Res*. 2011; 13:868–873. [PubMed: 21498427]
27. Jacob P 3rd, Wilson M, Benowitz NL. Improved gas chromatographic method for the determination of nicotine and cotinine in biologic fluids. *J Chromatogr*. 1981; 222:61–70. [PubMed: 6783675]
28. Benowitz N, Jacob P, Ahijevych K, et al. Biochemical verification of tobacco use and cessation. *Nicotine Tob Res*. 2002; 4:149–159. [PubMed: 12028847]
29. USDHHS. Behavioral Risk Factor Surveillance System (BRFSS). National Center for Chronic Disease Prevention and Promotion, Centers for Disease Control and Prevention; 2009.
30. Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. *Arch Intern Med*. 1998; 158:1789–1795. [PubMed: 9738608]
31. Giordano TP, Guzman D, Clark R, Charlebois ED, Bangsberg DR. Measuring adherence to antiretroviral therapy in a diverse population using a visual analogue scale. *HIV Clin Trials*. 2004; 5:74–79. [PubMed: 15116282]
32. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med*. 2005; 353:487–497. [PubMed: 16079372]
33. Irwin M, Artin KH, Oxman MN. Screening for depression in the older adult: criterion validity of the 10-item Center for Epidemiological Studies Depression Scale (CES-D). *Arch Intern Med*. 1999; 159:1701–1704. [PubMed: 10448771]
34. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol*. 1988; 54:1063–1070. [PubMed: 3397865]

35. Carver C, White T. Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment. *J Pers Soc Psychol.* 1994; 67:319–333.
36. Mitchell SH. Measures of impulsivity in cigarette smokers and non-smokers. *Psychopharmacology (Berl).* 1999; 146:455–464. [PubMed: 10550496]
37. Cohen S, Lichtenstein E. Perceived stress, quitting smoking, and smoking relapse. *Health Psychol.* 1990; 9:466–478. [PubMed: 2373070]
38. Resnicow K, Wallace D, Jackson A, et al. Dietary change through African-American churches: Baseline results and program description of the Eat for Life Trial. *Journal of Cancer Education.* 2000; 15:156–163. [PubMed: 11019764]
39. Hughes JR, Hatsukami D. Signs and symptoms of tobacco withdrawal. *Arch Gen Psychiatry.* 1986; 43:289–294. [PubMed: 3954551]
40. Cox LS, Tiffany ST, Christen AG. Evaluation of the brief questionnaire of smoking urges (QSU-brief) in laboratory and clinical settings. *Nicotine Tob Res.* 2001; 3:7–16. [PubMed: 11260806]
41. Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerstrom Test for Nicotine Dependence: a revision of the Fagerstrom Tolerance Questionnaire. *Br J Addict.* 1991; 86:1119–1127. [PubMed: 1932883]
42. Muscat JE, Stellman SD, Caraballo RS, Richie JP Jr. Time to first cigarette after waking predicts cotinine levels. *Cancer Epidemiol Biomarkers Prev.* 2009; 18:3415–3420. [PubMed: 19959690]
43. Program CTE. Common Terminology Criteria for Adverse Events, Version 3.0. DCTD, NCI, NIH, DHHS; Washington, DC: 2006.
44. Cohen, S.; Lichtenstein, E.; Mermelstein, R., et al. Social support interventions for smoking cessation. In: Gottlieb, B., editor. *Marshalling Social Support: Format, Processes, and Effects.* New York: Sage; 1998. p. 211–240.
45. Johnston AJ, Ascher J, Leadbetter R, et al. Pharmacokinetic optimisation of sustained-release bupropion for smoking cessation. *Drugs.* 2002; 62 (Suppl 2):11–24. [PubMed: 12109932]
46. Zhu AZ, Cox LS, Nollen N, et al. CYP2B6 and Bupropion's Smoking-Cessation Pharmacology: The Role of Hydroxybupropion. *Clin Pharmacol Ther.* 2012; 92:771–777. [PubMed: 23149928]
47. Kirchheiner J, Klein C, Meineke I, et al. Bupropion and 4-OH-bupropion pharmacokinetics in relation to genetic polymorphisms in CYP2B6. *Pharmacogenetics.* 2003; 13:619–626. [PubMed: 14515060]
48. Lerman C, Shields PG, Wileyto EP, et al. Pharmacogenetic investigation of smoking cessation treatment. *Pharmacogenetics.* 2002; 12:627–634. [PubMed: 12439223]
49. Zanger UM, Turpeinen M, Klein K, Schwab M. Functional pharmacogenetics/genomics of human cytochromes P450 involved in drug biotransformation. *Anal Bioanal Chem.* 2008; 392:1093–1108. [PubMed: 18695978]
50. Hsyu PH, Singh A, Giargiari TD, et al. Pharmacokinetics of bupropion and its metabolites in cigarette smokers versus nonsmokers. *J Clin Pharmacol.* 1997; 37:737–743. [PubMed: 9378846]
51. Walsh RA. Over-the-counter nicotine replacement therapy: a methodological review of the evidence supporting its effectiveness. *Drug Alcohol Rev.* 2008; 27:529–547. [PubMed: 18696300]
52. Balmford J, Borland R, Hammond D, Cummings KM. Adherence to and Reasons for Premature Discontinuation From Stop-Smoking Medications: Data From the ITC Four-Country Survey. *Nicotine Tob Res.* 2011; 13:94–102. [PubMed: 21147894]
53. Fucito LM, Juliano LM. Effects of instructions on responses to the nicotine patch: a laboratory study. *Psychopharmacology (Berl).* 2007; 194:475–483. [PubMed: 17619862]
54. Yerger VB, Wertz M, McGruder C, Froelicher ES, Malone RE. Nicotine replacement therapy: perceptions of African-American smokers seeking to quit. *J Natl Med Assoc.* 2008; 100:230–236. [PubMed: 18300540]
55. Lynam I, Catley D, Harris KJ, et al. African American smokers' intention to use pharmacotherapy for cessation. *Am J Health Behav.* 2012; 36:615–627. [PubMed: 22584089]
56. Jacob P 3rd, Hatsukami D, Severson H, et al. Anabasine and anatabine as biomarkers for tobacco use during nicotine replacement therapy. *Cancer Epidemiol Biomarkers Prev.* 2002; 11:1668–1673. [PubMed: 12496059]

57. Buchanan TS, Berg CJ, Cox LS, et al. Adherence to Varenicline among African American Smokers: An Exploratory Analysis Comparing Plasma Concentration, Pill Count, and Self-Report. *Nicotine Tob Res.* 2012; 19:1083–1091. [PubMed: 22367976]
58. Thompson N, Nazir N, Cox LS, et al. Unannounced telephone pill counts for assessing varenicline adherence in a pilot clinical trial. *Patient Prefer Adherence.* 2011; 5:475–482. [PubMed: 22003285]

Table 1

Association between Motivation, Behavioral, Individual, and Situational Factors^a and Continuation versus Discontinuation of Bupropion among Subjects in the Bupropion Arm (n=270)^b

	Total n=270	Continuation of Bupropion, Wk 3 (BUP level 1.0 ng/ml) n=154	Discontinuation of Bupropion, Wk 3 (BUP levels < 1.0 ng/ml) n=60	p
<i>Personal Motivation</i>				
Motivation to quit, mean (SD)	7.9 (2.1)	7.8 (2.1)	8.1 (2.0)	0.26
Bupropion 'very helpful'/'helpful' in quitting, Week 7, %	62.9	67.2	56.9	0.19
<i>Social Motivation</i>				
Social support, mean (SD)	40.1 (7.5)	40.3 (7.6)	39.4 (8.2)	0.44
<i>Behavioral Skills</i>				
Confidence to quit, mean (SD)	7.1 (3.1)	7.1 (3.7)	7.4 (3.5)	0.59
<i>Individual and Situational Factors</i>				
Age in years, mean (SD)	46.8 (11.1)	48.0 (11.4)	46.6 (9.5)	0.40
Gender, male, %	35.6	33.1	50.0	0.02
Marital status, not married or living with partner, %	66.2	67.3	58.3	0.22
Cigarettes per day, mean (SD)	8.0 (2.6)	8.1 (2.6)	7.8 (2.7)	0.34
Menthol cigarettes, %	83.0	77.9	85.0	0.25
Drinks in last 30 days, mean (SD)	4.3 (9.0)	4.6 (10.4)	4.6 (7.1)	0.94
Education, high school, %	83.6	83.6	75.0	0.15
Family income, \$1800/month, %	62.8	64.7	65.0	0.97
> 80% 3-day self-reported bupropion use, Week 3, %	75.2	84.4	49.2	<0.001
Depression, mean (SD)	7.2 (4.8)	7.2 (5.1)	7.3 (4.6)	0.87
Negative affect, mean (SD)	19.1 (7.6)	19.1 (7.8)	19.3 (8.1)	0.87
Positive affect, mean (SD)	38.4 (6.9)	38.0 (6.9)	39.9 (6.8)	0.07
Impulsivity, mean (SD)	18.8 (1.6)	18.9 (1.4)	18.7 (1.8)	0.51
Perceived stress, mean (SD)	4.9 (3.1)	5.0 (2.9)	4.6 (3.0)	0.53
Withdrawal, mean (SD)	9.0 (7.0)	9.1 (6.9)	8.9 (7.7)	0.87
Craving, mean (SD)	2.8 (1.6)	2.7 (1.6)	3.0 (1.8)	0.13
Nicotine dependence, first cig within 30 minutes of waking, %	70.7	68.8	68.3	0.94

	Total n=270	Continuation of Bupropion, Wk 3 (BUP level 1.0 ng/ml) n=154	Discontinuation of Bupropion, Wk 3 (BUP levels < 1.0 ng/ml) n=60	p
Adverse events, % experiencing no events during the 16 week treatment period, %	67.4	64.3	63.3	0.90
Pharmacotherapy not used in last quit attempt, %	72.2	72.1	75.9	0.58

^a All factors are at baseline unless otherwise noted;

^b 270 subjects were randomized to bupropion. Of these 270, 51 subjects were lost to follow-up & 5 did not provide plasma samples at Week 3, bringing the total number of subjects included in this analysis to 214.

Table 2

Association between Motivation, Behavioral, Individual, and Situational Factors^{a,b} and Continuation versus Discontinuation of Counseling among the Entire Sample (n=540)

	Total, n=540	Continuation of Counseling, Wks 0–16 ^c n=341	Discontinuation of Counseling, Wks 0–16 ^c n=199	p
<i>Personal Motivation</i>				
Motivation to quit, mean (SD)	7.9(2.0)	7.8 (2.0)	7.9 (2.0)	0.63
<i>Social Motivation</i>				
Social support, mean (SD)	39.8 (7.2)	39.7 (7.3)	40.0 (6.8)	0.67
<i>Behavioral Skills</i>				
Confidence to quit, mean (SD)	7.3 (3.4)	7.3 (3.4)	7.2 (3.6)	0.60
<i>Individual and Situational Factors</i>				
Age in years, mean (SD)	46.5 (11.3)	48.4 (11.2)	43.2 (10.7)	<0.001
Gender, male, %	33.9	35.2	31.7	0.40
Marital status, not married or living with partner, %	30.7	30.0	32.2	0.60
Cigarettes per day, mean (SD)	7.9 (2.5)	8.0 (2.5)	7.8 (2.5)	0.27
Menthol cigarettes, %	83.7	80.3	89.5	<0.01
Drinks in last 30 days, mean (SD)	4.4 (9.2)	4.8 (10.1)	3.6 (7.4)	0.14
Education, high school, %	84.1	84.3	83.4	0.69
Family income, \$1800/month, %	60.6	62.1	58.3	0.39
Depression, mean (SD)	7.7 (5.2)	7.5 (5.2)	8.0 (5.1)	0.35
Negative affect, mean (SD)	19.8 (8.0)	19.6 (8.0)	20.0 (7.9)	0.59
Positive affect, mean (SD)	37.5 (7.5)	37.3 (7.5)	37.9 (7.5)	0.37
Impulsivity, mean (SD)	18.8 (1.5)	18.8 (1.5)	18.8 (1.7)	0.78
Perceived stress, mean (SD)	5.2 (3.2)	5.1 (3.1)	5.5 (3.2)	0.14
Withdrawal, mean (SD)	9.6 (6.7)	9.5 (7.1)	9.8 (6.3)	0.62
Craving, mean (SD)	2.9 (1.7)	2.8 (1.7)	3.0 (1.6)	0.33
Nicotine dependence, first cig within 30 minutes of waking, %	72.2	71.0	74.4	0.39
Adverse event, % experiencing no events during the 16 week treatment period, %	68.1	65.1	73.4	0.05
Pharmacotherapy not used in last quit attempt, %	26.0	24.1	29.4	0.19

^a All factors are at baseline unless otherwise noted

^b Identical factors were examined as predictors of discontinuation of bupropion and discontinuation of counseling with the exception of two variables. Self-reported bupropion use and perceived helpfulness of bupropion were not analyzed as predictors of discontinuation of counseling because these variables were measured at follow-up time points (Weeks 3, 7) and responses could only be captured in subjects who returned for counseling.

^c Counseling session attendance represents global attendance across the 16 week treatment period. *Continuation of counseling* represents those who attended at least 5 out of 6 possible counseling visits. *Discontinuation of counseling* represents those who attended less than 5 counseling visits.