Predictors of cessation in African American light smokers enrolled in a bupropion clinical trial

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Abstract

Background.—This is the first study to examine predictors of successful cessation in African American (AA) light smokers treated within a placebo-controlled trial of bupropion.
Methods—We analyzed data from a randomized, double-blind, placebo-controlled trial of bupropion and health education for 540 African American light smokers. African American light smokers (≤ 10 cigarettes per day, cpd) were randomly assigned to receive 150mg bid bupropion SR (n=270) or placebo (n=270) for 7 weeks. All participants received health education counseling at Weeks 0, 1, 3, 5 and 7. Using chi-square tests, two sample t-tests, and multiple logistic regression analyses, we examined baseline psychosocial and smoking characteristics as predictors of cotinine-verified 7-day point prevalence smoking abstinence among study participants at the end treatment (week 7) and at the end of follow up (week 26).

Results—Participants who received bupropion were significantly more likely to quit smoking compared to those who received placebo (OR = 2.72, 95% CI = 1.60–4.62, P = 0.0002). Greater study session attendance (OR = 2.47, 95% CI = 1.76–3.46, P = 0.0001), and smoking non-menthol cigarettes increased the likelihood of quitting (OR = 1.84, 95% CI = 1.01–3.36, P = 0.05); while longer years of smoking (OR = 0.98, 95% CI = 0.96–1.00, P = 0.05) and higher baseline cotinine (OR = 0.97, 95% CI = 0.95–0.99, P = 0.002) significantly reduced the odds of quitting at Week 7. Conversely, at the end of follow-up (week 26), treatment with bupropion vs. placebo (OR = 1.14, 95% CI = 0.65–2.02, P = 0.64) was not significantly associated with quitting and type of cigarette smoked (menthol vs. non-menthol) did not appear in the final logistic regression model. Greater study session attendance (OR = 1.96, 95% CI = 1.44–2.66, P = 0.0001); BMI (OR = 1.03, 95% CI = 1.00–1.07, P = 0.04); and weight efficacy (OR = 1.03, 95% CI = 1.01–1.05, P = 0.01) increased the likelihood of quitting at Week 26. Similar to our findings at Week 7, longer years of smoking (OR = 0.96, 95% CI = 0.94–0.99, P = 0.01) and higher baseline cotinine (OR = 0.97, 95% CI = 0.95–0.99, P = 0.02) significantly reduced the odds of quitting at Week 26.

Conclusions—Baseline cotinine levels, number of years smoked and study session attendance are associated with both short- and long-term smoking cessation, while bupropion and the type of cigarette smoked were associated with quitting on short term only.

Keywords
African American; light smokers; bupropion; cotinine; menthol; smoking cessation

1. Introduction

Despite robust smoking cessation intervention programs in the United States, over 1.200 Americans die from smoking-related illnesses daily (CDC, 1990; Cinciripini, Hecht, Henningfield, Manley, & Kramer, 1997) and 19.3% of adult Americans still continue to smoke (CDC, 2011). Of the 45.3 million current adult smokers in the U.S in the year 2010, 68.8% were interested in quitting smoking, over half had made a quit attempt in the past year but fewer than 5% who tried to quit on their own succeeded in quitting (CDC, 2007, 2011). According to the US clinical practice guidelines, pharmacotherapy and counseling have been shown to increase the odds of quitting cigarettes smoking both in placebo-controlled trials (Fiore & Jaen, 2008; Fiore, Bailey, & Cohen, 2000) and in clinical settings (Ranney, Melvin, Lux, McClain, & Lohr, 2006; Rigotti et al., 2006; Rigotti, Munafò, & Stead, 2007). The majority of African American (AA) smokers smoke fewer cigarettes per day (cpd) than Whites (Benowitz, Bernert, Caraballo, Holiday, & Wang, 2009; Caraballo et al., 1998), are more likely to smoke mentholated cigarettes (Allen & Ünger, 2007; Castro, 2004), have slower rates of nicotine metabolism (Ho, Mwenifumbo, et al., 2009), and show higher levels of cotinine per cigarette smoked (Benowitz, Bernert, Caraballo, Holiday, & Wang, 2009; Benowitz et al., 1999; Ho, Faseru, et al., 2009). Despite smoking fewer cigarettes per day, African Americans find it more difficult to quit smoking compared to Whites (Gariti et al., 2009; Lawrence, Graber, Mills, Meissner, & Warnecke, 2003; Robles, Singh-Franco, & Ghin, 2008). While African American smokers are more likely than White smokers to have quit for at least one day during the previous year, the percentage of smokers...
who quit smoking successfully is higher among Whites than among African Americans (Lawrence et al., 2003; Robles et al., 2008). Furthermore, African Americans bear excess burden of tobacco-related morbidity and mortality compared to Whites (CDC, 2005; USDHHS, 1991).

Because African Americans are underrepresented in smoking cessation research, and little is known about effective cessation treatments in this and other under-represented minority populations (Webb, 2008), there is a critical need to investigate how best to treat racial and ethnic minority smokers (Fiore & Jaen, 2008). The Clinical Practice Guidelines specifically call for tobacco use treatment research targeting racial minorities including African Americans (Fiore et al., 2008) and there is paucity of data on treatment of light smokers Cox, Okuyemi, Choi, & Ahluwalia, 2011; Hughes, Stead, & Lancaster, 2007; S. Shiffman, 2005). The majority of African American smokers are light smokers (smoke ≤10 cigarettes per day; cpd) (Schoenborn, Adams, Barnes, Vickerie, & Schiller, 2004; Trinidad et al., 2009), and live below federal poverty level (CDC, 2008). In general, smokers with low socioeconomic status (SES) are less likely to quit smoking than the more affluent, partly because smokers of low SES generally have scarce resources for smoking cessation pharmacotherapy (Hiscock, Bauld, Amos, Fidler, & Munafo, 2011), and multiple cycles of treatment are often needed for an individual to successfully quit (Ellerbeck et al., 2009). Differential response to smoking cessation treatment by SES and among various disadvantaged ethnic groups provides a rationale for identifying specific factors that may predict and facilitate efficient and effective tailoring of smoking cessation treatment for African American light smokers.

We define “light smokers” as those who smoke ≤10 cpd (Coggins, Murrelle, Carchman, & Heidbreder, 2009; Husten, 2009; Saul Shiffman, 2009). Like heavy smokers, light smokers report nicotine dependence and experience substantial tobacco-related diseases (Bjartveit & Tverdal, 2005; Fletcher, Peto, & Tinker, 1976; Garfinkel & Stellman, 1988; Luoto, Uutela, & Puska, 2000; Rosengren, Wilhelmsen, & Wedel, 1992; Schane, Ling, & Glantz, 2010). Unfortunately, light smokers perceive less risk of disease compared to heavier smokers (Ayanian & Cleary, 1999), and the proportion of those who are light smokers continues to increase in the United States (Schane et al., 2010). Ahluwalia and colleagues previously treated African American light smokers, evaluating nicotine gum versus placebo combined with health education (HE) counseling or motivational interviewing (MI) within a 2 × 2 factorial design randomized trial (Ahluwalia et al., 2006). Findings demonstrated the efficacy of HE counseling in doubling smoking abstinence relative to MI, but found no measurable benefit of nicotine gum (Ahluwalia et al., 2006). The sample of light smokers demonstrated variations in daily smoking patterns and a wide range of baseline cotinine levels, suggesting that dosing using nicotine replacement might be challenging. Advancing the treatment of light smokers is therefore crucial. The current study evaluated the use of sustained release bupropion, a non-nicotine medication shown to be effective in producing abstinence in African American moderate to heavy smokers (≥10 CPD) (Ahluwalia, Harris, Catley, Okuyemi, & Mayo, 2002), for light smokers. Bupropion is an effective first-line medication for tobacco use treatment, shown to approximately double abstinence rates at 6 months compared to placebo (Ahluwalia et al., 2002; Fiore et al., 2008; Hughes, Stead, & Lancaster, 2007).

Several predictors of successful smoking cessation treatment have been identified. These include gender, age, age at smoking initiation, history of previous quit attempts, depression, anxiety, nicotine dependence including amount of cigarettes smoked, alcoholism, motivation, social/familial environment, and presence of smokers in the household and workplace (Boardman, Catley, Mayo, & Ahluwalia, 2005; Chandola, Head, & Bartley, 2004; Coppotelli & Orleans, 1985; Curry, Grothaus, & McBride, 1997; Scharf & Shiffman, 2005).
Among African American smokers who smoked more than 10 cigarettes per day enrolled in a placebo controlled trial, participants who received bupropion treatment were more than twice as likely to quit smoking at the end of treatment compared to participants who received placebo; smoking within 30 minutes of waking and higher salivary cotinine levels at baseline reduced the likelihood of quitting (Harris et al., 2004). Among African American light smokers enrolled in a 2 × 2 factorial, randomized clinical trial to evaluate the efficacy of nicotine gum (2 mg versus placebo) and counseling (motivational interviewing versus health education), factors which significantly increased the likelihood of quitting included health education rather than motivational interviewing counseling, older age and higher body mass index, while female gender, lower income, higher baseline cotinine and not completing all counseling sessions reduced the odds of quitting (Nollen et al., 2006).

The current study is the first to examine predictors of successful cessation in African American light smokers treated within a placebo-controlled trial of bupropion. A better understanding of the predictors of smoking cessation could help identify AA light smokers most likely to benefit from standard treatment and help recognize individuals for whom additional treatment resources may be needed.

2. Methods

2.1 Study Design

Data were obtained from the Kick It at Swope III (KIS-III) trial, a randomized, placebo-controlled trial of bupropion in combination with health education counseling (HE) for smoking cessation among African American light smokers (≤ 10 cigarettes per day; cpd) (Cox et al., 2012). Five hundred forty African American light smokers were randomly assigned to an active bupropion and HE counseling condition (n = 270) or to a placebo and HE comparison condition (n = 270). All participants received a 7-week supply of sustained release bupropion (150 mg daily for 3 days, then 150 mg twice daily) or placebo, six sessions of HE counseling, and a culturally targeted smoking cessation guide developed for African American light smokers and used previously (Ahluwalia et al., 2006). Participants were followed for a total of 6 months.

Health education (HE) included providing information about the risks of continued smoking and the benefits of quitting, developing a quit plan, outlining a concrete quit day preparation plan, discussing strategies for successful quitting, building social support, reducing stress, recognizing and managing withdrawal and craving, overcoming barriers to abstinence, and using pharmacotherapy. Recruitment methods, study methodology, and smoking abstinence outcomes are described in detail elsewhere (Cox, Faseru, et al., 2011; Cox et al., 2012; Faseru et al., 2011). Study sessions were conducted within an urban community medical clinic serving a predominantly African American population. Trial procedures were approved and monitored by the University of Kansas Medical Center’s Human Subjects Committee.

2.2 Participants

Five hundred and forty participants enrolled in the trial; eligibility criteria are described in detail elsewhere (Cox, Faseru, et al., 2011). In brief, eligible participants had to be interested in quitting smoking, ≥18 years of age, self-identify as African American or Black, smoke ≤ 10 cigarettes per day for ≥2 years, and have smoked on ≥25 days in the month prior to enrollment.
2.3 Measures

Participants completed a baseline assessment of demographic, smoking, and psychosocial characteristics. Items were derived from standardized instruments that have been described in detail elsewhere (Cox, Faseru, et al., 2011; Cox et al., 2012; Faseru et al., 2011) but are outlined briefly below. To reduce the number of variables included in the multivariable analyses, only those previously identified in the literature as being predictive of cessation or those thought to be clinically relevant were selected for evaluation as predictor variables.

2.3.1 Demographics—Baseline assessment of demographic information included age, gender, marital status, income, and education. Metric measurement of height and weight were collected to calculate body mass index (BMI).

2.3.2 Smoking characteristics—Cotinine (COT), a metabolite of nicotine found in blood, saliva, or urine, is the most widely used objective indicator of nicotine exposure (Benowitz et al., 2002). Nicotine is metabolized into cotinine (COT) (Howard, Sellers, & Tyndale, 2002; Malaiyandi, Sellers, & Tyndale, 2005; Messina, Tyndale, & Sellers, 1997; Tyndale & Sellers, 2002; Xu, Goodz, Sellers, & Tyndale, 2002). Cotinine, in turn, is metabolized into tran-3′-hydroxycotinine (3HC) (Messina et al., 1997; Nakajima et al., 1996a, 1996b). Whereas the half-life of nicotine is 2 hours, the half-life of 3HC is similar to the half-life of cotinine (16 hours); therefore, the ratio of 3HC to cotinine (3HC/COT) is fairly constant over time. Plasma 3HC/COT ratio is strongly correlated with nicotine clearance and this ratio can be a useful non-invasive marker for nicotine metabolism (Dempsey et al., 2004). For example, the 3HC/COT ratio has been shown to be significantly correlated with the number of cigarettes smoked per day in moderate and heavy smokers, suggesting that the rate of nicotine metabolism is a factor in the level of cigarette consumption (i.e., rapid metabolizers would need more nicotine and therefore would smoke more, while slower metabolizers would need less nicotine and would smoke less) (Benowitz, Pomerleau, Pomerleau, & Jacob, 2003). Cigarette per day has been found to be only modestly correlated with plasma cotinine in light smokers and therefore has not been a useful marker of nicotine intake in light smokers (Ho, Faseru, et al., 2009). We collected and assessed serum cotinine as a biomarker of tobacco use at baseline. We also measured serum nicotine and calculated nicotine per cpd, cotinine per cpd and 3hydroxycotinine/cotinine ratios. Self-reported smoking history included cigarettes per day, type of cigarettes used (menthol or non-menthol), depth of inhalation, number of years smoked, number of quit attempts in the past year, and use of pharmacotherapy in the most recent quit attempt. A single item was used from the Fagerström Test for Nicotine Dependence (FTND) to assess how soon after waking the first cigarette of the day was smoked as an indicator of nicotine dependence (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991). Responses were collapsed into two categories: smoking within 30 minutes of waking or smoking after 30 minutes of waking. The degree to which participants reported smoking for weight control and concerns over post-cessation weight gain were measured using 6-item Weight Concerns Scale (WCS) (Borrelli & Mermelstein, 1998a). Confidence to prevent post-cessation weight gain was assessed using the 6-item Weight Efficacy after Quitting Scale (Borrelli & Mermelstein, 1998a).

2.3.3 Psychosocial characteristics—Social support items included an assessment of the presence of other smokers in the home (Okah, Choi, Okuyemi, & Ahluwalia, 2002) and the 12-item Interpersonal Support Evaluation List (ISEL) that provides a global level of social support (Cohen et al., 1998). The ISEL measured domains of appraisal (perceived availability of someone to talk to about problems), belonging (perceived availability of people to do things with), and tangible support (perceived availability of material aid) (Cohen et al., 1998). The 4-item Perceived Stress Scale measured self-appraised global life
stress in the past month (Cohen & Lichtenstein, 1990). The Positive and Negative Affect Scales (PANAS) were administered to measure different positive (e.g., high energy, full of concentration) and negative (e.g., anger, fear) affective states (Watson, Clark, & Tellegen, 1988). The Center for Epidemiologic Studies Short Depression Scale (CESD-10) was used to assess distress associated with depressive symptoms (Irwin, Artin, & Oxman, 1999).

2.3.4 Outcome Variable—Cotinine-verified 7-day point prevalence smoking abstinence, defined as no cigarettes (not even a puff) in the previous 7 days at Week 7 (end of drug treatment), validated using salivary cotinine was our outcome variable (Benowitz et al., 2002). The cotinine cut-point of 15ng/ml was used to differentiate smokers from nonsmokers (Cummings & Richard, 1988).

3. Statistical Analyses

We analyzed data to identify predictors of abstinence among all participants (n=540) at the end of treatment (Week 7) and follow up (Week 26) while imputing those lost to follow-up as smokers. This approach enables us to describe participants who have or have not responded to drug at the end of the medication phase and also determine the predictors of sustained abstinence after the medication phase. Categorical variables were summarized by frequencies and percentages. Continuous variables were summarized by means and standard deviations. Categorical variables were compared between smoking status using the chi-square test and continuous variables were compared using two sample t tests. Given the known effect of treatment (bupropion SR vs. placebo) on quitting (Cox et al., 2012), treatment was included in the regression model. This approach allowed us to examine individual predictors of cessation over and above the effects of treatment. Factors whose individual association with cessation resulted in a p-value less than or equal to 0.10 were considered for inclusion in the regression model. Multiple logistic regression analysis with full stepwise and best subset variable selection procedures were performed to identify predictors of cotinine-verified 7-day point prevalence abstinence from smoking at Week 7, while controlling for treatment. The subsets of predictors in the final model were all statistically significant (p < 0.05).

4. Results

The majority of the study participants were female (66.1%), had at least a high school education (84.2%), and had a mean age of 46.5 (SD=11.3) years. Participants smoked, on average, 8.0 (SD=2.5) cigarettes per day at baseline, had cotinine levels of 275.8ng/ml (SD=155.8), had smoked for 17.6 (SD=11.9) years, and made 3.7 (SD=7.6) 24 hour quit attempts in the past year (Cox et al., 2012).

Differences in categorical and continuous baseline characteristics between abstinent and continuing smokers at Week 7 and Week 26 are presented in Tables 1 and 2. Compared to continuing smokers, participants who were abstinent were more likely to smoke non-menthol cigarettes (p<0.001 at Week 7 and p=0.005 at Week 26), had lower baseline serum cotinine (p<0.001 at Week 7 and p=0.001 at Week 26), lower serum nicotine (p<0.002 at Week 7 and p=0.005 at Week 26), higher weight efficacy (p<0.042 at Week 7 and p=0.012 at Week 26), smoked for fewer years (p=0.05 at Week 7 and p=0.006 at Week 26) and attended more counseling sessions (p<0.001 at both Weeks 7 and 26). There was no difference in body mass index (p=0.079), nicotine per CPD (p=0.332), and cotinine per CPD (p=0.588), between abstinent and continuing smokers at Week 7. However at Week 26, the differences in nicotine per CPD (p=0.031), cotinine per CPD (p=0.017), and body mass index (p=0.008) were statistically significant. There were no significant differences in
Results of the multiple logistic regression analyses are presented in Table 3. At the end of the 7-week medication phase of the intervention, the smoking abstinence rate was statistically significantly higher in the bupropion group compared with the placebo group (23.7% vs. 9.6%). Participants who received bupropion were more likely to be abstinent at Week 7 compared to those who received placebo (OR=2.72, 95% CI 1.60–4.62, p = 0.0002). Over and above the effect of treatment, four predictor variables were retained in the final model. Specifically, smoking non-menthol cigarettes (OR = 1.84, 95% CI = 1.01–3.36, p<0.05) and counseling attendance (OR = 2.47, 95% CI = 1.76–3.46, p<0.0001) at Week 7 increased the likelihood of quitting at Week 7, while longer years of smoking (OR= 0.98, 95% CI = 0.96–1.00, p<0.05) and higher baseline cotinine (OR = 0.97, 95% CI = 0.95–0.99, p=0.0022) significantly reduced the odds of quitting.

At Week 26, while there was no significant difference in abstinence rates between the bupropion group compared with the placebo group (13.3% vs. 10.0%, OR=1.14, 95% CI 0.647–2.02, p = 0.64), type of cigarette smoked (menthol vs. non-menthol) did not appear in the final logistic regression model. Counseling attendance (OR = 1.96, 95% CI 1.44–2.66, p=0.005), BMI (OR = 1.03, 95% CI 1.00–1.07, p=0.0425), and weight efficacy (OR = 1.03, 95% CI 1.01–1.05, p=0.0147), increased the odds of quitting while longer years of smoking (OR= 0.96, 95% CI = 0.94–0.99, p<0.0001) and higher baseline cotinine (OR = 0.97, 95% CI = 0.95–0.99, p=0.02) significantly reduced the odds of quitting.

5. Discussion

This paper is the first to examine predictors of successful cessation in African American light smokers treated within a placebo-controlled trial of bupropion. Following 7 weeks of treatment, predictors of smoking abstinence included treatment with bupropion, greater completion of counseling visits, lower baseline cotinine levels, use of non-menthol cigarettes, and fewer years of smoking cigarettes. While treatment with bupropion and the type of cigarettes smoked were no longer associated with quitting at Week 26 follow up, years smoked, counseling session attendance, cotinine levels, in addition to BMI and weight efficacy were factors associated with long term smoking abstinence.

African American light smokers who received bupropion were more likely to be abstinent compared to those who received placebo at Week 7 (24% vs. 13%) but not at Week 26 follow-up (13% vs. 10%), which is contrary to our previous study that found that standard bupropion treatment produced higher rates of both short (Week 7) and long-term abstinence (Week 26) compared to placebo in African American moderate to heavy smokers (≥10 CPD) (Ahluwalia, Harris, Catley, Okuyemi, & Mayo, 2002). In that study, 600 patients were randomized to receive bupropion 150 mg bid or placebo for 7 weeks and all patients participated in smoking cessation counseling. Biochemically confirmed abstinence rates at the end of 7 weeks of treatment were 36.0% in the bupropion SR group and 19.0% in the placebo group (17.0 percentage point difference; 95% confidence interval, 9.7–24.4; P<.001). At Week 26, the quit rates were 21.0% in the treatment and 13.7% in the placebo groups (7.3 percentage point difference; 95% confidence interval, 1.0–13.7; P = 0.02).

Those who were abstinent at Week 7 and Week 26 attended smoking cessation counseling more frequently than those who continued to smoke. This finding is consistent with previous studies that have shown a link between counseling adherence and improved smoking abstinence (Aveyard et al., 2007; Nollen et al., 2006; Thyrian et al., 2007). Among African American light smokers enrolled in a 2 × 2 factorial, randomized clinical trial to evaluate the efficacy of nicotine gum (2 mg versus placebo) and counseling (motivational interviewing...
versus health education), Nollen et al. (2006) found that participants who did not complete all counseling sessions were 52% less likely to quit at month 6 than participants who attended all sessions (Nollen et al., 2006). A dose–response relationship was also demonstrated between counseling attendance and cessation. Participants who attended at least 5 out of 6 smoking cessation counseling sessions were 3.3 times more likely to abstain from smoking at month 6 than those who attended fewer than 5 sessions (Nollen et al., 2006). While these findings suggest that counseling sessions and contact with research staff is beneficial and important, future studies should investigate why smokers did not attend counseling sessions, as we could not determine the reasons in the current study. It may be possible they did not attend sessions because of their level of motivation to quit, they failed to quit or because they experienced relapse.

To date, the role menthol plays in smoking cessation in response to pharmacotherapy remains unclear (Alexander, Crawford, & Mendiondo, 2010; Fagan et al., 2010; Fu et al., 2008). Our current study has demonstrated a robust effect of menthol on smoking cessation. African American light smokers of menthol cigarettes were less likely to quit smoking compared to non-menthol cigarette smokers. This finding is consistent with previous studies (Delnevo, Gunderson, Echeverria, & Steinberg, 2011; Foulds et al., 2006; Gandhi, Foulds, Steinberg, & Williams, 2009; Levy et al., 2011; K. Okuyemi et al., 2003; Stahre, Okuyemi, Joseph, & Fu, 2010; Trinidad, Pérez-Stable, Messer, White, & Pierce, 2010) and supports the Tobacco Products Scientific Advisory Committee (TPSAC) report of 2011 (TPSAC, 2011). We were able to replicate the results from the first double-blind, placebo–controlled randomized trial of bupropion in African American smokers (> 10 cpd) (Okuyemi et al., 2003). In that study, menthol smokers were less likely to be abstinent compared to non-menthol smokers. Specifically, in the group receiving bupropion, 28.3% of menthol cigarette smokers (n=417) compared with 41.5% of non-menthol cigarette smokers (n=118) were abstinent (p=0.006) while the abstinence rates were similar between mentholated cigarette smokers and non-menthol cigarette smokers among the placebo group (20.5% vs. 23.3%) (Okuyemi et al., 2003). Similarly, African American light smokers who smoked menthol cigarettes had lower cessation when treated with nicotine replacement therapy and counseling (Okuyemi, Faseru, Cox, Bronars, & Ahluwalia, 2007). On the other hand, Fu et al. conducted a secondary analysis of data from a multi-site randomized controlled trial of an intervention to facilitate repeat tobacco cessation treatment. Contrary to our findings, among 1,343 participants (54% White, 35% Black and 12% other) who had received a prescription for nicotine replacement therapy (NRT) or bupropion for smoking cessation of which 19% of Whites, 62% of Blacks, and 25% of other ethnicity smoked menthol cigarettes, the odds of quitting for menthol cigarette smokers was higher than for non-menthol smokers (adjusted odds ratio [OR] 1.31, 95% CI 0.95–1.8) (Fu et al., 2008). However the confidence interval indicates the difference was not statistically significant. By and large, the majority of the studies support the idea that menthol cigarette smoking is associated with a decreased likelihood of smoking abstinence, and the relationship is more pronounced among African Americans.

The higher prevalence of smoking menthol cigarettes may explain why African Americans generally find it more difficult to quit smoking compared to Whites despite smoking fewer cigarettes per day. More studies are needed to understand possible biologic mechanisms underlying differences in quit rates between menthol and non-menthol smokers. Menthol in cigarettes could also be a marker for another variable, (yet to be identified) related to quitting. As more evidence of cessation failures and potential harm of menthol in cigarettes emerge, TPSAC may reconsider banning menthol in cigarettes. For example, in a recent study, among a total of 5028 respondents (25.6% menthol cigarette smokers) mentholated cigarette smokers were found to have significantly increased odds of stroke compared with non-mentholated cigarette smokers (OR= 2.25; 95% CI, 1.33–3.78), and in particular...
women (OR = 3.28; 95% CI, 1.74–6.19) and non-African American smokers (OR = 3.48; 95% CI, 1.70–7.13) after adjusting for sex, age, education level, total household income, body mass index, and smoking quantity and duration (Vozoris, 2012).

We found an inverse dose-response relationship between cotinine levels and quitting. African American light smokers with higher levels of cotinine at baseline were less likely to stop smoking compared to those with lower cotinine levels. This is similar to findings reported in a study among African American smokers enrolled in a placebo controlled trial of bupropion who smoked more than 10 cigarettes per day in which higher salivary cotinine was inversely related to quitting (Harris et al., 2004). Other studies found relatively higher than expected levels of cotinine in African Americans compared to White light smokers (Faseru et al., 2011; Perez-Stable, Herrera, Jacob, & Benowitz, 1998). African Americans have been found to have slower clearance of nicotine and its proximal metabolite cotinine and to take in more nicotine per cigarette compared to Whites (Perez-Stable et al., 1998) and African American smokers have been found to be more nicotine dependent at lower levels of cigarette smoking (Edens, Glowinski, Pergadia, Lessov-Schlaggar, & Bucholz, 2010; Luo et al., 2008). From a clinical perspective, providers may be reluctant to prescribe pharmacotherapy to a light smoker or may under dose medications based on smoking fewer cigarettes per day than was tested in pivotal clinical trials. The results of this study and others suggest that AA light smokers have cotinine levels similar to White heavier smokers and, therefore, could benefit from pharmacotherapeutic interventions for smoking cessation similar to those used in clinical trials of heavier smokers.

The association between BMI and quitting in the current study is similar to findings in our previous study, where we also found that AA light smokers who had a higher BMI were more likely to quit smoking than those with a lower BMI (Nollen et al., 2006). BMI is often a marker for poorer overall health status (Flegal, Graubard, Williamson, & Gail, 2005) (Adams et al., 2006; Flegal, Graubard, Williamson, & Gail, 2007; Freedman, Ron, Ballard-Barbash, Doody, & Linet, 2006; Freedman, Sigurdson, et al., 2006). In this study, it is possible that participants with a higher BMI had other health problems or were concerned with improving their health status, and therefore, were more determined to quit.

The association between weight efficacy and quitting is similar to other studies that have found that fear of post-cessation weight gain and/or confidence in the ability to prevent post-cessation weight gain are positively associated with quitting smoking (Borrelli & Mermelstein, 1998b). The positive association between self-efficacy to control post-cessation weight gain and smoking abstinence found in this study is particularly important for AA women who have the highest rates of adult obesity (Ogden et al., 2006) and for whom quitting smoking may only seek to exacerbate tobacco- and obesity-related co-morbidities.

We explored a number of baseline psychosocial factors (depression, stress, social support, mood, weight concerns) and none of these factors was a significant predictor of cessation in this current evaluation of African American light smokers (see Table 2), although they have been found to be important predictors of cessation in other populations (Chandola et al., 2004; Curry et al., 1997; Venters et al., 1984; Venters et al., 1990). Possible explanations include limited variability in these factors among our sample—e.g., high depressive symptoms, low stress, high social support and limited weight concerns. For weight concerns in particular, we know that AA light smokers do not smoke to control or maintain their weight despite high rates of obesity (Thomas et al., 2008).

Limitations of this study have been described in greater detail elsewhere (Cox, Faseru, et al., 2011; Cox et al., 2012; Faseru et al., 2011). For example, our findings may not apply to the
general population of AA light smokers: only smokers interested in quitting and were medically eligible to take bupropion were enrolled, therefore the results of this study may be most applicable to treatment-seeking smokers.

In conclusion, this study provides insight into factors associated with successful smoking cessation in African American light smokers. Bupropion and counseling session attendance facilitated short-term smoking abstinence among African American light smokers. Higher baseline cotinine, menthol cigarette smoking, and greater number of years of smoking increased individual risk for continued smoking. Given that African American smokers consistently demonstrate higher cotinine levels and have a greater prevalence of menthol smoking compared to non-Hispanic White American smokers (Kandel & Chen, 2000; Trinidad et al., 2009), smoking cessation pharmacotherapy using Bupropion SR, improving attendance of counseling sessions and eliminating menthol in cigarettes, are necessary to enhance smoking cessation treatment in African American light smokers.

Acknowledgments
Role of Funding Sources

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References


Borrelli B, Mermelstein R. The role of weight concern and self-efficacy in smoking cessation and weight gain among smokers in a clinic-based cessation program. Addict Behav. 1998a; 23:609–622. [PubMed: 9768298]


Cox LS, Faseru B, Mayo MS, Krebhill R, Snow TS, Bronars CA, Nollen NL, Choi WS, Okuyemi KS, Salzman GA, Benowitz NL, Tyndale RF, Ahluwalia JS. Design, baseline characteristics, and


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Table 1
Baseline characteristics (categorical variables) of abstinent and continuing smokers at week 7 and week 26

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Week 7</th>
<th></th>
<th>Week 26</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>% Abstinent</td>
<td></td>
<td>% Abstinent</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>183 (33.9)</td>
<td>16.4</td>
<td>0.90</td>
<td>11.5</td>
<td>0.85</td>
</tr>
<tr>
<td>Female</td>
<td>357 (66.1)</td>
<td>16.8</td>
<td></td>
<td>12.0</td>
<td></td>
</tr>
<tr>
<td>Married or living with partner</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>373 (69.2)</td>
<td>17.4</td>
<td>0.50</td>
<td>11.8</td>
<td>0.90</td>
</tr>
<tr>
<td>Yes</td>
<td>166 (30.8)</td>
<td>15.1</td>
<td></td>
<td>11.4</td>
<td></td>
</tr>
<tr>
<td>High school graduate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>85 (15.7)</td>
<td>16.4</td>
<td>0.95</td>
<td>12.9</td>
<td>0.69</td>
</tr>
<tr>
<td>Yes</td>
<td>454 (84.2)</td>
<td>16.7</td>
<td></td>
<td>11.4</td>
<td></td>
</tr>
<tr>
<td>Income ≥$1,800/month</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>No</td>
<td>327 (60.7)</td>
<td>15.6</td>
<td>0.39</td>
<td>10.1</td>
<td>0.15</td>
</tr>
<tr>
<td>Yes</td>
<td>212 (39.3)</td>
<td>18.4</td>
<td></td>
<td>14.1</td>
<td></td>
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<tr>
<td>Smokes menthol cigarettes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>88 (16.3)</td>
<td>28.4</td>
<td>0.001</td>
<td>20.4</td>
<td>0.005</td>
</tr>
<tr>
<td>Yes</td>
<td>452 (83.7)</td>
<td>14.4</td>
<td></td>
<td>10.0</td>
<td></td>
</tr>
<tr>
<td>Smokes first cigarette within 30 min of waking b</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>150 (27.8)</td>
<td>21.3</td>
<td>0.07</td>
<td>14.0</td>
<td>0.29</td>
</tr>
<tr>
<td>Yes</td>
<td>390 (72.2)</td>
<td>14.9</td>
<td></td>
<td>10.7</td>
<td></td>
</tr>
<tr>
<td>Depth of inhalation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Into the chest</td>
<td>126 (23.3)</td>
<td>17.5</td>
<td>0.78</td>
<td>12.6</td>
<td>0.24</td>
</tr>
<tr>
<td>Into the throat, mouth, or don’t really inhale</td>
<td>414 (76.7)</td>
<td>16.4</td>
<td>8.7</td>
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<tr>
<td>Other smokers in the household</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>402 (74.4)</td>
<td>17.4</td>
<td>0.43</td>
<td>11.6</td>
<td>0.97</td>
</tr>
<tr>
<td>Yes</td>
<td>138 (25.6)</td>
<td>14.5</td>
<td></td>
<td>15.0</td>
<td>0.17</td>
</tr>
<tr>
<td>Use of pharmacotherapy on last quit attempt</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>378 (74.0)</td>
<td>16.9</td>
<td></td>
<td>10.5</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>133 (26.0)</td>
<td>17.3</td>
<td>0.92</td>
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Table 2

Baseline characteristics (continuous variables) of abstinent and continuing smokers at week 7 and week 26

<table>
<thead>
<tr>
<th></th>
<th>Overall mean (SD)</th>
<th>Week 7</th>
<th>Week 26</th>
<th>p^a</th>
<th>Abstinent, mean (SD)</th>
<th>Smoker, mean (SD)</th>
<th>p^b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>539</td>
<td>46.5 (11.3)</td>
<td>47.9 (11.6)</td>
<td>0.183</td>
<td>46.2 (11.2)</td>
<td>49.2 (11.8)</td>
<td>0.040</td>
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<tr>
<td>Cigarettes per day</td>
<td>540</td>
<td>8.0 (2.5)</td>
<td>7.7 (2.7)</td>
<td>0.250</td>
<td>8.0 (2.5)</td>
<td>8.2 (2.5)</td>
<td>0.350</td>
</tr>
<tr>
<td>Cotinine</td>
<td>536</td>
<td>275.8 (155.8)</td>
<td>220.7 (151.8)</td>
<td>&lt;0.001</td>
<td>286.9 (154.3)</td>
<td>215.2 (159.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Nicotine</td>
<td>536</td>
<td>14.1 (11.8)</td>
<td>11.3 (8.6)</td>
<td>0.002</td>
<td>14.7 (12.3)</td>
<td>11.0 (8.6)</td>
<td>0.025</td>
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<tr>
<td>Nicotine per CPD</td>
<td>536</td>
<td>2.0 (2.3)</td>
<td>1.8 (2.2)</td>
<td>0.332</td>
<td>2.1 (2.3)</td>
<td>1.4 (1.1)</td>
<td>0.031</td>
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<tr>
<td>Cotinine per CPD</td>
<td>536</td>
<td>39.0 (39.5)</td>
<td>37.0 (32.2)</td>
<td>0.588</td>
<td>39.47 (36.5)</td>
<td>27.9 (19.2)</td>
<td>0.017</td>
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<tr>
<td>3HC</td>
<td>539</td>
<td>82.7 (61.1)</td>
<td>72.9 (69.8)</td>
<td>0.138</td>
<td>84.7 (59.2)</td>
<td>74.9 (71.3)</td>
<td>0.279</td>
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<tr>
<td>Ratio 3HC Cotinine</td>
<td>530</td>
<td>0.375 (0.260)</td>
<td>0.377 (0.257)</td>
<td>0.931</td>
<td>0.374 (0.261)</td>
<td>0.421 (0.288)</td>
<td>0.369 (0.266)</td>
</tr>
<tr>
<td>Years smoked</td>
<td>540</td>
<td>17.6 (11.9)</td>
<td>15.4 (11.9)</td>
<td>0.053</td>
<td>18.0 (11.9)</td>
<td>13.7 (11.7)</td>
<td>0.006</td>
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<tr>
<td>Visit Attendance</td>
<td>540</td>
<td>4.5 (1.8)</td>
<td>5.7 (0.6)</td>
<td>&lt;0.001</td>
<td>4.3 (1.9)</td>
<td>5.6 (0.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Number of 24 hr quit attempts in past year</td>
<td>540</td>
<td>3.7 (7.6)</td>
<td>3.5 (6.1)</td>
<td>3.7 (7.9)</td>
<td>0.784</td>
<td>3.2 (4.8)</td>
<td>3.7 (7.9)</td>
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<tr>
<td>Body mass index</td>
<td>539</td>
<td>31.1 (7.9)</td>
<td>32.5 (8.6)</td>
<td>0.079</td>
<td>30.9 (7.7)</td>
<td>33.6 (9.0)</td>
<td>0.008</td>
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<tr>
<td>Weight Concern</td>
<td>540</td>
<td>26.9 (13.9)</td>
<td>27.3 (14.6)</td>
<td>0.801</td>
<td>26.9 (13.8)</td>
<td>27.6 (15.0)</td>
<td>0.702</td>
</tr>
<tr>
<td>Weight Efficacy</td>
<td>540</td>
<td>42.5 (13.0)</td>
<td>45.0 (12.4)</td>
<td>0.042</td>
<td>42.0 (13.1)</td>
<td>46.4 (11.0)</td>
<td>0.012</td>
</tr>
<tr>
<td>Social support, total score^b</td>
<td>539</td>
<td>39.8 (7.2)</td>
<td>40.1 (7.8)</td>
<td>39.7 (7.0)</td>
<td>0.677</td>
<td>39.3 (8.1)</td>
<td>39.8 (7.0)</td>
</tr>
<tr>
<td>Appraisal support^b</td>
<td>539</td>
<td>13.3 (3.0)</td>
<td>13.7 (3.0)</td>
<td>13.1 (3.1)</td>
<td>0.132</td>
<td>13.3 (3.1)</td>
<td>13.3 (3.0)</td>
</tr>
<tr>
<td>Belonging support^b</td>
<td>539</td>
<td>13.2 (2.7)</td>
<td>12.9 (2.9)</td>
<td>13.2 (2.7)</td>
<td>0.337</td>
<td>13.0 (2.8)</td>
<td>13.2 (2.6)</td>
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<tr>
<td>Tangible support^b</td>
<td>539</td>
<td>13.3 (2.7)</td>
<td>13.4 (2.9)</td>
<td>13.3 (2.7)</td>
<td>0.718</td>
<td>12.9 (2.7)</td>
<td>13.4 (2.7)</td>
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<tr>
<td>Depression^c</td>
<td>539</td>
<td>7.7 (5.2)</td>
<td>7.2 (5.4)</td>
<td>7.8 (5.1)</td>
<td>0.354</td>
<td>6.9 (5.3)</td>
<td>7.8 (5.2)</td>
</tr>
<tr>
<td>Perceived stress^d</td>
<td>539</td>
<td>5.2 (3.2)</td>
<td>5.0 (3.0)</td>
<td>5.2 (3.2)</td>
<td>0.597</td>
<td>4.8 (3.0)</td>
<td>5.3 (3.2)</td>
</tr>
<tr>
<td>Negative affect^e</td>
<td>540</td>
<td>19.7 (8.0)</td>
<td>20.0 (8.5)</td>
<td>19.7 (7.9)</td>
<td>0.733</td>
<td>19.7 (8.5)</td>
<td>19.8 (7.9)</td>
</tr>
<tr>
<td>Positive affect^e</td>
<td>540</td>
<td>37.5 (7.5)</td>
<td>38.2 (6.8)</td>
<td>37.4 (7.7)</td>
<td>0.343</td>
<td>37.5 (7.2)</td>
<td>37.5 (7.6)</td>
</tr>
</tbody>
</table>

^a ANOVA
^b Derived from the Interpersonal Support Evaluation List
^c Derived from the Center for Epidemiologic Studies Depression Scale
Derived from the Perceived Stress Scale

Derived from the Positive and Negative Affect Schedule

3HC-3Hydroxycotinine
Table 3

Final regression model of variables predicting cotinine verified quitting at week 7 and Week 26

<table>
<thead>
<tr>
<th>Week 7</th>
<th>Odds ratio (95% CI)</th>
<th>P</th>
<th>Week 26</th>
<th>Odds ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
<td></td>
<td></td>
<td>Variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment Bupropion vs Placebo&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.72 (1.60 – 4.62)</td>
<td>0.0002</td>
<td>Treatment Bupropion vs Placebo&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.14 (0.647 – 2.02)</td>
<td>0.6417</td>
</tr>
<tr>
<td>Type of Cigarette (Non-menthol vs. menthol) &lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.84 (1.01 – 3.36)</td>
<td>0.0459</td>
<td>Years smoked</td>
<td>0.964 (0.939 – 0.989)</td>
<td>0.0050</td>
</tr>
<tr>
<td>Visit Attendance&lt;sup&gt;b, c&lt;/sup&gt;</td>
<td>2.47 (1.76 – 3.46)</td>
<td>0.0001</td>
<td>Visit Attendance&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.96 (1.44 – 2.66)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Cotinine level&lt;sup&gt;b, c&lt;/sup&gt;</td>
<td>0.97 (0.95 – 0.99)</td>
<td>0.0022</td>
<td>Cotinine level&lt;sup&gt;b, c&lt;/sup&gt;</td>
<td>0.97 (0.95 – 0.99)</td>
<td>0.0201</td>
</tr>
<tr>
<td>Years smoked&lt;sup&gt;b, d&lt;/sup&gt;</td>
<td>0.98 (0.96 – 1.00)</td>
<td>0.0476</td>
<td>BMI</td>
<td>1.03 (1.00 – 1.07)</td>
<td>0.0425</td>
</tr>
<tr>
<td>Weight Efficacy</td>
<td></td>
<td></td>
<td></td>
<td>1.03 (1.01 – 1.05)</td>
<td>0.0147</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reference category- placebo, menthol  
<sup>b</sup> Visit attendance, cotinine and years smoked were modeled as continuous variables  
<sup>c</sup> The odd ratios shown is for a 10 unit change (e.g. increase of cotinine level from 20 to 30)  
<sup>d</sup> The odd ratios shown is for a 1 year unit change  
<sup>e</sup> Attendance was modeled on the continuum- integer range 0–6