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Attrition during a randomized controlled trial of reduced nicotine content cigarettes as a proxy for understanding acceptability of nicotine product standards

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Abstract

Aims—To determine (1) if nicotine content affects study attrition – a potential behavioral measure of acceptability – in a trial that required compliance with three levels of reduced nicotine content (RNC) cigarettes, and (2) if attrition is associated with subjective and behavioral responses to RNC cigarettes.

Design—Secondary analysis of a 35-day, parallel design, open-label, randomized controlled trial. After a 5-day baseline period, participants were randomized to smoke for three, 10-day periods: their preferred brand (control group), or RNC cigarettes with three nicotine levels in a within-subject, stepdown (1 group: high-moderate-low) or non-stepdown (5 groups: high-low-moderate, low-moderate-high, low-high-moderate, moderate-low-high, moderate-high-low) fashion.

Setting—A single site in Philadelphia, Pennsylvania, USA.

Participants—246 non-treatment-seeking daily smokers (M age = 39.52, CPD = 20.95, 68.3% White) were recruited from October 2007 to June 2013.

Measurements—The primary outcome was attrition. Key predictors were nicotine content transition and study period. Exploratory predictors were taste and strength subjective ratings, total puff volume, and carbon monoxide (CO) boost. Covariates included: age, gender, race, education, and nicotine dependence.

Findings—Overall attrition was 31.3% ($n = 77$): 24.1% of the control and 25.0% of the stepdown RNC cigarette groups dropped out vs. 44.6% of non-stepdown groups ($p = 0.006$). Compared with controls, attrition odds were 4.5 and 4.7 times greater among smokers transitioning from preferred and the highest RNC cigarettes to the lowest RNC cigarettes, respectively (p 's = .001 and .003).

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Providing more favorable initial taste ratings of study cigarettes decreased attrition odds by 2% ($p = .012$).

Conclusions—The majority of participants completed a 35-day trial of varying levels of reduced nicotine content cigarettes. Participant drop-out was greater for cigarettes with lower nicotine content and less in smokers reporting more favorable subjective ratings of the cigarettes.

Keywords

attrition; reduced nicotine; low nicotine; acceptability; product acceptance

INTRODUCTION

The signatories of the World Health Organization Framework Convention on Tobacco Control and the U.S. Food and Drug Administration (FDA) have the authority to set and enforce a nicotine content standard for cigarettes [1,2]. In clinical studies, reduced nicotine content (RNC) cigarettes generally decrease dependence and toxicant exposure without negatively impacting smoking behaviors, and may facilitate cessation [3–13]. This evidence demonstrates potential public health benefits of a reduced nicotine product standard, but offers little information regarding consumer acceptability of the product. Acceptability data are needed to determine if and how RNC cigarettes will be used; low acceptability could represent low abuse liability [14], indicate likelihood of alternative nicotine/tobacco product use, or signal adverse, unintended consequences (e.g., product tampering, a higher nicotine-containing product “black market”). Regulatory agencies would likely consider this information with the potential benefits and consequences of a reduced nicotine standard to address its overall public health impact [15].

Recent trials suggest that RNC cigarettes have reduced acceptability relative to own brand: smokers generally rate these products negatively [3,5,16], supplement their use with conventional cigarettes [7,9], or discontinue participation because they are unwilling to exclusively use these products [5]. These acceptability metrics, however, have limited utility given their assessment in the context of an unregulated environment with readily-available, higher nicotine-containing products in which smokers had little or no rationale for switching to RNC cigarettes. Thus, non-compliance and negative subjective ratings, as well as poor sales of industry-created RNC cigarettes [17], may not fully reflect acceptability in a regulatory environment where only RNC combustible cigarettes are available. Further, associations between these metrics and actual product use behaviors are unclear; subjective ratings of RNC cigarette characteristics such as “satisfaction from smoking” were not related to puffing behaviors or cigarette consumption in one recent trial [13], but were related to compliance in another [18].

Other proxies of acceptability may provide additional, important information as to whether smokers are likely to continue to use RNC cigarettes, and what factors might influence acceptability (e.g., immediate vs. gradual reduction). One potential proxy is study attrition, particularly during trials requiring RNC cigarette compliance. Unlike noncompliance and subjective ratings, which allow participants to remain in trials while disapproving of the product, attrition requires participants to forfeit future earnings (i.e., study compensation) to

express that dissatisfaction. Thus, when receiving participation incentives and free cigarettes, smokers' attrition is likely a strong indicator of low acceptability, at least within the context of a trial. Further, examining associations of behavioral and subjective responses to RNC cigarettes with subsequent attrition may identify additional influences on attrition and support its use as an acceptability measure.

Still, few RNC cigarette trials detail attrition rates or differences between completers and non-completers. Of those addressing the latter, attrition-distinguishing factors differ across studies. In the largest randomized controlled trial of RNC cigarettes, Donny and colleagues [7] found that non-completers were younger, less educated, and more likely to be White and male than completers. Attrition rates did not differ by smoking-related variables or assigned nicotine content. In contrast, others have found that non-completers were more nicotine dependent [5] or more likely to be female [9] than completers. Discrepancies may result from several factors, including differing RNC products, study designs, sample sizes/ populations, as well as degree of noncompliance. For example, retaining noncompliant participants may explain the lack of differences in attrition rates by assigned nicotine content in Donny and colleagues' study [7]. Exploring attrition in an environment that does not tolerate noncompliance provides a different metric that may clarify discrepant findings and provide better insight into consumer acceptance of these products when higher nicotine-containing combustible cigarettes are unavailable.

The purpose of this study was to examine the effect of RNC cigarette use on study attrition – a potential behavioral proxy of acceptability – using data from a randomized controlled trial that required product compliance [13]. Because smokers were randomized to use three types of RNC cigarettes in stepdown (i.e., progressively lowered) and non-stepdown sequences, this study was uniquely positioned to address how nicotine content reduction method (i.e., immediate vs. gradual) affected attrition. Specifically, our primary analysis examined whether attrition likelihood varied by nicotine content transition (i.e., switching from high to low vs. moderate to high RNC cigarettes), controlling for factors previously shown to influence attrition (e.g., gender). In an exploratory analysis, we also determined if subjective and behavioral responses to study-supplied cigarettes were associated with attrition to determine which factors have the greatest impact on acceptability. Thus, this study provides data on RNC cigarette acceptability without access to other nicotine products, as well as how it is affected by reduction method.

METHODS

Design

This study examined data from a 35-day parallel design, within-subject, open-label, randomized, controlled, laboratory trial ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01202942) Identifier: NCT01202942). The original trial assessed RNC cigarette effects on smoking behaviors and harm exposure by comparing an experimental group given three types RNC cigarettes in a stepdown reduction method for three 10-day periods, to a control group given their preferred brand. Specific procedural details and results are reported elsewhere [13]. Additional participants were recruited and randomized to the same three nicotine level RNC cigarettes in one of five counterbalanced non-stepdown sequences to determine the effects of reduction order. Other

than reduction order, procedures for the non-stepdown groups were identical to the stepdown and control groups.

Participants

Smokers recruited from the Philadelphia area through newspaper and internet postings or previous study participation completed a telephone interview to determine initial eligibility. Those eligible were 21 years old, smoked exclusively 15 filtered, non-menthol cigarettes per day (CPD), had smoked for five years, and were not planning to quit within two months. Participants were further excluded if they reported a psychiatric disorder other than depression, drank 25 alcohol-containing drinks per week, were currently using other nicotine-containing products or marijuana, had a past year myocardial infarction, were pregnant/lactating, had a substance use disorder within five years, or provided an exhaled carbon monoxide (CO) sample < 10 ppm at the initial laboratory visit.

Procedure

Briefly, all participants smoked their own preferred cigarettes for a 5-day baseline period. An independent database assignment tracking program then randomly allocated subjects to control, stepdown, or non-stepdown RNC groups, for three consecutive 10-day periods. Regardless of whether smokers were randomized to RNC or control groups, all participants received 25% more cigarettes than their self-reported CPD (rounded to the nearest pack) to allow for compensatory smoking by increasing daily consumption and to ensure that product supply would not be depleted if the next session was delayed (maximum of 1 day). RNC cigarettes were previously commercially available Quest® 1, 2, and 3 cigarettes (Vector Tobacco Inc., Durham, DC). Respective FTC-reported nicotine yields were 0.6, 0.3, and 0.05 mg nicotine; rod contents were estimated as 8.9, 5.1–8.4, and 0.48–1.5 mg nicotine per cigarette [9,19–21].

Laboratory visits occurred every 5 days. At each visit, participants smoked a cigarette *ad lib* to standardize time since last cigarette, and provided pre- and post-cigarette CO samples. Participants repeated this process twice more, with cigarettes interspersed by 45 minutes, using topography equipment to capture puffing behavior, and completed post-cigarette subjective rating questionnaires. RNC cigarette product switching occurred on Days 5, 15, and 25 prior to smoking the third cigarette. Participants were unaware of when switching days occurred, and how long they would use a given RNC cigarette type. Participants were not blinded to changes in packaging descriptions of nicotine content, but received no additional product information: Quest 1, 2, and 3 packages were labeled as “low nicotine”, “extra low nicotine”, and “nicotine free”, respectively. Additionally, packages contained the following nicotine yield descriptions in small text on package sides: “Quest 1 contains 0.6 mg of nicotine per cigarette”, “Quest 2 contains 0.3 mg of nicotine per cigarette”, and “Quest 3 contains only trace levels of nicotine – no more than 0.05 mg per cigarette. Written informed consent was obtained at the onset of the first visit, and all study procedures were approved by the university Institutional Review Board.

Compliance and incentives—The study consent form explicitly stated that participation required smoking only study-supplied cigarettes. Staff specified that participants did not

need to consume all provided cigarettes, and that using non-study-supplied cigarettes would result in study removal. Staff assessed noncompliance at each visit by asking participants about non-study-supplied cigarette use and through counting returned spent filters and unused study-supplied cigarettes; those who reported noncompliance at any two visits following randomization were removed. Participants were incentivized for returning spent filters and unused cigarettes that equaled the number of cigarettes distributed at the previous session. Incentives were: \$60 for completing the relatively long day 0 session, \$35 for completing behavioral measures at each session; \$25 for providing a urine sample per study period; and a \$25 bonus for proper cigarette collection per period.

Measures

Attrition—Attrition status was determined for each laboratory visit. Smokers were categorized as drop-outs if they: formally withdrew their participation, were removed due to non-compliance, or failed to attend and never rescheduled, a given visit (e.g., a participant who completed Day 10 but no sessions afterward was considered a Day 15 drop-out); there was no study re-entry. Completers were those who finished Day 35.

Primary predictors: RNC groups and transitions—Randomization occurred after the 5-day baseline period where all participants smoked their own preferred cigarettes. Participants were assigned to (1) a control group given their preferred brand, (2) the stepdown (i.e., high-moderate-low order) RNC group, or one of the five counterbalanced non-stepdown RNC groups, including: (3) low-moderate-high, (4) low-high-moderate, (5) moderate-low-high, (6) moderate-high-low, and (7) high-low-moderate orders. Due to imbalanced sample sizes within each randomization order, we were unable to test the interactive effects of nicotine content and randomization order on attrition. We instead created a variable representing each possible nicotine content transition (e.g., low to high, high to moderate), given that significant overlap in transitions occurred across groups (i.e., the high-low-moderate and moderate-high-low randomization groups both completed the high to low transition). Additionally, because all participants used their preferred brand during baseline, transitions also included preferred brand to high, moderate, and low RNC cigarettes (e.g., preferred brand to high).

Predictors of attrition in previous RNC cigarette trials—Sociodemographic and smoking-related variables previously shown to influence RNC cigarette trial attrition [5,9,14] were assessed at the initial visit and included participants': age, gender (male = reference; female), race (White = reference; non-White), highest education level (HS or less; some college or technical training; college graduate or higher = reference), and nicotine dependence as measured by the Fagerström Test for Nicotine Dependence [22].

Exploratory predictors of attrition—Additional measures explored for associations with attrition included subjective ratings, smoking behaviors, and smoke exposure. Participants rated cigarettes smoked during laboratory visits on a 14-item 100 mm visual analog scale of cigarette characteristics (e.g., taste) used by the tobacco industry [23] and previous research [16,24–26]. Anchors were item-specific (e.g., taste: 0=“very bad”; 100=“very good”); lower scores indicated negative ratings. We previously found that the

strength and taste items were most useful in discriminating RNC cigarette types [13]; thus exploratory analyses included only these two items.

Smoking behavior was assessed by total puff volume, the sum of all puff volumes taken from each cigarette smoked through topography equipment (Borwaldt KC, Richmond, VA). Smoke exposure was assessed by CO boost [16,27], the difference between pre- and post-cigarette CO values. CO samples were obtained 4 minutes before and after each cigarette (Vitalograph, Lenexa, KS).

Analytic Plan

Chi-square independence tests and unpaired t-tests compared categorical and continuous baseline measures, respectively, by attrition status. Separate generalized estimating equations (GEE) models examined differences in attrition independently by nicotine content and study period; a logistic regression model examined attrition differences by randomization group. Chi-square tests examined associations between attrition status and cigarette type at each study visit. Two GEE models then tested the primary aims of the study. For the primary analysis examining nicotine content effects on attrition (controlling for covariates), an initial GEE model regressed attrition status onto nicotine content transition, study period, age, gender, ethnicity, highest education level, and nicotine dependence. The second, exploratory model retained only significant predictors from the previous model, and added covariates of: strength and taste subjective ratings, CO boost, and total puff volume. Analyses were performed using IBM SPSS Statistics v23 [28] using two-tailed significance tests conducted at the $p = 0.05$ level.

RESULTS

Sample Characteristics

Study enrollment occurred from October 2007 through June 2013; recruitment and retention details are presented for each randomization group in Figure 1. Participants ($N = 246$), on average, were 39.52 years old (range = 21–66), reported smoking 20.95 CPD (range = 12–45) in the 7-days preceding their initial laboratory visit, had been smoking for 23.18 years (range = 5–51), and were moderately nicotine dependent (range = 1–10). Five telephone-eligible participants (three in the stepdown RNC group, two in the control group) reported smoking <15 CPD at the initial laboratory visit due to extenuating circumstances (e.g., illness, traveling). Table 1 provides additional demographic information.

Attrition Prevalence

Seventy-seven of the 246 participants (31.3%) dropped out of the trial (Fig 1). Missed visits were the primary reason for drop-out (84.8%), followed by study removal (8.9%) and voluntary withdrawal (6.3%); drop-out reasons did not differ among randomization groups. Compared to completers, non-completers were younger [$t(173.80) = -3.69, p < 0.001$], had been smoking for fewer years [$t(173.01) = -3.27, p = 0.001$], and were less likely to have a college degree or higher education [$\chi^2(2) = 11.2, p = 0.004$]; see Table 1. Attrition was greater among the non-stepdown group (44.6%) compared to both the control (24.1%) and stepdown RNC (25.0%) groups [$\chi^2(2) = 10.29, p = 0.006$]. Among all RNC cigarette groups

(i.e., excluding controls), attrition was highest during use of the lowest nicotine cigarettes (18.0%), followed by the moderate and high RNC cigarettes (9.0% and 7.8%, respectively).

Independent Associations with Attrition

Nicotine content was a significant predictor of attrition among all participants [*Wald* $\chi^2(3) = 13.95, p = 0.003$] and among those using RNC cigarettes only (i.e., excluding controls) [*Wald* $\chi^2(2) = 10.22, p = 0.006$]. Among all groups, relative to preferred brand use, odds of attrition were 2.6 times greater during use of the lowest RNC cigarette ($p = 0.002$). Among RNC groups only, relative to the lowest RNC cigarette, attrition odds decreased by 61% and 53% during use of the highest ($p = 0.005$) and moderate ($p = 0.018$) RNC cigarettes, respectively. Study period also predicted attrition status [*Wald* $\chi^2(2) = 6.67, p = 0.036$]; attrition odds were 53% lower during the fourth period relative to the second period ($p = 0.029$). Randomization group was a significant predictor of attrition [$\chi^2(6) = 12.67, p = 0.049$]. Relative to the control group, attrition odds were 3.9 and 3.2 times greater among participants in the low-moderate-high and moderate-high-low groups, respectively (p 's = 0.011 and 0.042, respectively).

Attrition status and cigarette type were associated for Days 10 [$\chi^2(3) = 20.85, p < 0.001$] and 30 [$\chi^2(3) = 9.122, p = 0.028$], and marginally associated for Day 20 [$\chi^2(3) = 7.32, p = 0.062$], but were not associated for Days 15, 25, and 35 (p 's > 0.2). Thus, attrition differences occurred only following product switching days, with greater attrition among participants switched to the lowest RNC cigarettes compared to another cigarette type.

Primary Analysis

The full GEE model regressing attrition status onto nicotine content transition, study period, gender, age, race, education level, and dependence found that only nicotine content transition [*Wald* $\chi^2(9) = 33.15, p < .001$], study period [*Wald* $\chi^2(2) = 9.73, p = 0.008$], and age were significant predictors of attrition (Table 2). We observed a trend in associations between reductions to the lowest RNC cigarette: compared to the control group, odds of attrition were 4.5 and 4.7 times greater when switching from preferred brand and the highest RNC, respectively, to the lowest RNC cigarette. Although not significant at the $p < .05$ level, compared to controls, attrition odds were 2.2 times greater when switching from the moderate to the lowest RNC cigarette. Attrition odds were also 3.2 times greater during the third study period compared to the final study period. Every one unit increase in age decreased the likelihood of drop-out by 3%.

Exploratory Analyses

The exploratory GEE model regressed attrition status onto nicotine content transition, study period, age, strength and taste subjective rating items, total puff volume, and CO boost. Nicotine content transition, study period, and age remained significant predictors of attrition (Table 3). Neither total puff volume nor CO boost significantly predicted attrition status or altered the pattern of previous model findings (i.e., their inclusion in models did not change that the transition to lowest RNC cigarette increased odds of drop-out). Taste, but not strength, significantly predicted attrition status, such that each 1-unit increase in taste ratings (i.e., increasing favorability) decreased attrition odds by 2%.

DISCUSSION

There is a need to understand the factors that influence acceptability of nicotine product standards despite being unable to simulate the environmental conditions of federal nicotine regulation. We propose that a useful behavioral proxy of acceptability is study attrition, as ending participation in a trial which requires compliance but provides free cigarettes and compensation is a relative indicator of low acceptability. The FDA could potentially use trial attrition data to anticipate potential responses to mandated nicotine reduction, and further evaluate its public health impact.

To place our findings within this context, we found that the majority (~70%) of a sample of non-treatment-seeking, daily smokers participating in a randomized controlled trial was compliant with using study-supplied RNC cigarettes and completed the trial; even among the non-stepdown RNC groups, 55% completed the full trial. Among non-completers, use of the lowest RNC cigarettes increased attrition likelihood, particularly when preceded by use of higher nicotine content cigarettes (both preferred brand and RNC cigarettes), despite receiving financial incentives and free cigarettes for 30 days. Attrition was also greater immediately following switching to the lowest RNC cigarette, rather than after 5 days of use. Regarding whether cigarette nicotine content should be immediately or gradually reduced, this study provides evidence – although based on limited, 10-day exposure periods – suggesting that immediate reduction to very low nicotine content with no available alternative products will most negatively affect their acceptability.

Exploratory findings demonstrated that subjective ratings of RNC cigarettes, and not topography or exposure measures, predicted attrition. Specifically, smokers who provided more favorable taste ratings of RNC cigarettes were less likely to drop out of the trial than those who provided negative ratings. Given that most non-completers ended their participation immediately after smoking the lowest RNC cigarettes, and thus had one or relatively few exposures to this nicotine level, these findings suggest that initial sensory responses to RNC cigarettes strongly influence subsequent acceptability.

Like Donny and colleagues [7], we found that non-completers were younger and less educated than completers, although we did not observe racial or gender differences in attrition. Divergence in findings between our study and Donny and colleagues may reflect differences in RNC noncompliance, as smoker presumably were less likely to drop out of the Donny trial due to low acceptability, given that they could continue to smoke their own cigarettes. Our findings align with tobacco industry documents [17] anticipating that older smokers concerned with the health consequences of smoking would be more willing to tolerate an unacceptable low nicotine product than younger smokers who value sensory experiences (e.g., taste) over health concerns.

Although findings suggest that larger, immediate reductions in nicotine content decrease acceptability of very low RNC cigarettes, it is unclear whether low acceptability is necessarily negative, as this is likely context-dependent. While not an exhaustive list of implications, low acceptability could indicate low abuse liability [14], which may be beneficial within the context of other policies that facilitate smoking cessation (e.g., widely

available NRT, access to alternative, non-combustible forms of tobacco, etc.) and minimize access to black markets. Such outcomes would further validate enforcing a low nicotine content standard as a strategy for protecting public health. Conversely, low acceptability within the context of more restrictive tobacco control policies could cause smokers to either use these products in ways that increase harm (e.g., increasing CPD or puffing intensity), or seek out higher nicotine-containing products from other, potentially illicit sources.

Interpreting these findings requires several considerations. Because most non-completers dropped out before providing urine samples, we could not verify compliance beyond self-report and returned filter discrepancies. However, this study differs from others in that continued eligibility required participants' used and unused cigarettes to equal the amount distributed [13]; thus, participants could be non-compliant but still had to return used RNC filters, minimizing the likelihood of non-compliance and underestimating the degree to which low acceptability affected attrition. Additionally, because non-compliant participants were removed, smokers had no alternatives available to express their dissatisfaction other than to end participation, but this also meant forgoing remuneration and free cigarettes. Findings thus reflect acceptability without access to higher nicotine-containing products, and may not represent acceptability in an environment with other regulated products (e.g., e-cigarettes). Research is needed to determine if other tobacco product availability affects RNC cigarette trial attrition. This may inform other regulatory changes that could accompany federal nicotine regulation to counter potential acceptability issues.

Additionally, our sample of heavy-smoking, mostly White, non-menthol smokers from a single city may not represent the larger smoking population. Participants' expectancies about RNC cigarettes may have influenced attrition [29], although expectancies would likely similarly influence acceptability under federal nicotine regulation. Like most RNC cigarette trials, this study did not replicate the exact environment of mandated nicotine reduction; for example, because use periods were 10 days only, findings may not generalize to longer exposure (i.e., less willingness to use RNC cigarettes for a 6-week vs. 35-day trial may increase attrition). Further, no context was provided for product switching; smokers were not informed of switching benefits (e.g., reduced addictiveness), which would likely occur under federal regulation. Still, this study is an important first step in assessing the utility of attrition as an acceptability measure. Future research should evaluate attrition during trials with more representative samples and longer use periods to further evaluate factors influencing acceptability.

In summary, this study suggests that relative attrition during RNC cigarette studies may be a useful proxy for understanding factors that influence acceptability when unable to simulate the conditions of mandated nicotine reduction. Although most participants completed the trial and were compliant with RNC cigarettes, non-completers were more likely to end participation when using the lowest RNC cigarettes. Attrition odds increased with larger reductions in cigarette nicotine content, but were reduced with positive subjective taste ratings. Findings suggest low acceptability of very low RNC cigarettes immediately following use of higher nicotine content cigarettes, in the absence of other available nicotine-containing alternatives.

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Figure 1.

Overall study recruitment and retention.

Note: C = completed session, NC = classified as session non-completers.

Table 1

Sample demographic and smoking history characteristics and differences by attrition status.

	Study completers (<i>n</i> = 169) <i>M</i> (<i>SD</i>)	Non-completers (<i>n</i> = 77) <i>M</i> (<i>SD</i>)	Total sample (<i>n</i> = 246) <i>M</i> (<i>SD</i>)
Demographic			
Age ***	41.34 (12.92)	35.51 (10.81)	39.52 (12.57)
Gender (<i>n</i> ; % male)	110 (65.1%)	58 (75.3%)	168 (68.3%)
Ethnicity (<i>n</i> ; % White)	149 (88.2%)	72 (93.5%)	221 (89.8%)
Highest level of education **			
High school/GED or less	38 (22.5%)	18 (23.4%)	56 (22.8%)
Some college/technical training	66 (39.1%)	45 (58.4%)	111 (45.1%)
College graduate or higher	65 (38.5%)	14 (18.2%)	79 (32.1%)
Smoking history			
Baseline daily cigarette consumption	20.68 (5.53)	21.53 (5.67)	20.95 (5.58)
Baseline carbon monoxide (ppm)	25.42 (11.26)	24.35 (11.87)	25.09 (11.44)
Years smoking ***	24.83 (13.13)	19.56 (11.04)	23.18 (12.73)
Nicotine dependence (FTND; 0]–10)	5.51 (1.83)	5.42 (1.84)	5.48 (1.83)
Randomization group (<i>n</i> ; %)			
Control (Preferred brand)	60 (75.9%)	19 (24.1%)	79
Stepdown (High-moderate-low)	63 (75.0%)	21 (25.0%)	84
Nonstepdown (collapsed)	46 (55.4%)	37 (44.6%)	83
Low-moderate-high	8 (44.4%)	10 (55.6%)	18
Low-high-moderate	9 (52.9%)	8 (47.1%)	17
Moderate-low-high	11 (68.8%)	5 (31.3%)	16
Moderate-high-low	8 (50.0%)	8 (50.0%)	16
High-low-moderate	10 (62.5%)	6 (37.5%)	16

Note:

* indicates significant difference at $p < .05$ level;** = $p < .01$;*** = $p < .001$.

Table 2

Results from the primary generalized estimating equations (GEE) model regressing attrition status onto nicotine content transition, study period, age, gender, nicotine dependence, race, and highest education level.

	B (SE)	Wald χ^2	P	Odds ratio	95% CI (LB,UB)
Intercept	-3.77 (.67)	31.79	< .001	.02	.01, .09
Nicotine content transition					
Control (no transition)	REF	REF	REF	REF	REF
High to moderate	-.26 (.47)	.32	.58	.77	(.30, 1.93)
High to low	1.54 (.53)	8.58	.003	4.65	(1.66, 12.99)
Moderate to high	.22 (.78)	.08	.78	1.25	(.27, 5.76)
Moderate to low	.80 (.47)	2.96	.09	2.23	(.89, 5.57)
Low to high	.52 (.65)	.64	.43	1.68	(.47, 5.97)
Low to moderate	.77 (.62)	1.53	.22	2.16	(.64, 7.29)
Preferred brand to high	-.26 (.51)	.27	.61	.77	(.29, 2.08)
Preferred brand to moderate	.25 (.63)	.16	.69	1.29	(.38, 4.40)
Preferred brand to low	1.50 (.47)	10.24	.001	4.48	(1.79, 11.23)
Study period					
Second	.92 (.54)	2.92	.09	2.50	(.87, 7.14)
Third	1.15 (.37)	9.70	.002	3.17	(1.53, 6.55)
Fourth	REF	REF	REF	REF	REF
Age	-.03 (.01)	12.91	< .001	.97	(.95, .99)
Gender					
Male	REF	REF	REF	REF	REF
Female	-.41 (.29)	1.92	.17	.67	(.38, 1.18)
Nicotine dependence	.07 (.07)	.91	.34	1.07	(.93, 1.23)
Race					
White	REF	REF	REF	REF	REF
Non-white	-.70 (.52)	1.85	.17	.50	(.18, 1.36)
Highest education level					
HS only	.54 (.39)	1.91	.17	1.71	(.80, 3.65)
Some college	.72 (.33)	4.69	.03	2.06	(1.07, 3.95)

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	B (SE)	Wald χ^2	P	Odds ratio	95% CI (LB,UB)
	REF	REF	REF	REF	REF
College grad					

Table 3

Results from the exploratory generalized estimating equations (GEE) model regressing attrition status onto nicotine content transition, study period, age, strength and taste subjective ratings, CO boost, and total puff volume.

	B (SE)	Wald χ^2	P	Odds Ratio	95% CI (LB,UB)
Intercept	-2.38 (.81)	8.58	.003	.09	(.02, .46)
Nicotine content transition					
Control (no transition)	REF	REF	REF	REF	REF
High to moderate	-.49 (.54)	.82	.37	.61	(.21, 1.78)
High to low	1.15 (.57)	4.02	.045	3.15	(1.03, 9.67)
Moderate to high	.06 (.80)	.01	.94	1.06	(.22, 5.05)
Moderate to low	.28 (.55)	.27	.60	1.33	(.46, 3.87)
Low to high	.34 (.64)	.29	.59	1.41	(.40, 4.91)
Low to moderate	.49 (.66)	.54	.46	1.63	(.45, 5.96)
Preferred brand to high	-.30 (.52)	.33	.57	.74	(.27, 2.07)
Preferred brand to moderate	.30 (.62)	.23	.63	1.35	(.40, 4.53)
Preferred brand to low	1.30 (.53)	5.96	.015	3.66	(1.29, 10.40)
Study period					
Second	1.02 (.55)	3.41	.065	2.76	(.94, 8.12)
Third	1.27 (.40)	10.07	.002	3.56	(1.63, 7.80)
Fourth	REF	REF	REF	REF	REF
Age	-.03 (.01)	10.52	.001	.97	(.95, .99)
Strength	-.01 (.01)	0.81	.37	.99	(.98, 1.01)
Taste	-.02 (.01)	6.34	.012	.98	(.97, 1.00)
CO boost	-.06 (.03)	2.81	.09	.95	(.89, 1.01)
Total puff volume	.00 (.00)	1.08	.30	1.00	(1.00, 1.00)