NICOTINE CONTENT DESCRIPTION EFFECTS ON SUBJECTIVE RESPONSES TO SMOKING AND SMOKING BEHAVIORS: IMPLICATIONS FOR NICOTINE REDUCTION STRATEGIES

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Abstract

INTRODUCTION: A federal policy requiring a gradual reduction in cigarette nicotine content is a promising strategy for reducing tobacco-related morbidity and mortality within the US. However, research on consumer response to reduced nicotine cigarettes (RNCs) is needed prior to policy implementation. Extant studies have shown that smokers provide lower subjective ratings of RNCs, but it is unknown if these low ratings result from deficient nicotine levels within these products, or from smokers’ biases about using cigarettes with less nicotine. As such, the primary aims of this dissertation were to examine the effects of nicotine content description – independent of the effect of actual cigarette nicotine content – on subjective responses (Aim 1) and smoking behaviors (Aim 2). Additionally, Aim 3 explored baseline RNC smoking outcome expectancies and willingness to use RNCs as moderators of nicotine content description effects.

METHODS: Participants (N = 33) were daily smokers (63.6% male, 69.7% White) aged 18-53 years old ($M \pm SD = 25.94 \pm 8.49$) who reported smoking 5-32 cigarettes per day (12.91 ± 7.03). After an initial baseline screening session, 12-h abstinent participants completed 3 laboratory sessions, during which they smoked a study-supplied cigarette and completed craving, withdrawal, and sensory effect assessments. When smoking, participants smoked a blinded version of their preferred brand cigarette, but were provided with deceptive descriptions regarding the cigarette's nicotine content, counterbalanced across participants. Cigarettes were described as containing (1) nicotine content similar to participants’ usual brand [“UBC”], (2) low nicotine content [“LNC”], and (3) very low nicotine content [“VLNC”].
RESULTS: Greater reductions in global craving and craving due to anticipation of negative affect relief were reported after smoking the “UBC” compared to “LNC” and “VLNC” cigarettes. Participants also took shallower puffs of and rated the “LNC” and “VLNC” cigarettes as being weaker (in general), too mild, and having weaker smoke compared to the “UBC.” Withdrawal suppression, reduction of craving due to desire to smoke, and other sensory effect and topography measures did not differ across nicotine content descriptions. Willingness to use RNCs did not moderate nicotine content description effects on subjective responses or smoking behaviors, but RNC outcome expectancies moderated effects on average puff volume; there was only an effect among those with negative (vs. positive/neutral) RNC outcome expectancies.

CONCLUSIONS: Results suggest that low subjective ratings given to RNCs in extant trials may be at least partially due to negative bias about using a cigarette containing less nicotine content. Additionally, these effects may be influenced by participants' pre-existing outcome expectancies about these products. These biases and expectancies may need to be addressed prior to implementation of a nicotine reduction policy to promote positive consumer response to RNCs, and ensure the success of this strategy.
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Abbreviations

ANOVA: analysis of variance
BPD: balanced placebo design
BS: between-subjects
CDC: Centers for Disease Control and Prevention
CO: carbon monoxide
CPD: cigarettes per day
CTP: Center for Tobacco Products
FDA: Food and Drug Administration
FSTPCA: Family Smoking Tobacco Prevention Control Act
LNC: low nicotine content
MANOVA: multivariate analysis of variance
NRT: nicotine replacement therapy
RM: repeated measures
RNC: reduced nicotine content [cigarette]
SD: standard deviation
SEM: standard error of the mean
UBC: usual brand nicotine content
USDHHS: U.S. Department of Health and Human Services
VLNC: very low nicotine content
WS: within-subjects
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Chapter 1: Introduction

Background

Cigarette smoking remains the leading cause of preventable death, responsible annually for over 480,000 deaths in the United States (U.S. Department of Health and Human Services [USDHHS], 2014) and over 5 million deaths worldwide (World Health Organization, 2011). Smoking directly causes numerous deleterious health issues – most notably cardiovascular disease, cancer, and lung disease – and negatively affects the prognosis of many other health conditions such as diabetes, pregnancy, and HIV (USDHHS, 2010). Accordingly, smoking is a significant economic burden to society, responsible for over $193 billion in lost productivity and health care expenditures in the U.S. from 2000 to 2004 (Centers for Disease Control and Prevention [CDC], 2008).

Although the prevalence of smoking within the U.S. has declined since 1965 (CDC, 2011a), current rates have changed little since 2000 and are unlikely to meet the 2020 Healthy People goal of 12% (USDHHS, 2014). Recently, the Surgeon General endorsed a policy approach to gradually reduce cigarette nicotine content to non-addictive levels (Benowitz & Henningfield, 1994) as a promising and realistic way of reducing overall cigarette use (USDHHS, 2014), and consequently, tobacco-related morbidity and mortality. Preliminary evidence from recent and ongoing studies (Benowitz et al., 2012; Donny et al., 2014; Hammond & O’Connor, 2014; Hatsukami, Kotlyar, et al., 2010; Hatsukami, Heishman, et al., 2012) supports the safety and efficacy of using reduced nicotine content (RNC) cigarettes, but additional research is needed on a number of remaining issues (e.g., effects of abrupt vs. gradual reduction, consumer response, use of RNCs by vulnerable populations) before such a policy may be
implemented. Of these issues, understanding consumer response to RNCs prior to the policy implementation is of importance given that policy success will depend, in part, upon smokers embracing and using these products as intended. However, this area of research has yet to be exhaustively explored.

The Potential of a Nicotine Reduction Policy

As originally proposed by Benowitz and Henningfield (1994), a federal nicotine reduction policy would require a widespread, gradual reduction of cigarette nicotine content over a 10-15 year period. Although cigarettes contain hundreds of harmful constituents, the proposal focused on nicotine because it is the primary addictive ingredient (USDHHS, 1988). Nicotine's pharmacological actions in the brain are exceptionally behaviorally reinforcing (USDHHS, 1988); smokers continually self-administer nicotine via cigarettes to achieve feelings of reward and pleasure, eventually resulting in long-term dependence. Benowitz and Henningfield (1994) theorized that reducing nicotine content should make cigarettes less reinforcing, leading to decreased consumption and, consequently, decreased exposure to tar and other harmful constituents. Further, reducing nicotine to non-addictive levels should deter new and infrequent smokers from developing dependence, preventing the transition of these smokers from experimental to long-term cigarette use (Benowitz & Henningfield, 1994).

Benowitz and Henningfield's proposal (1994) received much initial attention, yet its goals remained largely unrealized until the passing of the 2009 Family Smoking Prevention and Tobacco Control Act (FSPTCA). This act allowed the Food and Drug Administration (FDA) to regulate the tobacco industry for the purpose of protecting
public health (U.S. Congress, 2009). Under the FSPTCA, the FDA was given the authority to determine and enforce standards for cigarette nicotine and tar levels, with the exception that nicotine content cannot be reduced to zero (U.S. Congress, 2009). Thus, regulatory infrastructure now exists to support the implementation of a nicotine reduction policy, yet scientific evidence supporting the feasibility of such a policy is meager.

Since the passing of the FSPTCA, several studies have evaluated, or are currently evaluating, clinical response to RNCs (e.g., safety, efficacy). To date, these studies have generally found that RNCs do not pose any additional health risks to smokers beyond those already associated with use of commercially available cigarettes (Benowitz et al., 2007, 2009, 2012; Hammond & O’Connor, 2014). Previous studies of cigarettes whose product designs were manipulated to reduce nicotine yield (e.g., filter ventilation holes in “light” and “ultra-light” cigarettes) – vs. reducing content – have demonstrated that compensation, or increased smoking behaviors (e.g., greater number of puffs or cigarettes smoked, deeper puff volume), may result from the insufficient nicotine levels produced by these cigarettes (Scherer, 1999; Stepney, 1980). However, present studies of RNCs have found little evidence of compensation during long-term use, given that these cigarettes do not contain enough nicotine for smokers to extract via compensatory behaviors (Benowitz et al., 2012; Hatsukami, Donny, Koopmeiners, & Benowitz, 2015). Finally, there is some evidence that allowing smokers to taper nicotine content through using progressively lower RNCs results in decreased overall cigarette consumption (Benowitz et al., 2007, 2012; Hatsukami, Kotlyar, et al., 2010).

The findings of extant RNC studies suggest that a widespread nicotine reduction policy has significant potential to reduce tobacco-related morbidity and mortality within
the U.S. However, many remaining concerns about nicotine reduction must be addressed before such a policy may be implemented. Thus, the National Institutes of Health (NIH) and the FDA Center for Tobacco Products (CTP) have called for a range of studies including those which evaluate the impact of nicotine reduction on tobacco product use behavior (e.g., topography, compensation) and consumer perceptions of tobacco products (NIH, 2014). Findings from these studies will provide the FDA with scientific evidence to inform its regulatory decisions, which may result in the implementation of a nicotine reduction policy. Because the majority of RNC research to date has focused primarily on clinical response to these products (e.g., safety, efficacy), there is a particular need to evaluate consumer response prior to policy implementation.

**Addressing Consumer Response to Cigarettes with Reduced Nicotine Content**

A current research priority of the FDA CTP is to understand consumer response to tobacco products, specifically, RNCs (NIH, 2014). Despite the encouraging evidence from ongoing studies demonstrating the safety and efficacy of RNCs in reducing overall cigarette use, this evidence does not ensure the success of a nicotine reduction policy. Such a policy is unlikely to succeed if consumers do not accept RNCs or use these products as intended. For example, a growing concern about implementing a nicotine reduction policy is the consequent growth of a “black market” of tobacco products containing nicotine content greater than the federally regulated level (Hatsukami, Perkins, et al., 2010). It is possible that smokers who do not accept RNCs may seek out tobacco products with higher nicotine content from illegal sources, undermining policy goals.
Information on consumer response is needed to aid the FDA in anticipating potential challenges with adoption of RNC use.

A 2009 article by Rees and colleagues proposed a conceptual framework for understanding and assessing consumer response to potential reduced exposure products (PREPs), applicable to understanding consumer response to RNCs. This framework defined consumer response as “a set of subjective and behavioral responses that convey information, affect behavior and likelihood of long-term product use by the consumer, and his/her future intentions for product adoption (Rees et al., 2009).” Consumer response further comprised two separate, but interacting domains: product perceptions (e.g., attitudes and beliefs, outcome expectancies, risk perceptions) and response to product (e.g., reactions to initial use such as acute craving reduction). According to this framework, the combined influence of product perceptions and response to product dictate likelihood of experimentation with, as well as future long-term adoption of, that product. As such, studies seeking to evaluate consumer response to RNCs should assess constructs within each domain to determine likelihood of future use if a nicotine reduction policy were implemented.

To date, nearly all research on consumer response to RNCs has been within the “response to product” domain. Extant studies have found that smokers generally provide negative ratings of the subjective effects (e.g., milder taste, less satisfaction) of these cigarettes compared to their usual brand (Benowitz et al., 2012), suggesting that smokers may struggle with accepting RNCs if a nicotine reduction policy were implemented. These studies have generally not blinded participants to nicotine content (i.e., participants were aware they would receive a cigarette with less nicotine than their current brand) in
order to simulate real world use of RNCs. As such, it is unclear whether the negative
ratings given to RNCs are resultant from insufficient nicotine content (e.g., reductions in
nicotine content cause worse taste), or from participants’ biases about using a cigarette
with reduced nicotine (e.g., participants believe nicotine is responsible for cigarettes'
pleasant taste; they expect and consequently report a cigarette with less nicotine to have a
worse taste). Studies are needed to evaluate the influence of nicotine content description
– independent of actual nicotine content – on subjective and behavioral responses to RNC
use. If cigarettes described as containing reduced nicotine content (but which actually
have typical levels of nicotine) are still rated negatively, this might suggest that the FDA
should increase public education about the similarities between RNCs and traditional
cigarettes on rewarding and sensory aspects of smoking. Conversely, if subjective ratings
do not differ, this may instead suggest that the negative ratings given to RNCS in extant
trials are caused by deficient nicotine content.

**Effects of nicotine content descriptions on subjective effects of smoking.** A
number of laboratory studies have examined how descriptions about cigarette nicotine
content may bias subjective responses to smoking. These studies have generally
employed a 2 x 2 balanced placebo design (BPD) to separate the influence of nicotine’s
pharmacologic effects from expectations about smoking outcomes (manipulated through
descriptions of nicotine content) on study outcomes. In the 2 x 2 BPD, actual nicotine
dose (given nicotine vs. given no nicotine, or more likely, 0.05 mg nicotine
"denicotinized" cigarette) and nicotine dose description (told nicotine vs. told no
nicotine) are crossed, such that participants are assigned to one of four groups: (1) given
nicotine/told nicotine, (2) given nicotine/told no nicotine, (3) given no nicotine or
denicotinized/told no nicotine, and (4) given no nicotine or denicotinized/told nicotine.
Of note, denicotinized cigarettes are given because a true placebo cigarette (i.e.,
containing 0% nicotine) does not exist. Group differences in study outcomes can then be
attributed to either the effect of nicotine dose, nicotine dose description, or their
interaction. Using this design, Juliano and Brandon (2002) conducted a study in which 3-
hour abstinent smokers underwent a stress-inducing task, smoked a single blinded
cigarette, and then provided ratings of anxiety reduction, craving reduction, and
withdrawal suppression. All groups except the given denicotinized/told no nicotine group
reported similar reductions in craving and anxiety, but there was no group effect on
withdrawal. These results suggest the importance of nicotine dose descriptions, as the
description of receiving nicotine content produced the same magnitude of anxiety and
craving reduction as actually receiving nicotine.

A study by Perkins et al. (2008) also utilized a 2 (told nicotine vs. told no
nicotine) x 2 (given nicotine-containing cigarette vs. given 0.05 mg nicotine yield Quest
“denicotinized” cigarette) BPD to evaluate the influence of mood context on the effects
of actual nicotine dose and dose description on subjective ratings of smoking.
Participants experienced a manipulation to induce either positive or negative mood, and
were then allowed to smoke a blinded cigarette and provide ratings of that cigarette.
Across mood conditions, smokers in the given nicotine/told no nicotine group reported
lower ratings of liking and satisfaction for the study cigarette compared to smokers in the
given nicotine/told nicotine group. Similar to Juliano and Brandon (2002), this study
demonstrates that providing smokers with descriptions of nicotine dose – even in the
presence of sufficient nicotine content – can alter subjective responses to smoking, again suggesting the important influence of nicotine dose description on these outcomes.

Another study by Perkins et al. (2009) evaluated the same outcomes using a 2 (given nicotine vs. given no nicotine) x 2 (told nicotine vs. told no nicotine) BPD among users of nicotine nasal spray instead of cigarettes. Similar to the mood induction study, participants in the given nicotine/told no nicotine group reported lower liking of the nasal spray compared to those in the given nicotine/told nicotine group. These results replicate earlier findings demonstrating the effect of nicotine content descriptions on subjective responses to smoking (Juliano & Brandon, 2002; Perkins et al., 2008). More importantly, these results show that description effects generalize to other methods of nicotine administration beyond cigarette smoking.

Finally, a study by Darredeau, Stewart, & Barrett (2013) used a modified version of a 2 x 2 BPD to assess subjective responses to smoking and smoking reinforcement following 12 hours of abstinence. Participants completed two sessions in which they received either a regular nicotine content cigarette during both sessions, or a denicotinized cigarette for both sessions. However, nicotine dose description (told no nicotine vs. nicotine) was counterbalanced across sessions. As such, nicotine content descriptions could be compared within, but not between actual dose groups. Participants took 3 puffs of each session’s cigarette, provided subjective ratings, and were then given the opportunity to work for additional cigarettes puffs. Results found that among smokers actually given nicotine-containing cigarettes, smokers reported greater craving reduction after sampling puffs of the cigarette they were told contained no nicotine. Regardless of nicotine dose description, cigarettes that actually contained nicotine were rated higher on
the subjective ratings of “satisfied”, “stimulated”, and “head rush,” compared to
denicotinized cigarettes. Although somewhat contradictory to the findings of Juliano and
Brandon (2002) and Perkins et al. (2008), these findings further demonstrate that nicotine
dose descriptions can influence subjective responses to smoking. Additionally, such
descriptions may differentially affect types of subjective responses, given that description
affected craving responses but not ratings of subjective effects of smoking.

Taken together, the findings of Perkins and others provide evidence that nicotine
content description, independent of actual nicotine content, may bias subjective
responses to smoking. However, the relevance of these findings to nicotine reduction
efforts is limited by the fact that the descriptions employed by these studies reflected two
extreme ends of nicotine content descriptions; participants were told that the cigarettes
they smoked contained either a dose of nicotine similar to their usual brand or no nicotine
at all. These studies did not examine the effects of descriptions about gradations of
nicotine dose (e.g., no nicotine vs. “low” nicotine vs. “very low” nicotine). A better of
understanding of the effects of gradations in nicotine content description on subjective
responses would be useful for the FDA, because if a nicotine reduction policy were
implemented, such graded descriptions may be used to inform smokers of nicotine
content changes within their cigarettes. The specific “very low” nicotine content
description is critical, given that the FDA is permitted to reduce nicotine content to a non-
zero level, rather than eliminate it outright. Based on these studies, it is plausible that a
description of “low” nicotine would result in lower subjective ratings than a description
of normal nicotine content, but it is unclear if a description of “very low” nicotine would
result in ratings similar to, or above, those seen with the “no nicotine” description. Further research in this area is critical for informing nicotine reduction efforts.

To date, only Joel (2013) has specifically examined how the description of reduced (i.e., a gradation between no and typical) nicotine content influences subjective effects of smoking. This study comprised a single laboratory session in which 68 adult daily smokers first took four puffs of their usual brand cigarette, and were then given two identical blinded denicotinized (0.05 mg nicotine yield Quest) cigarettes to smoke ad lib. Participants were told one cigarette contained “average” nicotine content and the other contained “very low” nicotine content; description orders were counter-balanced across participants. Although both cigarettes contained the same actual nicotine content (i.e., 0.05 mg), participants provided lower subjective ratings (e.g., less satisfaction) for the “very low” cigarette compared to the “average” cigarette. Results suggest that merely describing a cigarette as having “very low” nicotine content may bias subjective responses to that cigarette, similar to the biases found for cigarettes described as having no nicotine. However, this study design did not allow for direct comparison of ratings between the “average” and “very low” cigarettes with participants' usual cigarette brand. Although participants provided lower ratings for the “very low” cigarette compared to the “average” cigarette, ratings for the “average” cigarette may be lower than how participants would rate their own brand due to deficient nicotine content within the “average” cigarette. Similar studies which control for nicotine content are needed to confirm that low subjective ratings given to RNCs result from bias and not insufficient nicotine levels. Additionally, future studies may be strengthened by having participants smoke and rate cigarettes on separate occasions, or after a period of abstinence, to control
for carry-over effects of prior cigarette smoking on the subjective ratings of subsequently smoked cigarettes during the study.

**Effects of nicotine content descriptions on smoking behavior.** A major concern with implementing a federal nicotine reduction policy is that smokers using RNCs may compensate for the insufficient nicotine levels contained within these cigarettes. Compensation can occur either in the form of increased puffing behaviors (i.e., smoking topography) or increased number of cigarettes smoked per day. If smokers do engage in compensatory smoking behaviors, this could potentially undermine the goals of the nicotine reduction strategy by increasing exposure to harmful non-nicotine cigarette constituents. As such, the FDA CTP has called for studies that evaluate the effects of nicotine reduction on smoking behavior. Smoking behavior is typically assessed in laboratory settings using electronic devices that measure aspects of smoking topography such as the number of puffs taken per cigarette smoked, the duration and volume of each puff, and the time elapsed between puffs. Laboratory topography assessments are consistent within participants (Perkins, Karelitz, Giedgowd, & Conklin, 2012), and are predictive of clinical outcomes such as cessation following treatment with nicotine replacement therapy (Franken, Pickworth, Epstein, & Moolchan, 2006; Strasser, Pickworth, Patterson, & Lerman, 2004). Thus, laboratory assessments of smoking topography during use of RNCs should serve as a reliable indicator of how smokers would use these products if a nicotine reduction policy were implemented.

Research examining smoking topography during use of RNCs has shown that smokers may initially engage in compensatory behaviors, but that the insufficient
nicotine content within these cigarettes does not allow smokers to extract enough nicotine to reinforce these behaviors long-term (Benowitz et al., 2012; Hatsukami et al., 2015). These findings are preliminary and should be further explored within the context of nicotine content descriptions. Studies are needed to determine if labeling a cigarette as having “reduced” or “low” nicotine – independent of actual nicotine content – affects smoking behaviors, and specifically, if such descriptions are responsible for initial attempts to compensate. Given that descriptions about receiving RNCs affect subjective ratings, it is plausible that these descriptions may influence smoking behaviors as well.

Studies that have examined the effects of nicotine content descriptions on smoking behaviors have produced mixed results. Of the four laboratory studies that examined nicotine content descriptions on subjective ratings, all except the study using nasal spray (Perkins et al., 2009) assessed description effects on smoking topography (e.g., number of puffs taken, mean puff volume). Perkins et al. (2008) found no effect of nicotine content description on either latency to first puff or number of puffs taken, while Darredeau et al. (2013) found that smokers in the given nicotine/told no nicotine group took fewer puffs than the given nicotine/told nicotine group. Regarding the effect of a specific “reduced” nicotine content description, Joel (2013) found no differences between cigarettes described as containing “average” and “very low” nicotine on any topography measures except mean puff volume. When smoking the cigarette described as having “average” nicotine content, participants demonstrated greater mean puff volume compared to the “very low” nicotine content cigarette.

Although mixed, overall results suggest that describing a cigarette as containing “no nicotine” or “very low” nicotine – independent of the cigarette’s actual nicotine
content – may lead to differences on some measures of smoking behavior compared to cigarettes of traditional nicotine content. Given the inconsistencies in which topography measures differed by content descriptions, additional studies are needed. Future studies are particularly needed to further explore how descriptions of gradations of nicotine content (e.g. “low” and “very low”) influence smoking behaviors, as these are most relevant for addressing the needs of the FDA CTP.

**Possible moderators of nicotine content description effects.**

*RNC outcome expectancies.* Assessing the influence of nicotine content descriptions on subjective responses and smoking behaviors may help to elucidate biases smokers have toward cigarettes labeled as “reduced” or “low” nicotine. However, these outcomes pertain only to the “response to product” domain of consumer response. As such, these studies reflect only one component of determining future adoption of RNCs. Further research is needed to examine factors that fall underneath the “product perceptions” domain of consumer response to RNCs, as these factors may have independent and interactive effects on future product adoption.

For example, previous studies have shown that dose description effects on subjective responses may vary based on whether smokers hold negative or positive smoking outcome expectancies (i.e., beliefs about outcomes following cigarette ingestion; e.g., smoking relieves stress, smoking improves weight control). In addition to assessing nicotine dose description effects on anxiety relief following stress induction, Juliano and Brandon (2002) also examined whether these effects were moderated by participants’ outcome expectancies regarding smoking’s ability to relieve anxiety.
Researchers found a significant interaction between the expectancy that smoking would relieve anxiety (low vs. high expectancy) and dose description; among participants who were told their cigarette contained no nicotine, those who held high expectancies about nicotine’s ability to relieve anxiety experienced less anxiety relief than those who held low expectancies. These findings demonstrate the importance of evaluating outcome expectancies about using RNCs, and examining the effects of these expectancies on initial responses to cigarettes described as containing reduced nicotine.

**Willingness to use RNCs.** Another component of determining consumer response to RNCs relates to assessing smokers’ likelihood of using RNCs in the future. The Theory of Reasoned Action [TRA] is a theoretical framework commonly applied to health behavior research because of its utility in predicting various future health behaviors based on current attitudes and beliefs. As such, the TRA may be applied to nicotine reduction studies to better understand and predict smokers’ likelihood of using RNCs if a nicotine reduction policy is implemented. According to the TRA, an individual’s likelihood of performing a given behavior is determined by that individual’s behavioral intentions, which are influenced by attitudes and norms about the behavior (Ajzen, 1991, 2003). Because RNCs are currently not commercially available, most smokers are either unaware of the existence of these products, or may mistakenly believe RNCs to be similar to cigarettes previously labeled as “light” and “ultra-light.” As such, smokers do not have well-defined behavioral intentions regarding using RNCs, which are not useful for predicting future use of RNCs. However, smokers may nonetheless be open, or willing, to use RNCs. The Prototype Willingness Model (Gibbons, Gerrard, Blanton, & Russell, 1998; Rivis, Sheeran, & Armitage, 2006) suggests then, that in
situations where reasoned behavioral intentions are not applicable, behavioral willingness to perform a behavior may serve as a better indicator of likelihood of performing that behavior. Because no extant RNC studies have prospectively assessed willingness to use RNCs, assessing these outcomes fills an important gap in the literature regarding consumer response of RNCs, as willingness to use RNCs may serve as a proxy for likelihood of future RNC use. Further, because willingness has been shown to explain unique variance in a number of health outcomes beyond that explained by behavioral intentions (Gibbons et al., 1998; Rivis et al., 2006), it is possible that willingness to use RNCs may moderate nicotine content description effects on subjective and behavioral responses to smoking.

Gaps in the Literature

In summary, a nicotine reduction policy holds potential for reducing tobacco-related morbidity and mortality in the US. However, further research is needed in areas beyond efficacy and safety trials to exhaustively determine its feasibility before policy implementation. Specifically, research is needed to evaluate domains related to consumer response to RNCs. Studies that examine both smokers’ responses to, and perceptions of, using RNCs (e.g., outcome expectancies, willingness to use) are needed, as these domains may dictate smokers’ intentions for future use and long-term product adoption (Rees et al., 2009). Few studies have examined how these domains may interact (e.g., outcome expectancies may moderate initial subjective responses) to influence consumer response to RNCs.
Study Purpose and Description

The purpose of this dissertation was to address the priorities of the FDA CTP to understand consumer response to RNCs. This study aimed to address consumer response in two ways, according to the framework proposed by Rees et al. (2009). First, the “response to product” domain of product acceptance was addressed by investigating the effects of nicotine content description (manipulated through supplying participants with their own brand of cigarette but providing deceptive descriptions about the nicotine content of these cigarettes) on subjective ratings and smoking behaviors. Second, the “product perceptions” domain was addressed by assessing initial RNC outcome expectancies and willingness to use RNCs, and exploring whether outcome expectancies and willingness moderate the effects of nicotine content descriptions.

In this study, 33 daily smokers (63.6% male) completed four laboratory sessions including a baseline session and three experimental sessions. During the baseline session, participants provided informed consent and completed initial assessments of RNC outcome expectancies and willingness to use RNCs. The three experimental sessions utilized a within-subjects crossover design, in which each session required participants to smoke a blinded study-supplied “research cigarette” through a smoking topography device and provide subjective ratings of sensory effects, craving reduction, and withdrawal suppression. For all experimental sessions, participants received their preferred cigarette brand as the study-supplied cigarette, but received one of three deceptive descriptions about the cigarette’s nicotine content: participants were told the cigarette contained (1) the same nicotine content as their usual brand [“UBC”], (2) a “low” level of nicotine compared to their usual brand [“LNC”]; (3) a “very low” level of
nicotine compared to their usual brand [“VLNC”]. Nicotine content description orders were counter-balanced across participants.

Specific Aims and Hypotheses

Aim 1: Determine the influence of nicotine content description on subjective responses to smoking (e.g., craving, withdrawal, sensory effects).

Rationale: Studies that have not blinded smokers to nicotine content have found that smokers generally provide more negative ratings of RNC subjective effects. It is unclear if these ratings result directly from reduced nicotine content, or from participants' biases about using RNCs. Extant literature on nicotine content descriptions suggests that the description of receiving a cigarette containing no nicotine – regardless of the actual nicotine content in the cigarette – will result in lower subjective ratings of that cigarette. Thus, it is possible that merely informing participants they are using a cigarette with reduced nicotine content immediately biases their subjective responses to that cigarette. Based on extant literature, it is expected that:

Hypothesis 1.1. There will be a dose-response relationship between nicotine content description and craving reduction, such that the magnitude of craving reduction will be greatest after smoking the cigarette with the greatest nicotine content description and lowest after smoking the cigarette with the lowest nicotine content description.

Hypothesis 1.2. There will be a dose-response effect of nicotine content description on withdrawal suppression. The magnitude of withdrawal suppression will be greatest after smoking the cigarette with the greatest nicotine content description, and will be the least after smoking the cigarette with the lowest nicotine content description.
**Hypothesis 1.3.** There will be a dose-response relationship between nicotine content description and ratings of sensory effects of smoking. The cigarette with the greatest nicotine content description will be given the most positive ratings; the cigarette with the lowest nicotine content description will be given the most negative ratings.

**Aim 2: Examine nicotine content description effects on smoking behaviors** (e.g., number of puffs taken, total puff volume).

**Rationale:** Although previous studies of RNCs have found that smokers generally dislike RNCs compared to their own brand, it is unclear how nicotine content descriptions affect how smokers actually smoke RNCs. While compensation is likely largely dependent upon physiological responses to the absence of nicotine, it is unclear if psychological factors (such as perceived content) also contribute to compensatory behaviors. It is possible that negative beliefs about the subjective effects associated with reduced nicotine content may cause smokers to smoke less of these cigarettes, or may cause smokers to initially increase puff volume due to beliefs that deeper puffs are necessary to obtain a greater amount of nicotine. Because previous RNC studies have shown initial attempts to compensate during use of RNCs, it is expected that:

**Hypothesis 2.1.** There will be a negative dose-response relationship between nicotine content description and smoking topography measures. Smokers will engage in fewer smoking behaviors (i.e., fewer puffs per cigarette, smaller average puff volume) when using the cigarette with the greatest nicotine content description, and will engage in more smoking behaviors when using the cigarette with the lowest content description.
Hypothesis 2.2. Nicotine content description and CO boost will have a negative dose-response relationship; the magnitude of the smoking-induced increase in CO level will be lowest after smoking the cigarette with the highest nicotine content description, and greatest after smoking the cigarette with the lowest nicotine content description.

Aim 3: Assess initial RNC outcome expectancies about and willingness to use RNCs, and evaluate willingness and attitudes as potential moderators of the effects of nicotine content descriptions on subjective ratings and smoking behaviors.

Rationale: To the author’s knowledge, no studies have prospectively assessed smokers’ outcome expectancies for RNC use, or willingness to use RNCS if such products were available. Given that smoking outcome expectancies have been shown to moderate nicotine dose expectancy effects on subjective of smoking (Juliano & Brandon, 2002), it is plausible that RNC outcome expectancies will have a similar effect on the influence of nicotine content descriptions on these outcomes. Additionally, given that willingness to engage in a behavior is a reliable predictor of performing a behavior, it is also plausible that willingness may moderate the relationships of nicotine dose descriptions with subjective ratings and smoking behaviors.

Hypotheses: Outcome expectancies and willingness will be significant moderators of the effects of nicotine content descriptions. The hypothesized dose-response relationship between nicotine content descriptions and subjective ratings and smoking behaviors will be stronger among those who are less willing to use RNCs and those who hold more negative outcome expectancies about RNCs compared to those who are more willing and hold more positive RNC outcome expectancies.
Innovation of the Present Research

Findings from this dissertation will inform tobacco policy by contributing to the accumulating literature regarding consumer acceptance of RNCs. Specifically, FDA CTP research priorities will be addressed by providing information on smokers’ initial perceptions of RNCs, as well as reactions to cigarettes that they are told contained reduced nicotine. This study will fill gaps in the literature by experimentally controlling for nicotine content and examining the true influence of nicotine content descriptions on subjective ratings of smoking and smoking behaviors. If participants provide lower subjective ratings of their own cigarette when it is labeled as “low” or “very low” nicotine, this taken together with the extant literature on nicotine content descriptions, might suggest that consumers may initially be biased toward RNCs regardless of their actual product characteristics. Smokers’ biases about the subjective effects of cigarettes described as containing reduced nicotine may need to be addressed prior to policy implementation in order to increase the acceptance of these products. Additionally, the information gained from the prospective assessment of outcome expectancies for, and willingness to use, RNCs may be useful for determining smokers’ openness to using these products if a nicotine reduction policy were implemented in the future.

Overall, this information will contribute to the accumulating body of literature which may be used to help regulatory agencies approach initial implementation strategies and public education about RNCs. Additionally, the information resulting from this study may be used to encourage agencies to fund future research into how perceptions of RNCs might be changed to promote consumer acceptance prior to intended implementation.
Chapter 2: Methods

Overview

This study used a crossover laboratory design to evaluate nicotine content description effects on subjective responses to smoking and smoking behaviors among a sample of 33 daily smokers. Additionally, participants’ initial RNC outcome expectancies and willingness to use RNCs were explored as moderators of nicotine content description effects. Eligible participants completed four laboratory sessions: a single, hour-long baseline session and three half-hour long experimental sessions. During the baseline session, participants provided informed consent and completed initial assessments of RNC outcome expectancies and willingness to use RNCs. During each experimental session (following 12-h abstinence), participants smoked a blinded version of their own cigarette brand through an electronic topography device. While smoking, participants received deceptive descriptions about that cigarette's nicotine content. Participants completed a number of pre- and post-cigarette measures of subjective and behavioral responses to smoking. All procedures were reviewed and approved by the Pennsylvania State University Institutional Review Board (CATS IRB #586).

Participants

Recruitment. Study participants were 33 (21 male, 12 female) smokers recruited from the Penn State University Park student population and surrounding State College community from September of 2014 through March of 2015. Participants were recruited primarily using websites such as Craigslist (https://pennstate.craigslist.org) and the PSU Office of Research Protections Study Volunteers (http://research.psu.edu/volunteer), and
secondarily through flyers and advertisements placed throughout Penn State's campus and on local business community boards (Appendix A1). A small number of participants were also recruited through participant databases from other on-campus smoking studies; individuals who had successfully completed these studies and indicated willingness to participate in future studies were contacted via email (Appendix A3). Recruitment methods were designed in consultation with Drs. Stephen Wilson and Charles Geier (personal communication), who had successfully recruited this population in previous studies (Lydon, Roberts, & Geier, 2014; Wilson et al., 2014).

Due to difficulties in recruiting female participants, recruitment materials were modified after three months of recruiting to specifically emphasize the need for female study volunteers (Appendix A4). Additional recruitment methods were also devised, which included sharing links to study listings on Craigslist through social media outlets (e.g., Facebook, Twitter) and placing study advertisements on various Penn State and community listservs (i.e., electronic mailing lists).

**Inclusion criteria.** To establish that participants were regular smokers, and to maintain consistency with the inclusion criteria of larger trials of RNCs (Donny et al., 2015), participants were required to report smoking at least 5 cigarettes per day for at least the past six months, and had to provide an initial breath carbon monoxide sample > 8 ppm during the baseline session (SRNT Subcommittee on Biochemical Verification, 2002). Given the legal age required to both provide consent and purchase cigarettes, participants had to be at least 18 years of age.

**Exclusion criteria.** Participants were excluded if they met any of the following criteria: (1) self-reported current diagnosis of an illnesses adversely affected by smoking
(e.g., thyroid, lung, heart, and kidney problems, diabetes, high blood pressure, asthma),
(2) self-report of or test positive for pregnancy, (3) primarily smoking self-rolled,
“crushable,” or otherwise unblindable/topography device-incompatible cigarettes (e.g.,
American Spirit, Marlboro NXT, Camel Crush), and (4) plans to quit within the next
month, as it is possible reactions to RNCs of those in or preparing for a quit attempt (i.e.,
treatment seeking smokers) may differ from non-treatment seeking smokers.

Procedure

**Telephone eligibility screen.** Potential participants responded to study
advertisements via e-mail or telephone. Regardless of contact method, all individuals
received a brief description of the study (Appendix A6), and then completed a short
fifteen-minute telephone interview (Appendix A2) to determine study eligibility. Those
who met eligibility criteria were provided with additional information about the study
protocol (Appendix A8), and if interested, were scheduled for the baseline session.

**Baseline (visit #1).** Participants were instructed to smoke as they normally would
prior to the baseline session, and to bring a pack of their preferred brand cigarette. Upon
arrival, participants provided informed consent. Participants then visually displayed their
preferred brand cigarette to research staff for purposes of verifying smoking status and
identifying brand of cigarette to be used as the blinded study-supplied cigarettes during
subsequent experimental sessions. Participants’ smoking status was further verified
biochemically through collection of an expired air carbon monoxide (CO) sample >8 ppm
(SRNT Subcommittee on Biochemical Verification, 2002), and female participants
provided a urine sample which was tested to rule out pregnancy. Participants then
completed a series of computerized questionnaires of demographic, smoking, and medical history information, as well as questions regarding willingness to use RNCs and RNC smoking outcome expectancies (Appendix B3 & B4). At the end of the baseline session, participants scheduled their first experimental session and were instructed to abstain from smoking and to avoid any products containing nicotine (e.g., e-cigarettes, hookah, NRT) for at least 12 hours before their scheduled session time.

**Experimental sessions (visit #’s 2-4).** Participants completed three experimental sessions during which they smoked a blinded, study-supplied cigarette (i.e., the participant’s usual brand cigarette) through a smoking topography device – an electronic device that captures measures of smoking behavior – and then provided ratings of the cigarette. Participants were required to abstain for 12 hours prior to their scheduled session time to eliminate the influence of prior cigarette consumption on subsequent smoking during experimental sessions. Because smokers experience the greatest subjective effects from smoking the first cigarette of the day (Pillitteri, Kozlowski, Sweeney, & Heatherton, 1997), sessions were generally scheduled between the hours of 7 a.m. and 1 p.m. to reflect the time during which participants would normally smoke their first cigarette of the day, and occurred within a 1-hour window across sessions. Sessions were scheduled with at least one day between to allow participants to resume normal smoking behaviors and to avoid order effects on pre-cigarette measures of craving and withdrawal (i.e., having back-to-back sessions would likely result in greater pre-cigarette craving during the second vs. first experimental session). The majority (75.8%) of the sample completed the study within two weeks (including the baseline session). On average, participants completed all four sessions in 14.67 (SD = 13.51) days.
At the beginning of each experimental session, participants provided a CO sample to verify 12-hour abstinence. If female, participants also provided a urine sample to be tested for pregnancy status. Participants who did not meet abstinence criteria (i.e., those with a CO ≥ 10 ppm or ≥ 50% of baseline CO, or who reported smoking ≥ 1 cigarettes during abstinence period) had that day's session rescheduled. Participants next completed pre-cigarette assessments of craving and withdrawal (Appendices C1 & C2). Following questionnaire completion, participants smoked a single, blinded cigarette through a smoking topography device. Participants were instructed to take at least one puff of the cigarette and were then given five minutes to smoke the remainder of the cigarette ad lib (i.e., without restrictions; participants were told they may smoke as much or as little of the cigarette as they wished). After smoking the cigarette, participants provided a post-cigarette CO sample and completed assessments of craving, withdrawal, and sensory ratings (Appendix C3). All experimental sessions were identical in format with the exception of the nicotine content descriptions participants were given. A brief, visual overview of the format for each study session is provided in Figure 1.
**Deception.** Study recruitment materials and procedures were designed specifically to deceive participants (as well as research staff) regarding the true purpose of the study. The consent form (Appendix A5) and all recruitment materials and study scripts (Appendices A6 and A8) stated that the purpose of the study was to determine if cigarettes containing “different levels of nicotine” affected smoking behaviors and ratings. Participants were informed that the study cigarettes they would be given would be “very similar to [their] preferred brand in all aspects except nicotine content.” However, during all sessions participants were given the exact type of cigarette they identified as their preferred brand cigarette. Thus, participants were aware that the cigarettes they would smoke during the study were similar to their preferred cigarette, but were deceived about being given their actual preferred brand cigarette. After the entire
study was completed, participants were sent a debriefing letter via email (Appendix A7) informing them of the true aims of the study.

**Nicotine content description.** Throughout the study, participants smoked three blinded versions of their own preferred brand cigarette. Participants were assigned to one of six possible description orders (see Table 1) using a simple randomization schedule, stratified by gender, created prior to participant recruitment. Description order was determined at the end of the baseline session and counterbalanced across participants.

<table>
<thead>
<tr>
<th>Order #</th>
<th>Experimental Session #</th>
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<tbody>
<tr>
<td>1 (ABC)</td>
<td>1 (ABC)</td>
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<tr>
<td>2 (BCA)</td>
<td>2 (BCA)</td>
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<tr>
<td>3 (CAB)</td>
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<td>5 (ACB)</td>
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<tr>
<td>6 (CBA)</td>
<td>6 (CBA)</td>
</tr>
</tbody>
</table>

Nicotine content descriptions for the study-supplied cigarettes were administered to participants via PowerPoint presentations created by the principal investigator. Three slideshows were created, one for each experimental session: 1) Slideshow A contained the description: “The cigarette you are smoking contains the same level of nicotine as your usual brand,” 2) Slideshow B contained the description: “The cigarette you are smoking contains a *low* level of nicotine compared to your usual brand,” and 3) Slideshow C contained the description: “The cigarette you are smoking contains a *very low* level of nicotine compared to your usual brand.” Slideshows were intentionally
labeled as “A” vs. “B” vs. “C” as opposed to “UBC” vs. “LNC” vs. “VLNC” to keep research staff blinded to the nicotine content of the study-supplied cigarette.

Prior to each experimental session, research staff retrieved a plastic bag from a laboratory refrigerator containing the blinded cigarette to be used during the session and the following information: participant ID and session number, session date and time, and slideshow letter (e.g., “Slideshow B”). Research staff opened the session-specific slideshow file after participants completed pre-smoking questions, but prior to receiving instructions on how to smoke the study-supplied cigarette. After research staff observed participants taking a single puff of the study-supplied cigarette, staff pressed a laptop button to initiate the slideshow. The slideshow consisted of three slides presented in the following order: 1) a blank slide lasting 30 seconds to allow research staff time to answer potential participant questions and exit the experiment room, 2) a slide with the nicotine content description lasting three minutes, and 3) a blank slide lasting indefinitely to allow research staff to remain blind about nicotine content description upon returning to the experiment room.

**Cigarette blinding.** Cigarettes were blinded using the same methods employed by similar cigarette deception studies (Perkins & Karelitz, 2013; Perkins, Mercincavage, Fonte, & Lerman, 2010; Strasser, Lerman, Sanborn, Pickworth, & Feldman, 2007) which required covering all branding or identifying marks with scientific labeling tape. Cigarette blinding was carried out solely by the principal investigator; research staff, like study participants, were unaware that participants were smoking their preferred brand cigarette. The principal investigator purchased participants’ identified preferred brand from retail outlets (e.g., Weis grocery store, Sheetz gas station) and blinded cigarettes
prior to experimental sessions. Blinded cigarettes were placed in a plastic bag containing participant- and session-specific slideshow information, and left in a laboratory refrigerator where research assistants retrieved them during subsequent study sessions.

**Study compensation.** Participants were paid at a rate of $10 per hour of participation, totaling $25 for the 2.5 total hours of study time (one hour-long and three half-hour long sessions). Participants received an additional $15 as an incentive for abstaining for 12 hours before each experimental session, totaling $45 for all three experimental sessions. To discourage attrition, a $30 “bonus” for completing all four sessions was provided at the end of the study. Successful completion of all study components resulted in participants receiving $100 total compensation.

**Measures**

**Overview.** Measures used to address Aims 1 and 2 have been previously used in similar laboratory-based smoking studies, and have demonstrated good psychometric properties. Because Aim 3 involved the exploratory assessment of constructs not yet applied to nicotine reduction research, the psychometric properties of Aim 3 measures are unknown, but were adapted from measures demonstrating high reliability and validity. Descriptions of measures specific to each aim are presented in detail below, followed by a summary of time points for when each measure was assessed in Table 2.

*Aim 1: Determine the influence of nicotine content description on subjective responses to smoking.* Participants’ subjective responses to smoking study-supplied
cigarettes were captured through assessments of craving, withdrawal, and sensory characteristics during each of the three experimental sessions.

**Craving.** Craving for cigarettes was assessed at the beginning and end (i.e., pre- and post-cigarette) of each experimental session using two factor subscales and an overall global craving score from the 10-item Brief Questionnaire of Smoking Urges (Cox, Tiffany, & Christen, 2001). Average QSU Factor 1 subscale scores represent intention or desire to smoke, and were created by taking the mean value of items 1, 3, 6, 7, and 10 (Cronbach’s α’s for pre- and post-cigarette Factor 1 scores across the three experimental sessions ranged from 0.93 to 0.97). Average QSU Factor 2 subscale scores represent craving due to anticipation of relief of negative affect and urgent desire to smoke, and were created by taking the mean value of items 2, 4, 5, 8, and 9 (Cronbach’s α’s = 0.85 to 0.92). The mean of all ten items was used as an average ‘global,’ or overall, craving score (Cronbach’s α’s = 0.93 to 0.96). Item responses ranged from 0-100 on a visual analog scale, anchored with 0 = "Strongly Disagree" and 100 = "Strongly Agree."

**Withdrawal.** The 15-item revised version of the Minnesota Nicotine Withdrawal Scale (MNWS; Hughes & Hatsukami, 1986) was administered prior to and after smoking each experimental session cigarette to assess withdrawal resulting from 12-h abstinence. Participants responded to each item on 0-100 point visual analog scale (0 = "None", 25 = "Slight", 50 = "Mild, 75 = "Moderate, 100 = "Severe"). Average pre- and post- cigarette withdrawal measures for each session were calculated by taking the mean of the validated 9 items (Cronbach’s α’s = 0.73 to 0.83).

**Sensory effects.** A 14-item visual analog scale (Strasser et al., 2004) was administered after smoking each study-supplied cigarette (Cronbach’s α’s = 0.41 to 0.69)
to assess sensory effects of smoking (e.g., taste, burn rate, strength). For this scale, participants were instructed to move a vertical slider to a position along a horizontal continuum which best represented their rating for the cigarette for a certain characteristic (e.g., “Strength”, “Harshness”). Continuum anchors were specific to each item (e.g., for the "Strength" item, response anchors were "Very weak" and "Very strong") and were analyzed on a 0-100 point scale (e.g., 0 = "Very weak," 100 = "Very strong").

**Aim 2: Examine nicotine content description effects on smoking behaviors.**
Smoking behaviors were captured through smoking topography measures and changes in expired air carbon monoxide (CO).

**Topography measures.** Measures of smoking topography were assessed using the Clinical Research Support System for Laboratories (CReSS) smoking topography device (Borgwaldt KC Inc., Richmond, VA). The CReSS device provides a variety of behavioral measures per puff of cigarette (e.g., puff duration, puff volume); however, composite and average variables were created to both maintain consistency with other topography studies (Perkins et al., 2008, 2009, 2012, 2010; Strasser et al., 2004), and to make direct comparisons between cigarettes (i.e., puff analysis was not an aim of this study). These measures included:

- **Total puff volume.** The volume (ml) of each cigarette puff was summed to create a total puff volume variable, representing the total smoke inhaled from each cigarette.

- **Total puff number.** The total number of puffs taken per cigarette.

- **Total puff duration.** The total length of inhalation for all puffs.

- **Average puff volume.** The average volume of each puff (ml).
Average interpuff interval. The average length of time between puffs (ms)

Average puff duration. The average length of each puff (ms).

Before conducting analyses of smoking topography measures, topography data were cleaned using procedures recommended by Plowshare Technologies (now Borgwaldt KC) to identify broken and aberrant puffs. First, all puffs with volumes less than 10 milliliters (ml) and an interpuff interval (IPI) less than 300 milliseconds (ms) were identified as broken puffs; as such, the volumes of these puffs were combined with the preceding puff, total puff count reduced by one, and the IPI of the previous puff replaced as the appropriate puff. Next, puffs with volumes greater than 150 milliliters and durations greater than 4000 milliseconds were identified as aberrant values. Cigarettes with more than 25% aberrant puff values were further excluded from analyses. Of the 72 conducted experimental sessions, the topography device recorded aberrant cigarette data for 7 cigarettes (9.72%), and failed to record data for 3 cigarettes (4.17%). Because topography analyses relied upon repeated measures assessments, this resulted in 8 participants (33.33%) being excluded from subsequent analyses of topography measures.

CO. Expired-air carbon monoxide was measured using the coVita/Bedfont Scientific Micro+ Smokerlyzer (Haddonfield, NJ). An initial CO sample was obtained during the baseline session to verify daily smoking status. Additional CO samples were taken at the beginning of each experimental session to verify 12-h abstinence and after smoking the study cigarette to observe changes following cigarette use.

Aim 3: Assess initial RNC outcome expectancies about and willingness to use RNCs, and evaluate willingness and attitudes as potential moderators of nicotine
content description effects on subjective ratings and smoking behaviors. In contrast to Aim 1 and 2 measures, both willingness to use RNCs and RNC outcome expectancies were assessed during participants' baseline session only (i.e., prior to use of any study cigarettes). Because these constructs have not yet been applied to nicotine reduction research, the present study served as pilot data for testing these measures.

**Willingness to use RNCs.** Participants' willingness to use RNCs was assessed according to the Theory of Planned Behavior/Theory of Reasoned Action (TPB/TRA; Ajzen, 1991, 2003) at baseline. According to TRA/TPB, behavioral intentions are those that individuals plan to do, and are strong predictors of future behavior (Ajzen, 2003). However, because RNCs are not commercially available and many smokers are unaware such products exist, participants did not have well-developed behavioral intentions regarding RNC use. As such, willingness – or openness – to use RNCs was assessed by asking participants, "If reduced nicotine cigarettes became available today..." to indicate how likely they were to engage in the following thirteen activities in the next 30 days: (1) use RNCs like [their] current brand, (2) use RNCs but smoke more CPD, (3) use RNCs to gradually quit smoking, (4) quit smoking immediately instead of using RNCs, (5) supplement RNC use with e-cigarettes, (6) supplement RNC use with other tobacco products, (7) supplement RNC use with nicotine replacement therapies, (8) supplement RNC use with roll-your-own cigarettes, (9) use e-cigs exclusively instead of RNCs, (10) use other tobacco products exclusively, (11) use NRT exclusively, (12) use roll-your-own cigarettes exclusively, and (13) buy cigarettes with higher nicotine content from "other potentially illicit sources." Participants responded to each item on a 4-point scale (1 = "Not at all", 2 = "Slightly willing", 3 = "Moderately willing", 4 = "Strongly willing").
Frequencies of responses were examined to determine which items contained reasonable variability for consideration for inclusion in a composite "general willingness to use RNCs" measure. A composite score was created by reverse scoring items 2, 4, and 9 through 13, and then summing these items with items 1 and 3. Items referring to supplementing RNCs with other types of tobacco use contained little variability between responses; as such, these items were excluded from the composite willingness measure.

**RNC Outcome Expectancies.** Participants' outcome expectancies for smoking RNCs were assessed using two modified versions of the modified Cigarette Evaluation Scale (mCES; Rose, 2005). The first version assessed outcome expectancies for participants’ preferred brand cigarette by asking participants to indicate their agreement with each item on the mCES for the statement, “I believe smoking my preferred cigarette brand….” The second version assessed outcome expectancies for RNCs by asking participants to complete the same items for the statement, “Compared to my preferred cigarette brand, I believe smoking a cigarette with reduced nicotine…” Six additional pilot items were included with each version of the mCES: (1) is addictive, (2) is safe, (3) is healthy, (4) increases risk of cardiovascular event, (5) increases chance of developing cancer, (6) helps me control my weight. Participants responded to each item on a 5-point scale (-2 = "Strongly disagree", -1 = "Slightly disagree", 0 = "Neither agree nor disagree", 1 = "Slightly agree", 2 = "Strongly agree"). Negative items (e.g. "...is addictive") were reverse scored, and a composite score for each cigarette type was created. Participants' composite scores of expectancies related to using a cigarette with reduced nicotine were subtracted from composite scores of expectancies related to using their preferred brand
cigarette. This resulted in the creation of an overall composite score of RNC outcome expectancies relative to expectancies for participants' own preferred brand cigarette.

Table 2. Questionnaire/Measure Administration across Study Sessions.

<table>
<thead>
<tr>
<th>Aim</th>
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<th>E2</th>
<th>E3</th>
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<td>X</td>
<td>X</td>
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<td></td>
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</tbody>
</table>

Additional measures. In addition to the measures described for each aim, participants also completed baseline questionnaires regarding their demographic information (e.g., age, gender, race/ethnicity, highest education level), smoking and drug use history (e.g., ever/never use, length of use), and nicotine dependence (Fagerstrom Test for Cigarette Dependence [FTCD; Fagerström, 1978; Heatherton, Kozlowski, Frecker, & Fagerström, 1991], Hooked on Nicotine Checklist [HONC; DiFranza et al., 2002], Wisconsin Inventory of Smoking Dependence Motives [WISDM; Piper et al., 2004]). Cronbach’s alphas for dependence measures were 0.40, 0.64, and 0.93, respectively.
Analytic Plan

**Overview.** Analyses of nicotine content description effects, as well as analyses of moderators of nicotine content description effects, utilized a series of repeated measures analysis of variance (RM-ANOVA) and repeated measures multivariate analysis of variance models (RM-MANOVA). Because of the similarities between analyses of constructs across Aims 1 and 2, brief descriptions are first provided for analyses specific to each construct (organized by aim), followed by more detailed descriptions by type of analysis. Given the exploratory nature of Aim 3, separate descriptions of Aim 3 analyses are presented following other data considerations.

**Basic descriptions of analyses used by aim.**

*Preliminary analysis: Validation of experimental manipulation.* To determine if the experimental manipulation of cigarette nicotine content description was successful, participants were asked after each session to estimate, on a scale of "None" to "Very Much" (scored 0-100), how much nicotine they thought was in that session's cigarette and how much nicotine they thought was in their own preferred brand cigarette. A RM-MANOVA was conducted to assess the effect of nicotine content description on two dependent variables: (1) estimated nicotine content of both the study-supplied cigarette and (2) participant’s preferred brand cigarette.

*Aim 1. Nicotine content description effects on subjective responses to smoking.*

1.1. *Craving reduction.* Two analyses were used: (1) a 3 (nicotine content description) x 2 (time) RM-ANOVA tested effects on the dependent variable of global
craving (i.e., average total score) and (2) a 3 x 2 RM-MANOVA tested effects on craving subscales. The multivariate analysis contained two dependent variables: craving due to intention/desire to smoke and craving due to anticipation of NA relief (i.e., QSU factor 1 and factor 2 subscales), given the correlations and conceptual relations between these subscales.

1.2. Withdrawal suppression. A single, univariate 3 (nicotine content description) x 2 (time) RM-ANOVA assessed effects on the dependent variable of withdrawal.

1.3. Sensory effects of smoking. A RM-MANOVA tested the effect of nicotine content description on sensory ratings, using the fourteen items of the visual analog scale as dependent variables.

Aim 2. Nicotine content description effects on smoking behaviors.

2.1. Smoking topography. Two RM-MANOVAs tested the effect of nicotine content description on (1) composite topography measures and (2) average topography measures. The first multivariate analysis contained three dependent variables: total puffs taken, total puff volume, and total puff duration. Due to statistical correlations and conceptual relations between composite topography measures (e.g., total puff volume is dependent, in part, upon total puff duration), all composite measures were included as dependent variables in a single multivariate analysis vs. as individual dependent variables in separate univariate analyses. The second multivariate analyses contained three dependent variables: average puff volume, average interpuff interval, and average puff duration. Similar to the multivariate analysis of composite topography measures, all
average topography measures were included together as dependent variables due to their conceptual and statistical associations.

2.2. CO boost. A single, 3 (nicotine content description) x 2 (time) RM-ANOVA was used to assess effects on the dependent variable of CO.

General descriptions of analyses used in Aims 1 and 2.

Univariate analyses. For all univariate (i.e., predicting a single outcome) repeated measures analyses (i.e., analyses of global craving reduction, withdrawal suppression, and CO boost), there were three IVs: the main effect of nicotine content description (“UBC” vs. “LNC” vs. “VLNC”), the main effect of time (pre- vs. post-cigarette assessments), and the interaction effect of nicotine content description x time. Given that the aims of the study were to compare the magnitude of change over time by nicotine content description, the primary term of interest in all analyses was the interaction of nicotine content description x time.

Significant interactions of nicotine content description x time were explored using two sets of follow-up ANOVAs. The first set of follow-up ANOVAs explored the main effect of nicotine content description on ratings for each time point by conducting:

1) A RM-ANOVA of nicotine content description on pre-cigarette ratings
2) A RM ANOVA of nicotine content description on post-cigarette ratings

The second set of follow-up ANOVAs explored the main effect of time on ratings for each nicotine content description by conducting:

1) A RM-ANOVA of time on ratings for the “UBC” description
2) A RM-ANOVA of time on ratings for the “LNC” description
3) A RM-ANOVA of time on ratings for the “VLNC” description

Main effects of time were explored by visual comparison of means, while main effects of nicotine content description were explored using pairwise comparisons. Pairwise comparisons used Bonferroni adjustments to correct for multiple comparisons.

_Multivariate analyses including time_. The analysis of craving reduction subscales (Aim 1.1.) was the only multivariate analysis that also included changes over time. As such, this RM-MANOVA included the same three IVs as univariate analyses (i.e., nicotine content description, time, and nicotine content description x time), but predicted two dependent variables instead of one, given the conceptual relations and correlations between QSU factor subscales. Similar to univariate analyses involving time, the multivariate interaction of nicotine content x time was the primary term of interest. Univariate results from multivariate analyses were only interpreted if multivariate effects were significant. Significant univariate main effects and interactions were then further explored using the same procedures as in univariate analyses discussed earlier (i.e., pairwise comparisons and sets of follow-up ANOVAs).

_Multivariate analyses not including time_. For all multivariate analyses of outcomes assessed at a single time-point (i.e., sensory effects of smoking, composite and average topography measures), nicotine content description was the only (three-level) IV. Univariate results were only interpreted if the overall multivariate effect of nicotine content description was significant. Significant univariate main effects were then further explored using Bonferroni-adjusted pairwise comparisons.
**Other analytic considerations.**

**Normality.** Prior to conducting all analyses, the distributions of each dependent variable – overall and at each level of the independent variable – were examined and determined to meet assumptions of normality. Skewness values of ± 2 and kurtosis values of ± 5 were considered acceptable.

**Sphericity.** Due to the use of a three-level repeated measures independent variable (i.e., nicotine content description), Mauchly’s test results were examined prior to interpreting univariate analyses to determine if the assumption of sphericity was met. In cases where sphericity was violated, epsilon values were examined to determine which correction should be applied to univariate results. As recommended by Girden (1992) Huynh-Feldt and Greenhouse-Geisser corrections were used for violations with epsilon values greater and less than 0.75, respectively.

**Power.** A priori power analyses were conducted for Aims 1 and 2 using G*Power v3.1.2 (Buchner, Erdfelder, Faul, & Lang, 2009). These analyses determined that a target sample size of 36 was necessary for the detection of the main within-subjects effect of nicotine content descriptions on a univariate outcome. This sample size would power analyses to detect a medium-large effect size (0.25-0.5) with 90% power, using a two-tailed significance test with alpha set to 0.05. A target sample of 50 was necessary to conduct multivariate versions of this analysis using the same parameters. Because the current study restricted analyses to include only the 24 participants who believed the experimental manipulation, the desired sample size was not met. However, post-hoc power analyses conducted for each specific outcome revealed that several analyses
obtained sufficient power despite this limitation (e.g., observed power for multivariate analyses of craving subscales and sensory ratings were 86% and 99%, respectively).

**Missing data.** Because data for this study were collected under highly controlled conditions, all variables had 0% missingness with the exception of the data collected by the smoking topography device (additional details provided under Measures section).

**Covariates.** Preliminary analyses revealed significant associations between gender and nicotine dependence (as assessed by the FTND) with several study outcomes (e.g., craving, withdrawal). As such, Aim 1 and 2 analyses were repeated including these variables as covariates. To separate gender and dependence effects, analyses were first repeated including gender as a covariate, and then again including both gender and dependence as covariates. Because main and interaction effects of gender and dependence were beyond the scope of this dissertation, detailed statistical results were not reported for these analyses; rather, results focused on whether nicotine content effects on study outcomes remained after controlling for these factors.

**Description of Aim 3 analyses**

**Aim 3. Assess initial RNC outcome expectancies about and willingness to use RNCs, and evaluate willingness and outcome expectancies as potential moderators of the effects of nicotine content descriptions on subjective ratings and smoking behaviors.**

**Normality.** Prior to examining willingness to use RNCs and RNC outcome expectancies as moderators of nicotine content description effects, the distributions for
each composite measure were examined among the 24 participants who believed the experimental manipulation. Both composite measures met assumptions of normality.

_creation of dichotomous moderators._ In order to create equal group sizes for exploratory analyses of moderating variables, a median split was used to divide the sample on measures of willingness to use RNCs and RNC outcome expectancies. Participants above the median score on the continuous willingness to use RNCs variable were classified as “more willing to use RNCs” while those below the median score were classified as “less willing to use RNCs.” Given that all participants expressed negative RNC outcome expectancies relative to their own brand cigarette, those who were above the median outcome expectancies score were classified as having “positive/neutral” RNC outcome expectancies and those below as having “negative” RNC outcome expectancies.

_willingness analyses._ To examine willingness as a moderator of nicotine content description effects, every analysis used in Aims 1 and 2 was repeated with the additional between-subjects variable of willingness to use RNCs. As such, the interaction of willingness with the primary terms of interest in previous analyses (e.g., nicotine content description main effect or nicotine content description x time) became the focal point of moderation analyses.

In analyses including time, a significant triple interaction of willingness x nicotine content description x time was explored using three sets of follow-up ANOVAs. First, two RM ANOVAs were conducted to explore the interaction effect of nicotine content description x time by each willingness category (more willing vs. less willing). Next, three RM ANOVAs were conducted to explore the interaction effect of willingness x time by each nicotine content description (“UBC” vs. “LNC” vs. “VLNC”). Finally, two
RM ANOVAs were conducted to explore the interaction effect of willingness x nicotine content description by each time of assessment (pre vs. post- cigarette). If any of these seven follow-up ANOVAs were significant, additional follow-up ANOVAs were conducted, similar to those outlined either in the description of univariate analyses (i.e., nicotine content description x time), or below for analyses not involving time (i.e., nicotine content description x willingness).

In analyses not including time, significant interactions of willingness x nicotine content description were explored by first conducting two follow-up RM-ANOVA examining the effects of nicotine content description effects first among only those who were more willing to use RNCs, and then only among those who were less willing to use RNCs. Next, three one-way ANOVAs were conducted to examine the effects of willingness by each separate nicotine content description. Similar to post-hoc analyses used in Aims 1 and 2, significant main effects for nicotine content description were evaluated using pairwise comparisons utilizing a Bonferroni adjustment to correct for multiple comparisons.

_RNC outcome expectancy analyses._ Similar to analyses of willingness, all analyses used for Aims 1 and 2 were repeated with the additional between-subjects variable of RNC outcome expectancies. As such, the interaction of RNC outcome expectancies with the primary terms of interest in previous analyses (e.g., nicotine content description main effect or nicotine content description x time) became the focal point of moderation analyses. All analyses were identical to those used to determine the moderating effects of willingness on nicotine content description influences on subjective and behavioral responses.
Chapter 3: Results

Study Recruitment and Retention

One-hundred sixty-nine prospective participants completed a telephone interview to determine initial eligibility for the study. Of these individuals, 99 were excluded from further participation for the following reasons: smoked < 5 CPD ($n = 61$), reported exclusive use of either a crushable (e.g., Camel Crush) or unblindable (e.g., American Spirit) brand of cigarette ($n = 15$), inconsistent smoking patterns ($n = 8$), health issues ($n = 8$), reported exclusive use of roll-your-own cigarettes ($n = 4$), or other reason (e.g., lived too far away, participant collusion; $n = 3$). Seventy individuals met over-the-phone eligibility criteria and were invited to participate in the initial in-person baseline session; five of these individuals either actively declined to participate or else did not return calls to schedule the baseline session (and were assumed to decline participation). Three individuals scheduled but did not show up for the baseline session. No-shows were given the opportunity to reschedule the missed baseline session; in all instances, these individuals again did not show up for the rescheduled baseline session.

Fifty-nine individuals arrived for the baseline session and signed consent forms to enroll in the study. Only 44 individuals met in-person eligibility criteria; the most common reason for exclusion ($n = 13$) was low CO (i.e., CO value < 9 ppm), followed by providing an unblindable preferred brand cigarette (e.g., Marlboro NXT), thereby conflicting information given during the telephone screen ($n = 2$). Individuals with low CO were given at least one additional attempt to provide a CO sample above 9 before being excluded indefinitely. Those who provided an unblindable cigarette brand were asked if they had a second preferred brand, and what the percentage of time spent
smoking each brand was; if the percentage of time spent smoking the second brand was <50%, the participant was excluded.

Participants who were eligible after the baseline session were then randomized to one of six potential nicotine content description orders. Of the 44 participants eligible after the baseline session, two were in the process of completing the ongoing study protocol, and four dropped out of the study. Of the four drop-outs (50% male), two attritted prior to the first experimental session; the remaining two attritted prior to the second experimental session. Although formal analyses comparing drop-outs to completers were statistically underpowered, drop-outs did not appear to differ from study completers in age, gender, description order, nicotine dependence, or CPD.

Thirty-eight of the 44 baseline-eligible participants completed the entire study. However, post-hoc examination of CO data revealed that five participants had at least one pre-cigarette CO value, indicating that these individuals were not 12-h abstinent, violating study protocol. Because these individuals should have had the sessions on which their CO values were ≥10 rescheduled, these participants' responses to the experimental protocol while non-abstinent could not be considered to be under the same experimental conditions as abstaining participants. As such, data for the five non-abstinent individuals were not included in this dissertation. All subsequent data and analyses refer to the 33 participants who were 12-h abstinent and completed all four study sessions. Overall study recruitment and retention figures are depicted in Figure 2.
Figure 2. Overall Study Recruitment and Retention.

Note: Letter orders refer to order of nicotine content description given across experimental sessions; A = “UBC”; B = “LNC”; C = “VLNC.” For example, ABC = receipt of UBC description during first experimental session, LNC during second experimental session, and VLNC during third experimental session.
Preliminary Analyses

Descriptive analyses. Participants were 33 daily smokers (21 male, 12 female) aged 18-53 years old ($M \pm SD = 25.94 \pm 8.49$) who reported smoking 5-32 CPD ($12.91 \pm 7.03$) and provided a baseline CO of 9-29 ppm ($15.73 \pm 5.84$). 69.7% of participants identified their race/ethnicity as White/Caucasian, 9.1% as Asian, 6.1% as Hispanic, 9.1% as more than one race, 3.0% as Black/African American, and 3.0% as another/unknown. Additional demographic and smoking history information are shown by gender in Table 3. Independent samples t-tests revealed no significant gender differences for any of the continuous variables. For categorical variables, Chi-square tests of independence found a significant association of gender with cigarette length [$\chi^2 (2, N = 33) = 6.03, p = 0.049$]; male participants were significantly more likely than females to smoke short (i.e., 70 mm) and long (i.e., 100 mm) lengths of cigarettes.

Table 3. Demographic Characteristics and Smoking History Behaviors of Sample by Gender and Whole Sample. Data are means + standard deviation or n (% of sample).

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>($n = 21$)</td>
<td>($n = 12$)</td>
<td>($N = 33$)</td>
</tr>
<tr>
<td><strong>Demographic Characteristics</strong></td>
<td>$M (SD)$</td>
<td>$M (SD)$</td>
<td>$M (SD)$</td>
</tr>
<tr>
<td>Age</td>
<td>24.81 (6.73)</td>
<td>27.79 (10.97)</td>
<td>25.94 (8.48)</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>13 (61.9%)</td>
<td>10 (83.3%)</td>
<td>23 (69.7%)</td>
</tr>
<tr>
<td>Black</td>
<td>1 (4.8%)</td>
<td>0 (0%)</td>
<td>1 (3.0%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>2 (9.5%)</td>
<td>0 (0%)</td>
<td>2 (6.1%)</td>
</tr>
<tr>
<td>Asian</td>
<td>2 (9.5%)</td>
<td>1 (8.3%)</td>
<td>3 (9.1%)</td>
</tr>
<tr>
<td>More than one race</td>
<td>2 (9.5%)</td>
<td>1 (8.3%)</td>
<td>3 (9.1%)</td>
</tr>
<tr>
<td>Unknown/other</td>
<td>1 (4.8%)</td>
<td>0 (0%)</td>
<td>1 (3.0%)</td>
</tr>
<tr>
<td>Education (highest level)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school graduate</td>
<td>5 (23.8%)</td>
<td>1 (8.3%)</td>
<td>6 (18.2%)</td>
</tr>
<tr>
<td>Partial college</td>
<td>10 (47.6%)</td>
<td>7 (58.3%)</td>
<td>17 (51.5%)</td>
</tr>
<tr>
<td>College graduate</td>
<td>3 (14.3%)</td>
<td>2 (16.7%)</td>
<td>5 (15.2%)</td>
</tr>
</tbody>
</table>
Among the six possible nicotine content description orders created to counterbalance the study design and control for order effects, one-way ANOVAs and Chi-square tests of independence also revealed no significant description order differences on any of demographic characteristics or smoking history measures. Additional information on demographic and smoking history variables is presented by nicotine content description order in Table 4.

<table>
<thead>
<tr>
<th>smoking history and behaviors</th>
<th>3 (14.3%)</th>
<th>2 (16.7%)</th>
<th>5 (15.2%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline CPD</td>
<td>13.19 (6.94)</td>
<td>12.42 (7.47)</td>
<td>12.91 (7.03)</td>
</tr>
<tr>
<td>Baseline CO (ppm)</td>
<td>16.14 (5.71)</td>
<td>15.00 (6.24)</td>
<td>15.73 (5.84)</td>
</tr>
<tr>
<td>Age first tried cigarette</td>
<td>16.10 (3.70)</td>
<td>14.75 (4.18)</td>
<td>15.61 (3.87)</td>
</tr>
<tr>
<td>Age started smoking regularly</td>
<td>17.76 (3.43)</td>
<td>19.67 (9.75)</td>
<td>18.45 (6.39)</td>
</tr>
<tr>
<td>Nicotine dependence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FTND (0-10)</td>
<td>3.95 (1.72)</td>
<td>3.58 (1.73)</td>
<td>3.82 (1.70)</td>
</tr>
<tr>
<td>WISDM</td>
<td>53.24 (8.88)</td>
<td>54.45 (9.27)</td>
<td>53.68 (8.89)</td>
</tr>
<tr>
<td>HONC (0-10)</td>
<td>7.62 (1.63)</td>
<td>7.33 (1.82)</td>
<td>7.52 (1.68)</td>
</tr>
<tr>
<td>Cigarette flavor preference</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menthol</td>
<td>6 (28.6%)</td>
<td>4 (33.3%)</td>
<td>10 (30.3%)</td>
</tr>
<tr>
<td>Non-menthol</td>
<td>15 (71.4%)</td>
<td>8 (66.7%)</td>
<td>23 (69.7%)</td>
</tr>
<tr>
<td>Cigarette strength</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full flavor</td>
<td>15 (71.4%)</td>
<td>5 (41.7%)</td>
<td>20 (60.6%)</td>
</tr>
<tr>
<td>Light</td>
<td>2 (28.6%)</td>
<td>5 (41.7%)</td>
<td>10 (21.2%)</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>4 (19.0%)</td>
<td>2 (16.7%)</td>
<td>6 (18.2%)</td>
</tr>
<tr>
<td>Cigarette length*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short (70-75 mm)</td>
<td>1 (4.8%)</td>
<td>0 (0.0%)</td>
<td>1 (3.0%)</td>
</tr>
<tr>
<td>Regular/King (80-85 mm)</td>
<td>13 (61.9%)</td>
<td>12 (100%)</td>
<td>25 (75.8%)</td>
</tr>
<tr>
<td>Long (100 mm)</td>
<td>7 (33.3%)</td>
<td>0 (0.0%)</td>
<td>7 (21.2%)</td>
</tr>
</tbody>
</table>

Note: * = p < 0.05; ** = p < 0.01; *** = p < 0.001
Table 4. Demographic Characteristics and Smoking History Behaviors of Sample by Nicotine Content Description Order. Data are means + standard deviation or n (% of sample).

<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>A (n = 4)</th>
<th>B (n = 7)</th>
<th>C (n = 7)</th>
<th>D (n = 5)</th>
<th>E (n = 5)</th>
<th>F (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>30.75 (8.46)</td>
<td>29.43 (13.02)</td>
<td>23.57 (4.72)</td>
<td>21.80 (1.79)</td>
<td>22.40 (4.34)</td>
<td>28.20 (10.71)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3 (75.0%)</td>
<td>5 (71.4%)</td>
<td>4 (57.1%)</td>
<td>3 (60.0%)</td>
<td>3 (60.0%)</td>
<td>3 (60.0%)</td>
</tr>
<tr>
<td>Female</td>
<td>1 (25.0%)</td>
<td>2 (28.6%)</td>
<td>3 (42.9%)</td>
<td>2 (40.0%)</td>
<td>2 (40.0%)</td>
<td>2 (40.0%)</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>4 (100%)</td>
<td>4 (57.1%)</td>
<td>4 (57.1%)</td>
<td>2 (40.0%)</td>
<td>5 (100%)</td>
<td>4 (80.0%)</td>
</tr>
<tr>
<td>Black</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (20.0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0 (0%)</td>
<td>2 (28.6%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Asian</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2 (28.6%)</td>
<td>1 (20.0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>More than one race</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (14.3%)</td>
<td>1 (20.0%)</td>
<td>0 (0%)</td>
<td>1 (20.0%)</td>
</tr>
<tr>
<td>Unknown/other</td>
<td>0 (0%)</td>
<td>1 (14.3%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Smoking History</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline CPD</td>
<td>18.75 (10.45)</td>
<td>10.14 (2.61)</td>
<td>11.71 (3.73)</td>
<td>10.20 (4.76)</td>
<td>10.40 (3.91)</td>
<td>19.00 (11.45)</td>
</tr>
<tr>
<td>Baseline CO (ppm)</td>
<td>18.75 (7.63)</td>
<td>15.00 (5.39)</td>
<td>14.86 (6.23)</td>
<td>14.00 (6.21)</td>
<td>15.00 (3.00)</td>
<td>18.00 (7.58)</td>
</tr>
<tr>
<td>Age first tried cigarette</td>
<td>15.25 (2.87)</td>
<td>17.14 (5.96)</td>
<td>15.14 (3.67)</td>
<td>15.60 (2.19)</td>
<td>13.80 (4.32)</td>
<td>16.20 (2.78)</td>
</tr>
<tr>
<td>Age started smoking regularly</td>
<td>17.75 (1.71)</td>
<td>22.43 (13.02)</td>
<td>17.14 (2.61)</td>
<td>17.80 (0.45)</td>
<td>16.40 (2.70)</td>
<td>18.00 (3.94)</td>
</tr>
<tr>
<td>Nicotine dependence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FTND</td>
<td>5.25 (1.50)</td>
<td>3.57 (1.40)</td>
<td>3.43 (1.40)</td>
<td>3.20 (2.59)</td>
<td>3.80 (1.30)</td>
<td>4.20 (2.05)</td>
</tr>
<tr>
<td>WISDM</td>
<td>57.64 (11.09)</td>
<td>54.08 (8.67)</td>
<td>58.14 (4.95)</td>
<td>53.62 (6.50)</td>
<td>46.60 (11.02)</td>
<td>50.89 (10.21)</td>
</tr>
<tr>
<td>HONC</td>
<td>9.00 (0.82)</td>
<td>7.43 (2.37)</td>
<td>7.86 (1.21)</td>
<td>7.20 (1.48)</td>
<td>6.20 (1.79)</td>
<td>7.60 (1.14)</td>
</tr>
<tr>
<td>Cigarette flavor preference</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menthol</td>
<td>1 (25.0%)</td>
<td>4 (57.1%)</td>
<td>0 (0%)</td>
<td>3 (60.0%)</td>
<td>1 (20.0%)</td>
<td>1 (20.0%)</td>
</tr>
<tr>
<td>Non-menthol</td>
<td>3 (75.0%)</td>
<td>3 (42.9%)</td>
<td>7 (100%)</td>
<td>2 (40.0%)</td>
<td>4 (80.0%)</td>
<td>4 (80.0%)</td>
</tr>
<tr>
<td>Cigarette strength</td>
<td>Full flavor</td>
<td>Light</td>
<td>Other/unknown</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
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<td>-------</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>2 (50.0%)</td>
<td>5 (71.4%)</td>
<td>1 (25.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 (28.6%)</td>
<td>3 (42.9%)</td>
<td>1 (14.3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 (80.0%)</td>
<td>0 (0%)</td>
<td>1 (20.0%)</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>3 (60.0%)</td>
<td>1 (20.0%)</td>
<td>1 (20.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 (80.0%)</td>
<td>2 (20.0%)</td>
<td>0 (0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cigarette length</th>
<th>Short (70-75 mm)</th>
<th>Regular/King (80-85 mm)</th>
<th>Long (100 mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 (0.0%)</td>
<td>2 (50.0%)</td>
<td>2 (50.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0.0%)</td>
<td>5 (71.4%)</td>
<td>2 (28.6%)</td>
</tr>
<tr>
<td></td>
<td>1 (14.3%)</td>
<td>6 (85.7%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>3 (60.0%)</td>
<td>2 (40.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>5 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>4 (80.0%)</td>
<td>2 (20.0%)</td>
</tr>
</tbody>
</table>
Belief of experimental manipulation. Of the 33 study completers, nine smokers (27.3%) rated at least one of the cigarettes they were told contained reduced nicotine (i.e., either the “LNC” or “VLNC” cigarette) as containing more nicotine than the “UBC” cigarette, suggesting that these subjects did not believe the experimental manipulation. Four of the nine “non-believers” rated both of the “reduced” nicotine cigarettes as containing more nicotine than the “UBC” cigarette; two of these four participants estimated the nicotine content of these cigarettes to be within 3-10% of the nicotine content in the “UBC” cigarette, indicating that these individuals knew or suspected they had received the same cigarette. There was no obvious pattern to the other two participants' estimates. Of the remaining five participants, all rated the “LNC” cigarette as containing comparable or greater nicotine than the “UBC” cigarette; notably, none rated the “VLNC” cigarette as having more nicotine than the “UBC” cigarette.

Exclusion of “non-believers.” Given discrepancies in estimated content of the study cigarettes, conclusions drawn from results of the entire sample (n = 33) may not be accurate. Consistent with the methods demonstrated by other nicotine dose descriptions (Juliano & Brandon, 2002; Perkins, 2009; Perkins et al., 2008), all subsequent analyses of nicotine content description effects are presented only for the subset of “believers,” i.e., those participants who provided estimates of study-supplied cigarette nicotine content congruent with nicotine content descriptions (n = 24). Although exclusion of the “non-believers” comprised a substantial portion of the total sample, this proportion is similar to those seen in other nicotine dose description studies (Juliano & Brandon, 2002; Perkins, 2009; Perkins et al., 2008). Additionally, independent samples t-tests and Chi-square tests
of independence revealed no significant differences between “believers” and “non-believers” on any demographic or smoking behavior characteristics (see Table 5 below).

Table 5. Demographic Characteristics and Smoking History Behaviors by Belief of Experimental Manipulation. Data are means ± standard deviation or n (% of sample).

<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>Believers (n = 24)</th>
<th>Non-believers (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>25.33 (8.10)</td>
<td>27.56 (9.76)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16 (66.7%)</td>
<td>5 (55.6%)</td>
</tr>
<tr>
<td>Female</td>
<td>8 (33.3%)</td>
<td>4 (44.4%)</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>19 (79.2%)</td>
<td>4 (44.4%)</td>
</tr>
<tr>
<td>Black</td>
<td>0 (0.0%)</td>
<td>1 (11.1%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1 (4.2%)</td>
<td>1 (11.1%)</td>
</tr>
<tr>
<td>Asian</td>
<td>1 (4.2%)</td>
<td>2 (22.2%)</td>
</tr>
<tr>
<td>More than one race</td>
<td>3 (12.5%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Unknown/other</td>
<td>0 (0.0%)</td>
<td>1 (11.1%)</td>
</tr>
<tr>
<td>Smoking History and Behaviors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline CPD</td>
<td>12.33 (7.14)</td>
<td>14.44 (6.89)</td>
</tr>
<tr>
<td>Baseline CO (ppm)</td>
<td>15.46 (5.60)</td>
<td>16.44 (6.75)</td>
</tr>
<tr>
<td>Age first tried cigarette</td>
<td>15.79 (4.25)</td>
<td>15.11 (2.76)</td>
</tr>
<tr>
<td>Age started smoking regularly</td>
<td>18.71 (7.34)</td>
<td>17.78 (2.82)</td>
</tr>
<tr>
<td>Nicotine dependence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FTND (0-10)</td>
<td>3.58 (1.67)</td>
<td>4.44 (1.74)</td>
</tr>
<tr>
<td>WISDM</td>
<td>52.35 (8.99)</td>
<td>57.24 (8.02)</td>
</tr>
<tr>
<td>HONC (0-10)</td>
<td>7.33 (1.83)</td>
<td>8.00 (1.12)</td>
</tr>
<tr>
<td>Cigarette flavor preference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menthol</td>
<td>8 (33.3%)</td>
<td>2 (22.2%)</td>
</tr>
<tr>
<td>Non-menthol</td>
<td>16 (66.7%)</td>
<td>7 (77.8%)</td>
</tr>
<tr>
<td>Cigarette strength</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full flavor</td>
<td>16 (66.7%)</td>
<td>4 (44.4%)</td>
</tr>
<tr>
<td>Light</td>
<td>3 (12.5%)</td>
<td>4 (44.4%)</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>5 (20.8%)</td>
<td>1 (11.1%)</td>
</tr>
<tr>
<td>Cigarette length</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short (70-75 mm)</td>
<td>1 (4.2%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Regular/King (80-85 mm)</td>
<td>20 (83.3%)</td>
<td>5 (55.6%)</td>
</tr>
<tr>
<td>Long (100 mm)</td>
<td>3 (12.5%)</td>
<td>4 (44.4%)</td>
</tr>
</tbody>
</table>

Note: * = p < 0.05; ** = p < 0.01; *** = p < 0.001
Validation of experimental manipulation. Multivariate analyses testing the effect of nicotine content description on estimated nicotine content of both the study-supplied cigarette and participant’s preferred cigarette brand revealed a substantial effect of nicotine content description on the combined dependent variables \[ Wilk's \, \lambda = 0.26, \, F(4, \, 90) = 21.42, \, p = 0.000, \, \eta_p^2 = 0.49 \]. When considered separately in univariate analyses, a main effect of nicotine content description was found only for estimated nicotine content of the study-supplied cigarette \[ F(2, \, 46) = 66.94, \, p = 0.000, \, \eta_p^2 = 0.73 \].

As shown in Figure 3 below, Bonferroni-adjusted pairwise comparisons revealed that participants estimated the “LNC” and “VLNC” cigarettes to have lower nicotine content than the “UBC” cigarette, indicating that the study was successful in deceiving participants that they received reduced nicotine content cigarettes, despite all study cigarettes containing identical nicotine content. On average, participants estimated that the “LNC” and “VLNC” cigarettes had \(~48\%\) \((37.58 \pm 3.15, \, p = 0.000)\) and \(~53\%\) \((34.54 \pm 4.02, \, p = 0.000)\) less nicotine, respectively, than the “UBC” cigarette \((73.04 \pm 3.09)\).

Although the raw average estimated nicotine content of the “VLNC” cigarette was lower than the “LNC” cigarette, this difference was not statistically significant.

There was no main effect of nicotine content description on estimated nicotine content of participants' own preferred brand \[ F(2, \, 46) = 0.11, \, p = 0.89, \, \eta_p^2 = 0.01 \], suggesting that participants' estimates of the nicotine content of their preferred cigarette brand were reliable across all three experimental sessions. To empirically ensure that the estimated nicotine content of the “UBC” cigarette was the same as participants’ preferred cigarette brand, three paired-samples t-tests were used to compare each of these nicotine content estimates to the “UBC” cigarette. All tests were non-significant \([t(23)']s = -1.00\) to
-0.35, \(p\)'s = 0.35 to 0.73], indicating that on average, participants believed the “UBC” cigarette contained as much nicotine as their own preferred brand.

Figure 3. Estimated Nicotine Content in Study-Supplied Cigarette and Participants’ Usual Brand Cigarette across Nicotine Content Descriptions (\(n = 24\)).

Note: * = \(p < 0.05\); ** = \(p < 0.01\); *** = \(p < 0.001\)

**Primary Aim Analyses**

**Aim 1**: Determine the influence of nicotine content descriptions on subjective ratings of smoking.

**Craving.**

*Hypothesis 1.1.* There will be a dose-response relationship between nicotine content description and craving reduction (i.e., greater craving reduction will be associated with the greatest nicotine content description; lower craving reduction will be associated with the lowest nicotine content description).
Global craving reduction. A RM-ANOVA examining the effects of nicotine content description ("UBC" vs. "LNC" vs. "VLNC") and time (pre- vs. post-cigarette) on global craving found a significant main effect of time \([F(1, 23) = 45.58, p = 0.000, \eta_p^2 = 0.67]\), but not nicotine content description \([F(2, 46) = 0.93, p = 0.40, \eta_p^2 = 0.04]\).

Average global craving ratings were similar across nicotine content descriptions, but differed by time of assessment; as expected, average post-cigarette global craving scores \((33.24 \pm 4.63)\) were significantly lower than pre-cigarette scores \((60.69 \pm 3.88)\).

The interaction of nicotine content description x time (i.e., the effect of nicotine content description on magnitude of craving reduction from pre- to post-cigarette) – had a significant effect on global craving \([F(1.31, 30.09) = 5.29, p = 0.02, \eta_p^2 = 0.19]\); Greenhouse-Geisser correction, \(\epsilon = 0.65\). To explore this interaction, two one-way ANOVAs were conducted to examine the main effect of nicotine content description separately for pre- and post-cigarette global craving ratings. Three RM-ANOVAs were used to examine the main effect of time on global craving separately by each nicotine content description. These analyses found that a significant main effect of time on craving for each separate nicotine content description (all \(p's < 0.001\)); post-cigarette global craving was lower than pre-cigarette global craving (Figure 4). Additionally, there was a significant main effect of nicotine content description on pre-cigarette global craving \([F(2, 46) = 5.08, p = 0.01, \eta_p^2 = 0.18]\) but not post-cigarette global craving \([F(1.65, 38.02) = 1.65, p = 0.21, \eta_p^2 = 0.07]; \text{Huynh-Feldt correction, } \epsilon = 0.83\].

Bonferroni-adjusted pairwise comparisons revealed that average pre-cigarette global craving scores were greater before participants smoked the “UBC” cigarette \((65.27 \pm 4.46)\) compared to ratings prior to smoking the “LNC” cigarette \((57.28 \pm 4.00, p = \)
0.014), but not the “VLNC” cigarette (59.53 ± 3.98, p = 0.20). Thus, due to greater pre-cigarette global craving, the magnitude of global craving reduction was greatest after using the “UBC” cigarette compared to the “LNC” and “VLNC” cigarettes.

Figure 4. Effects of Nicotine Content Description on Pre- and Post-cigarette Global Craving among Compliant Participants (n = 24)

![Graph showing effects of nicotine content description on pre- and post-cigarette global craving](image)

Note: * = p < 0.05; ** = p < 0.01; *** = p < 0.001

When gender was added as a covariate in the previous analysis, the interaction effect of nicotine content description x time on global craving was no longer significant [F(1.39, 30.63) = 0.42, p = 0.59, ηp² = 0.02]. Thus, after controlling for gender, there was no difference in craving reduction by nicotine content description. The addition of FTND dependence as a covariate (i.e., gender remaining as a covariate in the model) did not alter this finding. In conclusion, after controlling for gender and dependence, there was no difference in global craving reduction by nicotine content description.

Analyses of subscale craving reduction. A 2 x 3 RM-MANOVA was used to examine the effects of nicotine content description and time on the combined dependent
variables of intention/desire to smoke (QSU factor 1 subscale) and anticipation of negative affect (NA) relief (QSU factor 2 subscale). Multivariate analyses found no main effect of nicotine content description on the combined craving subscales \[\textit{Wilk's } \lambda = 0.83, \quad F(4, 90) = 2.26, \quad p = 0.07, \quad \eta_p^2 = 0.09\], indicating that across time, average craving on the combined subscales did not differ by nicotine content description. Similar to global craving analyses, there was a significant main effect of time \[\textit{Wilk's } \lambda = 0.32, \quad F(2, 22) = 22.98, \quad p = 0.000, \quad \eta_p^2 = 0.68\], which in univariate analyses was significant for both craving due to intention/desire to smoke \[F(1, 23) = 47.06, \quad p = 0.000, \quad \eta_p^2 = 0.67\], and due to anticipation of NA relief \[F(1, 23) = 26.44, \quad p = 0.000, \quad \eta_p^2 = 0.54\]. These results indicated that across nicotine content description, average post-cigarette ratings of craving due to intention/desire to smoke and craving due to anticipation of NA relief were lower than pre-cigarette ratings (intention/desire to smoke: 41.34 ± 5.39 vs. 76.48 ± 4.29; anticipation of NA relief: 25.15 ± 4.21 vs. 44.91 ± 4.31).

There was a significant multivariate effect of the primary term of interest – the interaction of nicotine content description x time – on the combined craving subscales \[\textit{Wilk's } \lambda = 0.74, \quad F(4, 90) = 3.63, \quad p = 0.009, \quad \eta_p^2 = 0.14\]. When considered separately in univariate analyses, the nicotine content description x time interaction effect was only significant for craving due to anticipation of NA relief \[F(1.60, 36.82) = 7.89, \quad p = 0.003, \quad \eta_p^2 = 0.26; \quad \text{HF correction}, \quad \varepsilon = 0.80\]. When this interaction was explored further with follow-up one-way ANOVAs, nicotine content description had a significant effect on pre-cigarette ratings for this subscale \[F(2, 46) = 7.34, \quad p = 0.004, \quad \eta_p^2 = 0.24\], but not post-cigarette ratings \[F(2, 46) = 1.28, \quad p = 0.29, \quad \eta_p^2 = 0.05\]. Bonferroni-adjusted pairwise comparisons found that pre-cigarette ratings were significantly higher prior to receiving
the “UBC” description (51.90 ± 5.12) compared to the “LNC” description (40.24 ± 4.46, \( p = 0.003 \)), but not the “VLNC” description (42.58 ± 4.46, \( p = 0.075 \)). Additional follow-up RM ANOVAs of craving reduction by nicotine content description revealed that as expected, there was a significant decrease in craving over time for each nicotine content description (\( p \)'s < 0.001). Thus, greater pre-cigarette ratings for this subscale resulted in a larger overall craving reduction after smoking the “UBC” cigarette when compared to the “LNC” and “VLNC” cigarettes (see Figure 5 below).

Figure 5. Effects of Nicotine Content Description on Pre- and Post-cigarette Craving due to Anticipation of Negative Affect Relief Ratings (\( n = 24 \))

When gender was added as a covariate in multivariate analyses, there was no longer an interaction effect of nicotine content description x time on the combined craving subscales [\( \text{Wilk's } \lambda = 0.93, F(4, 86) = 0.81, p = 0.52, \eta^2_p = 0.04 \)]. As with the global craving analyses, this indicates that after controlling for gender, there was no
difference in reduction in craving subscales by nicotine content description. When FTND dependence was added as an additional covariate (i.e., gender remaining as a model covariate), this did not change the effects of the previous analyses. Thus, after controlling for gender and dependence, there was no difference in global craving reduction across nicotine content description.

Summary. Analyses of global craving and craving subscales produced somewhat mixed results. There was no difference in reduction in craving due to intention/desire to smoke by nicotine content description, but the “UBC” nicotine content description produced greater reduction in global craving and craving due to anticipation of NA relief compared to the “LNC” description. As such, the hypothesis predicting a dose-response relationship with craving reduction was partially supported for global craving and craving due to anticipation of NA relief, but was not supported for craving due to intention/desire to smoke. However, after controlling for gender and nicotine dependence, there was no support for hypotheses.

Withdrawal.

Hypothesis 1.2. There will be a dose-response relationship between nicotine content description and withdrawal suppression (i.e., greater withdrawal suppression will be associated with the greatest nicotine content description).

Withdrawal analyses. A RM-ANOVA examining the effects of nicotine content description and time on withdrawal revealed a significant main effect of time \( [F(1, 23) = 49.54, p = 0.000, \eta_p^2 = 0.68] \); across nicotine content descriptions, (as expected) average post-cigarette withdrawal ratings were lower than pre-cigarette withdrawal ratings (18.73
Nicotine content description had no effect on withdrawal \([F(1.65, 37.85) = 1.65, p = 0.21, \eta_p^2 = 0.07; \text{Huynh-Feldt correction, } \varepsilon = 0.82]\), indicating that across time, average withdrawal ratings were similar for each nicotine content description. As shown in Figure 6 below, there was no interaction effect of time x nicotine content description on withdrawal \([F(1.51, 36.59) = 0.75, p = 0.45, \eta_p^2 = 0.03; \text{Huynh-Feldt correction, } \varepsilon = 0.80]\); smoking-induced withdrawal suppression was similar across all nicotine content descriptions.

Figure 6. Effects of Nicotine Content Description on Pre- and Post-cigarette Withdrawal among Compliant Participants (\(n = 24\))

The interaction effect of nicotine content x time on withdrawal remained non-significant when gender was added as a covariate in analyses \([F(1.59, 35.06) = 1.24, p = 0.29, \eta_p^2 = 0.05]\). The addition of FTND dependence as a covariate (i.e., gender remaining as a covariate in the model) also did not alter this finding.
Summary. Regardless of whether analyses did or did not control for gender and dependence, there was no effect of nicotine content description on withdrawal suppression. The hypothesis predicting a dose-response effect of nicotine content description on withdrawal suppression was not supported.

Sensory effects of smoking.

Hypothesis 1.3. There will be a dose-response relationship between nicotine content description and sensory effects of smoking (i.e., positive sensory ratings will be associated with the greatest nicotine content description).

Analyses of sensory effects of smoking. A RM-MANOVA examining the effect of nicotine content description on sensory effects of smoking revealed a significant main effect of description on the combined 14 sensory effect items of the Visual Analog Scale \[ \text{Wilk's } \lambda = 0.28, F(28, 66) = 2.09, p = 0.09, \eta_p^2 = 0.47 \]. When considered separately in univariate analyses, there was a significant main effect of nicotine content description for each of the following items: strength \( F(2, 46) = 10.72, p = 0.000, \eta_p^2 = 0.32 \), “too mild” \( F(2, 46) = 7.71, p = 0.001, \eta_p^2 = 0.25 \), and strength of smoke \( F(2, 46) = 6.83, p = 0.003, \eta_p^2 = 0.23 \). As shown in Figures 7 and 8, after applying a Bonferroni correction, pairwise comparisons revealed that both the “LNC” cigarette \( p's = 0.000, 0.005, 0.03 \) and “VLNC” cigarette \( p's = 0.016, 0.027, 0.015 \) were rated as weaker (in general), having weaker smoke, and being too mild in comparison to the “UBC” cigarette.

Although not significant at the \( p = 0.05 \) level, the main effect of nicotine content description trended toward significance for items related to cigarette harshness and smoke harshness \( p's = 0.07 \) and 0.09, respectively). Nicotine content description had no
effect on the following items: heat, draw, taste, satisfaction from smoking, burn rate, mildness of taste, after taste, staleness, and smoke smell ($p's = 0.23$ to $0.84$). However, examination of the raw means revealed a dose-dependent trend in ratings for several items. Ratings for each item are depicted below in Figures 7 and 8.

Figure 7. Effects of Nicotine Content Description VAS Sensory Items 1-7 ($n = 24$)

Figure 8. Effects of Nicotine Content Description on VAS Sensory Items 8-14 ($n = 24$)

Note: # = $p < 0.1$, * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.001$
When gender was added as a covariate in multivariate analyses, the main effect of nicotine content description on the combined sensory effect items remained \( \text{Wilk's } \lambda = 0.22, F \left( 28, 62 = 2.46, p = 0.02, \eta^2_p = 0.53 \right) \). This finding suggests that even after controlling for gender, smokers reported nicotine content description-induced differences in sensory effects of smoking. When further explored in univariate analyses, a main effect of nicotine content description was found for five additional items: cigarette harshness \( F(2, 44) = 7.28, p = 0.002, \eta^2_p = 0.25 \), draw \( F(2, 44) = 6.76, p = 0.003, \eta^2_p = 0.24 \), taste \( F(2, 44) = 3.54, p = 0.038, \eta^2_p = 0.14 \), satisfaction from smoking \( F(2, 44) = 6.74, p = 0.003, \eta^2_p = 0.24 \), and taste (mildness) \( F(2, 44) = 3.84, p = 0.029, \eta^2_p = 0.15 \).

When FTND dependence was added as an additional covariate (i.e., gender remaining as a covariate in the model), nicotine content description no longer had a significant multivariate effect \( \text{Wilk's } \lambda = 0.37, F \left( 28, 58 = 1.35, p = 0.16, \eta^2_p = 0.40 \right) \), and thus univariate results could not be interpreted.

**Summary.** The hypothesis predicting a dose-response effect of nicotine content description on sensory ratings was partially supported; the “UBC” description resulted in more positive ratings for measures of strength, strength of smoke, and "too mild" compared to the reduced nicotine content descriptions. This effect was not fully dose-dependent; there were no differences between the “LNC” and “VLNC” descriptions. This hypothesis was further partially supported after controlling for gender, as there was a main effect of nicotine content description on additional sensory items. However, after controlling for both gender and nicotine dependence, this hypothesis was not supported.
Aim 2: Examine the effects of nicotine content descriptions on smoking behaviors.

*Smoking topography measures.*

*Hypothesis 2.1.* There will be a negative dose-dependent relationship between nicotine content description and smoking topography measures (i.e., greater measures of smoking topography will be associated with the lowest nicotine content description; lower measures of smoking topography will be associated with the greatest nicotine content description).

*Analyses of composite topography measures.* Among the subsample of participants with complete and valid topography data \((n = 16)\), multivariate analyses revealed no effect of nicotine content description on the combined composite dependent variables of total puff count, total puffing duration, and total puff volume \([Wilk’s \, \lambda = 0.71, \, F(6, 56) = 1.71, \, p = 0.14, \, \eta_p^2 = 0.16]\). As such, univariate results were not explored. The effect of nicotine content description remained non-significant when gender was added as a covariate in multivariate analyses \([Wilk’s \, \lambda = 0.71, \, F(6, 52) = 1.62, \, p = 0.16, \, \eta_p^2 = 0.16]\), and when FTND dependence was added as an additional covariate. Thus, regardless of whether or not analyses controlled for gender and nicotine dependence, the composite smoking topography measures of puff count, total puff volume, and total puff duration did not differ by nicotine content description.

*Analyses of average topography measures.* Among the subsample of participants with complete and valid topography data \((n = 16)\), multivariate analyses revealed a significant main effect of nicotine content description on the combined dependent variables of average puff volume, average puff duration, and average interpuff interval.
Wilk's $\lambda = 0.61, F(6, 56) = 2.62, p = 0.026, \eta_p^2 = 0.22$. Univariate analyses revealed a main effect of nicotine content description for average puff volume only $[F(2, 30) = 7.69, p = 0.002, \eta_p^2 = 0.34]$. This effect is shown in Figure 9 below. Bonferroni-corrected pairwise comparisons revealed that participants’ average puff volume was greater during use of the “UBC” cigarette (66.04 ± 4.19 ml) compared to both the “LNC” (52.16 ± 3.72 ml, $p = 0.034$) and “VLNC” cigarettes (50.40 ± 3.22 ml, $p = 0.023$). There was no main effect of nicotine content description on either average puff duration $[F(2, 30) = 0.37, p = 0.69, \eta_p^2 = 0.02]$ or average interpuff interval $[F(2, 30) = 0.44, p = 0.65, \eta_p^2 = 0.03]$, indicating that these measures did not differ by nicotine content description.

Figure 9. Effect of Nicotine Content Description on Average Puff Volume ($n = 16$)

Note: * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.001$

When gender was added as a covariate in multivariate analyses, nicotine content description no longer had a significant effect on the combined average topography measures $[Wilk’s \lambda = 0.71, F(4, 52) = 1.63, p = 0.16, \eta_p^2 = 0.16]$, thus univariate analyses
of nicotine content description effects on the individual average topography measures were not explored. The addition of FTND dependence as a covariate (i.e., gender remaining as a model covariate) did not alter any of these effects. Thus, after controlling for gender and dependence, there was no difference in average topography measures by nicotine content description.

**Summary.** Results provided partial support for the hypothesis predicting a dose-response effect of nicotine content description on smoking topography measures. Average puff volume was greater during use of the “UBC” cigarette compared to the “LNC” and “VLNC” cigarettes, but there was no difference between the puff volumes of the reduced nicotine content descriptions. Nicotine content description had no effect on other measures of topography. After controlling for gender and nicotine dependence, nicotine content description had no effect on any topography measures.

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**Carbon monoxide.**

**Hypothesis 2.2.** There will be a negative dose-response effect of nicotine content description on CO boost (i.e., the lowest nicotine content description will produce the greatest CO boost; the greatest description will produce the lowest CO boost).

**Analyses of CO.** A RM-ANOVA examining the effects of nicotine content description and time on carbon monoxide (CO) found a significant main effect of time \(F(1, 23) = 133.94, p = 0.000, \eta^2_p = 0.85\], demonstrating that average post-cigarette CO values were greater than pre-cigarette CO values \((11.24 \pm 0.82 \text{ ppm vs. } 5.02 \pm 0.42 \text{ ppm, respectively, } p = 0.000)\). There was no main effect of nicotine content description on CO \(F(2, 46) = 0.01, p = 0.99, \eta^2_p = 0.001\], indicating that CO values averaged across time
did not differ by nicotine content description. The primary term of interest – the interaction of time x nicotine content description – had no effect on CO \( [F(2, 46) = 1.28, p = 0.29, \eta_p^2 = 0.05] \). Thus, CO increased from pre- to post- cigarette assessments, but increases in CO similar regardless of which nicotine content description participants received. This interaction also had no effect on CO when gender was added as a covariate in analyses \([F(2, 44) = 42.71, p = 0.10, \eta_p^2 = 0.10]\). The addition of FTND dependence as a covariate (i.e., gender remained a covariate in the model) did not affect this result.

**Summary.** Regardless of whether analyses controlled for gender and dependence, nicotine content description had no effect on CO boost. The hypothesis predicting a dose-response effect of nicotine content description on CO boost was not supported.

**Aim 3: Assess initial RNC outcome expectancies about and willingness to use RNCs, and evaluate willingness and outcome expectancies as potential moderators of the effects of nicotine content descriptions on subjective ratings and smoking behaviors.**

**Assessment of initial willingness to use RNCs.**

**Hypothesis 3.1.** Participants will, in general, express low willingness to engage in behaviors that promote positive use of RNCs, and will express high willingness to engage in behaviors to avoid use of RNCs.

**Exploratory summary of willingness to use RNCs.** Contrary to the hypothesis, exploratory examinations of response frequencies for individual items on a willingness to use RNCs questionnaire given at baseline revealed that participants were fairly willing to engage in behaviors encouraging appropriate use of RNCs (e.g., using RNCs to either
continue normal smoking or to gradually quit smoking). Interestingly, participants reported that if RNCs became available in the next 30 days, they were least willing to either supplement with or exclusively use alternative tobacco products and nicotine replacement therapy. In general, participants were more willing to supplement with or exclusively use e-cigarettes and roll-your-own tobacco cigarettes, as well as engage in negative behaviors like increasing smoking behaviors or purchasing high nicotine content cigarettes for illegal sources. More detailed information on the items and sample responses are provided in Table 6 below.
<table>
<thead>
<tr>
<th>Item</th>
<th>Not at all</th>
<th>Slightly willing</th>
<th>Moderately willing</th>
<th>Strongly willing</th>
<th>M (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Use RNCs like I smoke my current brand</td>
<td>2 (6.1%)</td>
<td>10 (30.3%)</td>
<td>12 (36.4%)</td>
<td>11 (27.3%)</td>
<td>2.85 (0.91)</td>
</tr>
<tr>
<td>2. Use RNCs but smoke more cigarettes/day</td>
<td>11 (33.3%)</td>
<td>16 (48.5%)</td>
<td>4 (12.1%)</td>
<td>2 (6.1%)</td>
<td>1.91 (0.84)</td>
</tr>
<tr>
<td>3. Use RNCs to gradually quit smoking</td>
<td>7 (21.1%)</td>
<td>8 (24.2%)</td>
<td>8 (24.2%)</td>
<td>10 (30.3%)</td>
<td>2.64 (1.14)</td>
</tr>
<tr>
<td>4. Quit smoking immediately instead of using RNCs</td>
<td>18 (54.5%)</td>
<td>8 (24.2%)</td>
<td>5 (15.2%)</td>
<td>2 (6.1%)</td>
<td>1.73 (0.94)</td>
</tr>
<tr>
<td>5. Supplement using RNCs with e-cigarettes</td>
<td>19 (57.6%)</td>
<td>8 (24.2%)</td>
<td>4 (12.1%)</td>
<td>2 (6.1%)</td>
<td>1.67 (0.92)</td>
</tr>
<tr>
<td>6. Supplement using RNCs with other tobacco products (chewing tobacco, cigars)</td>
<td>28 (84.8%)</td>
<td>2 (6.1%)</td>
<td>1 (3.0%)</td>
<td>2 (6.1%)</td>
<td>1.30 (0.81)</td>
</tr>
<tr>
<td>7. Supplement using RNCs with nicotine replacement therapy (gum, patch, lozenge)</td>
<td>26 (78.8%)</td>
<td>4 (12.1%)</td>
<td>2 (6.1%)</td>
<td>1 (3.0%)</td>
<td>1.33 (0.74)</td>
</tr>
<tr>
<td>8. Supplement using RNCs with roll-your-own cigarettes</td>
<td>18 (54.5%)</td>
<td>7 (21.2%)</td>
<td>6 (18.2%)</td>
<td>2 (6.1%)</td>
<td>1.76 (0.97)</td>
</tr>
<tr>
<td>9. Use e-cigarettes exclusively or instead of using RNCs</td>
<td>22 (66.7%)</td>
<td>5 (15.2%)</td>
<td>4 (12.1%)</td>
<td>2 (6.1%)</td>
<td>1.58 (0.94)</td>
</tr>
<tr>
<td>10. Use other tobacco products (chewing tobacco, cigars) exclusively or instead of using RNCs</td>
<td>29 (87.9%)</td>
<td>3 (9.1%)</td>
<td>1 (3.0%)</td>
<td>0 (0.0%)</td>
<td>1.15 (0.44)</td>
</tr>
<tr>
<td>11. Use nicotine replacement therapy (gum, patch, lozenge) exclusively or instead of using RNCs</td>
<td>26 (78.8%)</td>
<td>6 (18.2%)</td>
<td>1 (3.0%)</td>
<td>0 (0.0%)</td>
<td>1.24 (0.50)</td>
</tr>
<tr>
<td>12. Use roll-your-own cigarettes instead of using RNCs</td>
<td>19 (57.6%)</td>
<td>8 (24.2%)</td>
<td>5 (15.2%)</td>
<td>1 (3.0%)</td>
<td>1.64 (0.86)</td>
</tr>
<tr>
<td>13. Buy cigarettes with higher nicotine content from other, potentially illicit sources</td>
<td>22 (66.7%)</td>
<td>4 (12.1%)</td>
<td>6 (18.2%)</td>
<td>1 (3.0%)</td>
<td>1.58 (0.90)</td>
</tr>
</tbody>
</table>
Assessment of initial RNC smoking outcome expectancies.

Hypothesis 3.2. Participants will have more negative smoking outcome expectancies for RNCs compared to their preferred cigarette brand.

Exploratory summary of RNC outcome expectancies. Paired t-tests comparing participants’ smoking outcome expectancies for their preferred brand cigarette and a reduced nicotine cigarette revealed significant differences between cigarette types for almost all expectancy items. Compared to their preferred brand cigarette, participants held more negative expectancies regarding reduced nicotine cigarettes' ability to be satisfying, taste good, provide enjoyable throat/chest sensations, be calming, make participants feel awake and less irritable, reduce hunger for food, relieve craving, and be enjoyable. However, compared to their preferred brand cigarette, participants provided less negative expectancies regarding the reduced nicotine cigarettes' ability to be addictive, be healthy, increase risk of cardiovascular disease, and increase risk of lung disease. There were no significant differences between participants’ preferred brand cigarette and a reduced nicotine cigarette on smoking outcomes expectancies about causing nausea, being safe, or helping with weight control. Detailed results specific to expectancy items for each cigarette type are shown in Table 7 below.

Table 7. Paired t-test Comparisons of Baseline Smoking Outcome Expectancies between Participants' Preferred Brand Cigarette and a Reduced Nicotine Cigarette (RNC) among Whole Sample (n = 33).

<table>
<thead>
<tr>
<th>I believe [cigarette type]...</th>
<th>Usual brand M (SD)</th>
<th>RNC M (SD)</th>
<th>Mean difference [95% CI]</th>
<th>t(32)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ...is satisfying.</td>
<td>1.48 (0.76)</td>
<td>-0.27 (0.98)</td>
<td>1.76 [1.25, 2.27]</td>
<td>7.03</td>
<td>0.000</td>
</tr>
<tr>
<td>2. ...tastes good.</td>
<td>1.21 (0.78)</td>
<td>0.00 (0.87)</td>
<td>1.21 [0.79, 1.64]</td>
<td>5.84</td>
<td>0.000</td>
</tr>
</tbody>
</table>
3. ...provides enjoyable sensations in my throat/chest.  
   0.52 (1.15) -0.09 (1.01) 0.61 [0.15, 1.07] 2.68 0.011
4. ...calms me down.  
   1.36 (0.74) 0.42 (0.97) 0.94 [0.53, 1.35] 4.72 0.000
5. ...makes me feel more awake.  
   0.73 (0.94) -0.09 (0.91) 0.82 [0.46, 1.18] 4.64 0.000
6. ...makes me feel less irritable.  
   1.33 (0.65) 0.42 (0.94) 0.91 [0.55, 1.27] 5.17 0.000
7. ...helps me concentrate.  
   0.82 (0.88) -0.03 (1.05) 0.85 [0.50, 1.19] 5.01 0.000
8. ...reduces my hunger for food.  
   -0.06 (1.22) -0.52 (1.03) 0.46 [0.13, 0.78] 2.89 0.007
9. ...makes me dizzy.  
   0.91 (1.01) 0.82 (1.01) 0.09 [-0.34, 0.52] 0.43 0.669
10. ...makes me nauseous.  
    1.36 (0.93) 0.85 (1.09) 0.52 [0.17, 0.86] 3.04 0.005
11. ...immediately relieves my craving for a cigarette.  
    1.27 (0.72) 0.09 (1.10) 1.18 [0.73, 1.64] 5.28 0.000
12. ...is enjoyable.  
    1.24 (0.79) 0.30 (0.88) 0.94 [0.52, 1.36] 4.61 0.000
13. ...is addictive.  
    -1.64 (0.65) -0.67 (1.11) -0.97 [-1.41,-0.53] -4.50 0.000
14. ...is safe.  
    -1.30 (0.98) -1.12 (0.86) -0.18 [-0.54,0.18] -1.03 0.311
15. ...is healthy.  
    -1.73 (0.57) -1.45 (0.71) -0.27 [-0.51,-0.03] -2.32 0.027
16. ...increases my risk of having CVD.  
    -1.61 (0.70) -1.06 (1.14) -0.55 [-0.91,-0.18] -3.03 0.005
17. ...increases my chance of developing lung disease.  
    -1.67 (0.60) -1.18 (1.04) -0.49 [-0.83,-0.14] -2.87 0.007
18. ...helps me control my weight.  
    -0.67 (1.11) -0.70 (0.95) 0.03 [-0.24,0.30] 0.23 0.823

**Moderating effects of willingness to use RNCs on influence of nicotine content description on subjective ratings.**

**Craving.**

**Hypothesis 3.3.** Willingness will moderate nicotine content description effects on craving reduction, such that smokers who are less willing to use RNCs will experience a more robust dose-response effect of nicotine description on craving reduction compared to smokers who are more willing to use RNCs.
Analysis of global craving. A mixed effects RM-ANOVA was used to examine the moderating effects of willingness on the interaction effect of nicotine content description x time on global craving (i.e., the effect of nicotine content description on craving reduction). The primary interaction term of interest – willingness x nicotine content description x time – had no effect on global craving \([F(1.31, 28.77) = 0.05, p = 0.89, \eta_p^2 = 0.002,\) Greenhouse-Geisser correction, \(\varepsilon = 0.65\)], suggesting that willingness did not moderate nicotine content description effects on global craving reduction.

Additionally, the main effect of willingness \([F(1, 22) = 0.03, p = 0.88, \eta_p^2 = 0.001\] and interaction effects of willingness x nicotine content description \([F(2, 44) = 0.13, p = 0.88, \eta_p^2 = 0.006\] on craving were not significant. However, there was a significant interaction of willingness x time on global craving \([F(1, 22) = 5.00, p = 0.036, \eta_p^2 = 0.19]\).

Analysis of craving subscales. A mixed effects RM-MANOVA was used to examine the moderating effects of willingness to use RNCs on the interaction effects of nicotine content description x time on craving subscales (i.e., craving due to intention/desire to smoke and craving due to anticipation of NA relief). Multivariate analyses of the primary interaction of interest – willingness x nicotine content description x time – on the combined craving subscales were not significant \([\text{Wilk’s } \lambda = 0.98, F(4, 86) = 0.23, p = 0.92, \eta_p^2 = 0.01]\). As such, univariate analyses of this interaction were not further explored. Additionally, the interactions of willingness with nicotine content description \([\text{Wilk’s } \lambda = 0.99, F(4, 86) = 0.11, p = 0.98, \eta_p^2 = 0.005]\) and time \([\text{Wilk’s } \lambda = 0.82, F(2, 21) = 2.39, p = 0.12, \eta_p^2 = 0.19]\) were also not significant. Finally, willingness had no main effect on either intention to smoke \([F(1, 22) = 1.12, p = 0.74, \eta_p^2 = 0.05]\) or anticipation of NA relief \([F(1, 22) = 0.003, p = 0.96, \eta_p^2 = 0.000]\). These results suggest
that willingness did not moderate the effects of nicotine content description on reduction in craving due to either intention to smoke or anticipation of NA relief.

Summary. Willingness to use RNCs did not moderate nicotine content description effects on reduction of global craving, craving due to intention/desire to smoke, or craving due to anticipation of NA relief. As such, there was no support for the hypothesis predicting a more robust dose-response effect of nicotine content description on craving reduction among smokers who were less (vs. more) willing to use RNCs.

 Withdrawal.

 Hypothesis 3.4. Willingness will moderate nicotine content description effects on withdrawal suppression, such that smokers who are less willing to use RNCs will experience a more robust dose-response effect of nicotine description on withdrawal suppression compared to smokers who are more willing to use RNCs.

Analysis. A mixed effects RM-ANOVA was used to examine the moderating effects of willingness on the interaction effect of nicotine content description x time on withdrawal. The primary interaction term of interest – willingness x nicotine content description x time – had no effect on withdrawal \[F(1.63, 35.96) = 0.32, p = 0.68, \eta^2_p = 0.01\; \text{Huynh-Feldt correction, } \varepsilon = 0.82\], suggesting that willingness did not moderate nicotine content description effects on withdrawal suppression. Additionally, the main effect of willingness \[F(2, 44) = 1.23, p = 0.30, \eta^2_p = 0.05\], and interaction effects of willingness x nicotine content description \[F(2, 44) = 2.53, p = 0.091, \eta^2_p = 0.10\] and time \[F(1, 22) = 0.42, p = 0.53, \eta^2_p = 0.02\] on withdrawal were not significant.
**Summary.** Willingness to use RNCs did not moderate the effect of nicotine content description on withdrawal suppression, providing no support for the hypothesis predicting a more robust dose-response effect of nicotine content description on withdrawal suppression among smokers who were less (vs. more) willing to use RNCs.

**Sensory effects of smoking.**

*Hypothesis 3.5.* Willingness will moderate nicotine content description effects on sensory effects of smoking, such that smokers who are less willing to use RNCs will experience a more robust dose-response effect of nicotine description on sensory ratings compared to smokers who are more willing to use RNCs.

*Analysis.* A mixed effects RM-MANOVA was used to examine willingness as a moderator of nicotine content description effects on the combined 14 items of the Visual Analog Scale of Sensory Effects. In multivariate analyses, there was no interaction effect of willingness x nicotine content description on the combined dependent variables 

\[ \text{Wilk's } \lambda = 0.47, F(28, 62) = 1.00, p = 0.48, \eta^2_p = 0.31 \]; as such, univariate analyses of this interaction term were not explored. There was a main effect of willingness on the individual sensory items of strength \( F(1, 22) = 10.36, p = 0.004, \eta^2_p = 0.32 \), satisfaction from smoking \( F(1, 22) = 5.43, p = 0.029, \eta^2_p = 0.20 \) and staleness \( F(1, 22) = 5.75, p = 0.025, \eta^2_p = 0.21 \), such that across nicotine content descriptions, participants who were more willing to use RNCs provided more positive ratings of strength (63.17 vs. 48.25, \( SEM = 3.28 \)), satisfaction from smoking (73.72 vs. 57.22, \( SEM = 4.23 \)), and staleness (54.31 vs. 68.75, \( SE = 4.26 \)), than those who were less willing to use RNCs, respectively. These findings suggest that although there was an overall main effect of willingness on
some sensory effects of smoking, willingness did not moderate the nicotine content
description effects on sensory ratings.

Summary. Willingness to use RNCs did not moderate the effects of nicotine content
description on sensory effects of smoking. There was no support for the hypothesis predicting a more robust dose-response effect of nicotine content description on sensory effects of smoking among smokers who were less (vs. more) willing to use RNCs.

Moderating effects of willingness to use RNCs on influence of nicotine content
description on smoking behaviors.

Topography.

Hypothesis 3.6. Willingness will moderate nicotine content description effects on smoking topography, such that smokers who are less willing to use RNCs will experience a more robust dose-response effect of nicotine description on topography measures compared to smokers who are more willing to use RNCs.

Analyses of composite measures. A mixed effects RM-MANOVA was used to examine the interaction effect of nicotine content description x willingness on the combined composite topography measures (total puff count, total puff volume, total puff duration) among the 16 participants who had complete and valid topography data. In multivariate analyses, the interaction of nicotine content description x willingness had no effect on the combined measures \([Wilk’s \lambda = 0.66, F(6, 52) = 1.99, p = 0.084, \eta_p^2 = 0.19]\). As such, this interaction was not explored further in univariate analyses. Additionally, there was no main effect of willingness on the individual measures of total puff count.
analyses of average measures. a similar mixed effects rm-manova was used to examine the interaction effect of nicotine content description x willingness on the combined composite topography measures (average puff volume, average puff duration, average interpuff interval) among participants with complete and valid topography data ($n = 16$). in multivariate analyses, there was no interaction of nicotine content description x willingness on the combined measures was not significant [$wilk’ s \lambda = 0.85, F(6, 52) = 0.73, p = 0.63, \eta_p^2 = 0.08$]. thus, univariate analyses were not explored. additionally, there was no main effect of willingness on the individual measures of average puff volume [$F(1, 14) = 2.10, p = 0.17, \eta_p^2 = 0.13$], average puff duration [$F(1, 14) = 0.13, p = 0.73, \eta_p^2 = 0.01$], or average interpuff interval [$F(1, 14) = 0.06, p = 0.81, \eta_p^2 = 0.004$].

summary. willingness to use rncs did not moderate the effects of nicotine content description on either the combined (total puff count, volume, and duration) or average (average puff volume, duration, and interpuff interval) measures of smoking topography. there was no support for the hypothesis predicting that smokers who were less willing to use rncs would have experienced more robust dose-response effects of nicotine content description on smoking topography measures.

carbon monoxide.

hypothesis 3.7. willingness will moderate nicotine content description effects on CO boost, such that smokers who are less willing to use rncs will experience a more
robust dose-response effect of nicotine description on CO boost compared to smokers who are more willing to use RNCs.

*Analysis.* A mixed effects RM-ANOVA was used to examine the moderating effects of willingness on the interaction effect of nicotine content description x time on CO. This analysis found no interaction effect of willingness x nicotine content description x time on CO \([F(2, 44) = 1.22, p = 0.31, \eta^2_p = 0.05]\), suggesting that willingness did not moderate nicotine content description effects on CO boost. Additionally, the main effect of willingness \([F(1, 22) = 0.09, p = 0.76, \eta^2_p = 0.004]\), and interaction effects of willingness x nicotine content description \([F(2, 44) = 2.01, p = 0.15, \eta^2_p = 0.08]\) and time \([F(1, 22) = 0.08, p = 0.78, \eta^2_p = 0.004]\) on CO were not significant.

*Summary.* Willingness to use RNCs did not moderate the effects of nicotine content description on CO boost, contradicting the hypothesis predicting a more robust dose-response effect of nicotine content description on CO boost among smokers who were less (vs. more) willing to use RNCs.

*Moderating effects of RNC outcome expectancies on influence of nicotine content description on subjective ratings.*

*Craving.*

*Hypothesis 3.8.* RNC outcome expectancies will moderate nicotine content description effects on craving, such that smokers with more negative RNC outcome expectancies will experience a more robust dose-response effect of nicotine description on craving compared to smokers with more positive RNC outcome expectancies.
Analyses of global craving. A mixed effects RM-ANOVA was used to examine
the moderating effects of RNC outcome expectancies on the interaction effect of nicotine
content description x time on craving. The primary interaction of interest – RNC outcome
expectancies x nicotine content description x time – had no effect on global craving
\[F(1.33, 29.35) = 2.62, p = 0.11, \eta^2_p = 0.11; \text{Greenhouse-Geisser correction, } \varepsilon = 0.67\].
This finding suggests that nicotine content description effects on reductions global in
 craving from pre- to post-cigarette were not moderated by RNC outcome expectancies.
Additionally, there was no effect of RNC outcome expectancies \(F(1, 22) = 0.93, p =
0.35, \eta^2_p = 0.04\) or the interaction of RNC outcome expectancies x time \(F(1, 22) = 0.24,
 p = 0.63, \eta^2_p = 0.01\) on global craving. However, there was a significant interaction of
RNC outcome expectancies x nicotine content description on global craving \(F(2, 44) =
3.76, p = 0.031, \eta^2_p = 0.15\).

Analyses of craving subscales. A mixed effects RM-MANOVA was used to
examine RNC outcome expectancies as a moderator of the interaction effects of nicotine
content description x time on craving subscales. Multivariate analyses of the primary
interaction of interest – RNC outcome expectancies x nicotine content description x time
– found no significant effect on the combined craving subscales \(\text{Wilk’s } \lambda = 0.84, F(4, 86)
= 1.63, p = 0.17, \eta^2_p = 0.07\]. As such, univariate analyses of this interaction were not
further explored. Additionally, the interactions of RNC outcome expectancies with
nicotine content description \(\text{Wilk’s } \lambda = 0.85, F(4,86) = 1.85, p = 0.13, \eta^2_p = 0.08\) and
time \(\text{Wilk’s } \lambda = 0.97, F(2, 21) = 0.37, p = 0.70, \eta^2_p = 0.03\) were also not significant.
Finally, there was no main effect of RNC outcome expectancies on either intention to
smoke \(F(1, 22) = 1.27, p = 0.27, \eta^2_p = 0.05\) or anticipation of NA relief \(F(1, 22) = 0.47,\)
These results suggest that RNC outcome expectancies did not moderate the effects of nicotine content description on either intention to smoke or anticipation of NA relief.

Summary. RNC outcome expectancies did not moderate nicotine content description effects on reduction of global craving, craving due to intention/desire to smoke, or craving due to anticipation of NA relief. There was no support for the hypothesis predicting a more robust dose-response effect of nicotine content description on craving reduction among smokers holding negative (vs. positive/neutral) RNC smoking outcome expectancies.

Withdrawal.

Hypothesis 3.9. RNC outcome expectancies will moderate nicotine content description effects on withdrawal suppression, such that smokers with more negative RNC outcome expectancies will experience a more robust dose-response effect of nicotine description on withdrawal suppression compared to smokers with more positive RNC outcome expectancies.

A mixed effects RM-ANOVA was used to examine the moderating effects of RNC outcome expectancies on the interaction effect of nicotine content description x time on withdrawal. This analysis found that the primary interaction term of interest – RNC outcome expectancies x nicotine content description x time – had no significant effect on withdrawal \([F(1.72, 37.76) = 1.56, p = 0.22, \eta^2_p = 0.07,\) Huynh-Feldt correction, \(\xi = 0.86\)], suggesting that RNC outcome expectancies did not moderate nicotine content description effects on withdrawal suppression. Additionally, the main effect of RNC
outcome expectancies \( [F(1, 22) = 0.92, p = 0.35, \eta^2_p = 0.04] \), and interaction effects of RNC outcome expectancies with nicotine content description \( [F(2, 44) = 2.53, p = 0.091, \eta^2_p = 0.10] \) and time were not significant \( [F(1, 22) = 0.74, p = 0.40, \eta^2_p = 0.03] \).

**Summary.** RNC outcome expectancies did not moderate nicotine content description effects on withdrawal suppression. There was no support for the hypothesis predicting a more robust dose-response effect of nicotine content description on withdrawal suppression among smokers holding negative (vs. positive/neutral) RNC smoking outcome expectancies.

**Sensory effects.**

**Hypothesis 3.10.** RNC outcome expectancies will moderate nicotine content description effects on sensory effects of smoking, such that smokers with more negative RNC outcome expectancies will experience a more robust dose-response effect of nicotine description on sensory effects compared to smokers with more positive RNC outcome expectancies.

A mixed effects RM-MANOVA was used to examine RNC outcome expectancies as a moderator of nicotine content description effects on the combined 14 VAS sensory items. In multivariate analyses, the interaction effect of nicotine content description x RNC outcome expectancies on the combined dependent variables was not significant \( [\text{Wilk's } \lambda = 0.40, F(28, 62) = 1.30, p = 0.20, \eta^2_p = 0.37] \); as such, univariate analyses of this interaction term were not explored. There was a main effect of RNC outcome expectancies on the "too mild" item \( [F(1, 22) = 5.79, p = 0.025, \eta^2_p = 0.21] \), and a marginally significant effect on strength \( [F(1, 22) = 4.14, p = 0.054, \eta^2_p = 0.16] \). When
averaged across nicotine content descriptions, participants who held more negative RNC outcome expectancies rated the study-supplied cigarette as being milder and weaker in strength compared to those who held neutral/positive RNC outcome expectancies (too mild: 50.17 ± 5.66 vs. 68.00 ± 4.78, p = 0.025; strength: 49.5 ± 3.99 vs. 60.14 ± 3.38, p = 0.054).

Summary. Although there was main effect of RNC outcome expectancies on some sensory effects of smoking, RNC outcome expectancies did not moderate the overall effects of nicotine content description on sensory effects of smoking. There was no support for the hypothesis predicting a more robust dose-response effect of nicotine content description on sensory ratings among smokers holding negative (vs. positive/neutral) RNC smoking outcome expectancies.

**Moderating effects of RNC outcome expectancies of nicotine content description on smoking behaviors.**

**Topography.**

Hypothesis 3.11. RNC outcome expectancies will moderate nicotine content description effects on smoking topography, such that smokers with more negative RNC outcome expectancies will experience a more robust dose-response effect of nicotine description on topography measures compared to smokers with more positive RNC outcome expectancies.

**Composite measures.** A mixed effects RM-MANOVA was used to examine the moderating effects of RNC outcome expectancies on nicotine content description effects on composite topography measures (puff count, total puff volume, total puff duration). In
multivariate analyses, the primary term of interest – the interaction of nicotine content description x RNC outcome expectancies – had no effect on the combined measures \( [Wilk’s \lambda = 0.66, \ F(6, 52) = 2.03, \ p = 0.078, \ \eta^2_p = 0.19] \), suggesting that RNC outcome expectancies did not moderate nicotine content description effects on composite topography measures. Further, there was no main effect of RNC outcome expectancies on puff count \( [F(1, 14) = 1.54, \ p = 0.24, \ \eta^2_p = 0.10] \), total puff volume \( [F(1, 14) = 1.07, \ p = 0.32, \ \eta^2_p = 0.07] \), or total puff duration \( [F(1, 14) = 1.51, \ p = 0.24, \ \eta^2_p = 0.10] \). This finding suggests that across nicotine content descriptions, smokers with negative RNC outcome expectancies had total puff volumes, puff counts, and puff durations similar to smokers with positive/neutral RNC outcome expectancies.

**Analyses of average measures.** A mixed effects RM-MANOVA was used to examine the effects of nicotine content description and RNC outcome expectancies on the combined average topography measures (average puff volume, average puff duration, average interpuff interval). In multivariate analyses, there was a marginally significant interaction effect of nicotine content description x RNC outcome expectancies on the combined measures \( [Wilk’s \lambda = 0.63, \ F(6, 52) = 2.29, \ p = 0.049, \ \eta^2_p = 0.21] \). When explored in univariate analyses, similar to the main effect of nicotine content description (Aim 2), the interaction effect of RNC outcome expectancies x nicotine content description was significant for average puff volume only \( [F(2, 28) = 6.32, \ p = 0.005, \ \eta^2_p = 0.31] \). To explore this interaction, separate one-way ANOVAs examined RNC outcome expectancy effects on average puff volume by each nicotine content description. There was no effect of RNC outcome expectancies on average puff volume for either the UBC \( [F(1, 14) = 2.39, \ p = 0.15, \ \eta^2_p = 0.15] \) or VLNC \( [F(1, 14) = 0.29, \ p = 0.60, \ \eta^2_p = 0.02] \).
cigarettes. Follow-up RM-ANOVAs examining nicotine content description effects on average puff volume separately by RNC expectancy group found a significant main effect of nicotine content description among participants holding negative \( F(1.32, 10.58) = 11.37, p = 0.004, \eta_p^2 = 0.59 \), Huynh-Feldt correction, \( \varepsilon = 0.80 \), but not neutral/positive RNC expectancies \( F(2, 12) = 2.19, p = 0.15, \eta_p^2 = 0.27 \). As shown in Figure 10, Bonferroni-adjusted pairwise comparisons revealed that participants holding negative RNC outcome expectancies took deeper average puffs while smoking the “UBC” cigarette \((71.50 \pm 6.33 \text{ ml})\) compared to the “LNC” \((45.94 \pm 4.25, p = 0.012)\) and “VLNC” \((48.84 \pm 3.24 \text{ ml}, p = 0.027)\) cigarettes.

Figure 10. Moderating Effects of RNC Outcome Expectancies on Average Puff Volume by Nicotine Content Description \((n = 16)\)

Note: * = \( p < 0.05 \); ** = \( p < 0.01 \); *** = \( p < 0.001 \)
The main effect of RNC outcome expectancies on average puff volume of the LNC cigarette was marginally significant \( F(1, 14) = 4.42, p = 0.054, \eta^2_p = 0.24 \); participants with neutral/positive RNC expectancies took marginally deeper puffs of the LNC cigarette compared to those with negative RNC expectancies \((60.17 \pm 5.08 \text{ ml vs. } 45.94 \pm 4.48 \text{ ml})\).

**Summary.** RNC outcome expectancies did not moderate nicotine content description effects on total topography measures, but did moderate the effects of nicotine content description on average puff volume, such that only participants who held negative RNC outcome expectancies engaged in different puff average volumes dependent upon nicotine content description. There was partial support for the hypothesis predicting a more robust dose-response effect of nicotine content description on smoking topography among smokers holding negative (vs. positive/neutral) RNC smoking outcome expectancies.

**Carbon monoxide.**

**Hypothesis 3.12.** RNC outcome expectancies will moderate nicotine content description effects on CO boost, such that smokers with more negative RNC outcome expectancies will experience a more robust dose-response effect of nicotine description on CO boost compared to smokers with more positive RNC outcome expectancies.

**Analysis.** A mixed effects RM-ANOVA was used to examine the moderating effects of RNC outcome expectancies on the interaction effect of nicotine content description x time on CO. The interaction of RNC outcomes expectancies x nicotine content description x time had no effect on CO \( F(2, 44) = 0.44, p = 0.65, \eta^2_p = 0.02 \),
suggesting that RNC outcome expectancies did not moderate nicotine content description effects on CO boost. Additionally, there was no main effect of RNC outcome expectancies on CO \( [F(1, 22) = 0.04, p = 0.84, \eta^2_p = 0.002] \), and no significant interactions of RNC outcome expectancies with either nicotine content description \( [F(2, 44) = 0.08, p = 0.92, \eta^2_p = 0.04] \) or time \( [F(1, 22) = 0.001, p = 0.97, \eta^2_p = 0.00] \).

**Summary.** RNC outcome expectancies did not moderate nicotine content description effects on CO boost. There was no support for the hypothesis predicting a more robust dose-response effect of nicotine content description on CO boost among smokers holding negative (vs. positive/neutral) RNC smoking outcome expectancies.
Chapter 4: Discussion

Overview

Cigarette smoking is the leading preventable cause of death (USDHHS, 2014; WHO, 2011); decreasing its prevalence remains a priority for significantly reducing tobacco-related morbidity and mortality. A federal nicotine reduction policy is a promising strategy for decreasing cigarette use in the US (Benowitz & Henningfield, 1994; Donny et al., 2014; Hatsukami, Perkins, et al., 2010; Hatsukami, Benowitz, Donny, Henningfield, & Zeller, 2012), but research is needed regarding consumer acceptance of reduced nicotine content cigarettes (RNCs). The limited extant research on consumer response to RNCs has shown that smokers generally provide lower subjective ratings of these products (Benowitz et al., 2012), but it is unclear if such ratings result from bias or deficient nicotine content. Previous studies have shown that merely describing a cigarette as containing no nicotine – regardless of actual content – results in more negative subjective responses to that cigarette (Darredeau et al., 2013; Juliano & Brandon, 2002; Perkins et al., 2008, 2009). Applied to nicotine reduction strategies, these findings suggest that a federal policy that informs smokers that their cigarettes will contain “reduced” or “low” nicotine content may consequently negatively bias responses to these products. This may result in challenges with consumer acceptance of RNCs during initial stages of policy implementation, which may lead to unintended consequences such as the expansion of a black market of higher nicotine-containing tobacco products. As such, more research on consumer response to RNCs is needed prior to policy implementation.

To date, one study (Joel, 2013) has examined how a reduced nicotine content description – in contrast to a description of no nicotine – influences responses to
smoking. In this study, participants smoked two blinded identical denicotinized cigarettes described as having either “average” or “very low” nicotine content in counter-balanced order. Smokers provided lower subjective ratings for the “very low” nicotine content cigarette despite both cigarettes containing identical nicotine content (Joel, 2013). However, because this study used denicotinized cigarettes, it is possible that ratings given to both cigarettes are lower than how participants would rate their preferred brand due to deficient cigarette nicotine content in the denicotinized cigarettes. Thus, studies which control for nicotine content and examine the influence of reduced nicotine content description only are needed to both replicate these results and further determine the extent to which bias about RNCs results in lower ratings.

The goal of this dissertation was to address this gap in the RNC consumer response literature by assessing the effect of reduced nicotine content descriptions - while controlling for nicotine content - on subjective responses to smoking and smoking behaviors in a laboratory study. The first aim of this study was to determine the influence of nicotine content description on subjective responses to smoking: craving reduction, withdrawal suppression, and sensory effects of smoking. The second aim was to examine nicotine content description effects on smoking behaviors: measures of smoking topography and increases in carbon monoxide levels (CO boost). The third and final aim was to explore willingness to use and smoking outcome expectancies about using RNCs as possible moderators of nicotine content description effects. The present chapter examines the findings of this study in greater detail. Specifically, the results of each aim are first compared and contrasted with initial hypotheses and the existing literature, and then discussed to emphasize implications for regulatory efforts. Limitations are
acknowledged with suggested directions for future studies, and a final overall summary of study findings is presented.

**Validation of Experimental Manipulation**

**Belief of manipulation.** To confirm that participants believed the deceptive nicotine content descriptions for the study-supplied cigarettes, participants were asked after each experimental session to estimate how much nicotine was in both their preferred cigarette brand and the cigarette they just smoked. Nine (27.3%) participants estimated the nicotine content of either the “LNC” or “VLNC” cigarette to be greater than the nicotine content of the “UBC” cigarette, indicating that these participants did not believe the experimental manipulation. As such, subsequent subjective and behavioral responses to nicotine content descriptions could not be interpreted given that these differences were not truly attributable to the experimental manipulation. Consistent with the methods of previous nicotine dose description studies (Juliano & Brandon, 2002; Perkins et al., 2008, 2009), these nine participants were excluded from analyses directly pertaining to nicotine content description effects. For example, these participants were not included in craving analyses, but were included in analyses of baseline willingness to use RNCs. As discussed in the results section, excluded participants did not differ from included participants on any major demographic or smoking variables.

It is unclear why some participants did not believe the experimental manipulation. One possibility is that defining features of participants’ preferred brand cigarette might have been visible to participants despite blinding efforts (e.g., recessed filter on Parliament cigarettes). However, cigarettes were intentionally inserted into and removed
from the topography device away from participants’ view to minimize recognition opportunities. Another possibility is that study completers who did not believe the manipulation then informed subsequent participants of their suspicions. Although this possibility cannot be verified, it should be noted that participants were not debriefed about the experimental manipulation until the entire study was completed. As such, it is unlikely that study completers who did not believe the manipulation were both aware of the extent of the deception (i.e., that all cigarettes were actually their own preferred brand) and able to convey this to future participants.

The fact that approximately 27% of the sample did not believe the manipulation is consistent with other dose description studies, in which 30-40% of participants were not deceived. Of most relevance to the present study, Juliano & Brandon (2002) found that 39% of the individuals in the told no nicotine/given nicotine condition reported receiving a nicotine-containing cigarette, while Perkins and colleagues (2008) found that 27.5% and 32.5% of the smokers in the told de-nic/given nicotine condition reported receiving a nicotine-containing cigarette during negative and positive mood induction conditions, respectively. Interestingly, many of these studies found that significant proportions of participants who were not deceived (e.g., told nicotine/given nicotine) still reported receiving doses inconsistent with description (e.g., 3%-27% in Juliano & Brandon, 2002; 15-20% in Perkins et al., 2008). Because other studies have shown similar proportions of “non-believers,” and that proportions of “non-believers” do not vary by described or actual nicotine dose, the failure to deceive 27% of the current sample does not appear to be unique to the present study.
Confirmation of manipulation. Among the 24 participants who provided nicotine content estimates congruent with descriptions, there was no difference in mean estimated nicotine content for participants’ preferred cigarette brand across sessions. There was also no difference between any of these estimates and the estimated nicotine content of the study-supplied cigarette described as containing “as much nicotine as [participants’] usual brand cigarette [UBC].” These findings confirm that overall, participants believed that the “UBC” description was accurate. Further, these findings suggest participants’ subjective responses following, and smoking behaviors during, use of the “UBC” cigarette simulated responses to their own preferred cigarette brand. Thus, comparisons of responses between the cigarettes described as containing reduced nicotine and “UBC” cigarette should serve as accurate representations of how smokers would initially respond to RNCs compared to their own brand of cigarette.

Participants estimated the nicotine content of both the “LNC” and “VLNC” cigarettes to be considerably less than the “UBC” cigarette (~48% and ~53%, respectively). These findings indicate that the experimental manipulation was successful in convincing participants that they received cigarettes with reduced nicotine content. These findings demonstrate that differences in subjective and behavioral responses between the “UBC” cigarette and the “LNC” and “VLNC” cigarettes may be attributed to manipulation of nicotine content description, given that all other aspects of the experiment remained consistent across experimental sessions.

Interestingly, there was no statistically significant difference between the estimated average nicotine content of the “LNC” and the “VLNC” cigarettes, although the raw mean estimated nicotine content of the “VLNC” cigarette was lower than the
“LNC” cigarette. This finding may have two possible explanations. First, because all study-supplied cigarettes contained substantial nicotine content, it is possible that the pharmacological properties of nicotine overrode the “VLNC” description. In other words, a limit was imposed on how little nicotine participants could reasonably believe was in a cigarette that still reduced craving and withdrawal. Second, the absence of a major discrepancy between estimated contents may reflect the intentionally vague wording (i.e., “low” vs. “very low” nicotine) of the nicotine content descriptions. It is unclear which explanation is responsible for this finding; however, because participants estimated the “LNC” and “VLNC” to have similar nicotine content, this suggests that a full dose-response effect of nicotine content description on subsequent subjective and behavioral responses to smoking may not be possible. As such, the most pronounced differences in subjective and behavioral responses to smoking were expected to occur between the “UBC” and either the “LNC” cigarette or the “VLNC” cigarette; substantial differences in responses between the “LNC” and “VLNC” cigarettes were not anticipated.

**Summary.** An experimental manipulation check revealed that, similar to other dose description studies (Juliano & Brandon, 2002; Perkins et al., 2008), 72.7% of participants provided nicotine content estimates congruent with the descriptions they received, and as such, were retained in subsequent analyses. Participants reported no difference between estimated nicotine content of their preferred brand cigarette and the “UBC” cigarette, suggesting that subsequent responses to the “UBC” cigarette reflected use of their own preferred brand cigarette. Participants also estimated both the “LNC” and “VLNC” cigarettes to contain significantly less nicotine than the “UBC” cigarette suggesting they believed these cigarettes contained reduced nicotine content. However,
similar estimates of nicotine content within the “LNC” and “VLNC” cigarettes may prevent a full dose-response effect of nicotine content description on responses to smoking. As such, the most marked differences in subjective and behavioral responses to smoking are expected to occur between the “UBC” and either the “reduced nicotine” cigarette, but not between the “LNC” and “VLNC” cigarettes.

Primary Findings of Aims 1 and 2

Aim 1: Determine the influence of nicotine content description on subjective responses to smoking.

Overview. Overall, analyses examining the effect of nicotine content description on subjective responses to smoking produced mixed results. Nicotine content description affected some measures of craving reduction and sensory characteristics, but not others, and had no effect on withdrawal suppression. Additionally, significant effects of nicotine content description on some measures of craving reduction and sensory characteristics were not fully dose-dependent. Aim 1 findings are discussed in detail below, by specific hypotheses for each subjective response construct.

Craving Findings.

Hypothesis 1.1. There will be a dose-response relationship between nicotine content description and craving reduction (i.e., greater craving reduction will be associated with the greatest nicotine content description).

Nicotine dose description significantly affected some measures of smoking-induced craving reduction. Specifically, participants reported greater reductions in global
craving (i.e., total QSU score) and craving due to anticipation of negative affect relief (i.e., QSU factor 2 subscale) after smoking the “UBC” cigarette compared to the “LNC” and “VLNC” cigarettes. These findings might suggest that cigarettes described as having reduced nicotine content – regardless of “low” vs. “very low” description – results in lower craving reduction because of biases about these cigarettes. However, when explored further, greater craving reduction after smoking the “UBC” cigarette appeared to be explained by participants providing greater craving ratings before smoking the “UBC” cigarette compared to the other cigarettes. Because participants were unaware of which nicotine content description they would receive prior to smoking, the greater reduction in craving observed after smoking the “UBC” cigarette is unlikely the result of that cigarette’s nicotine content description. In other words, if craving ratings prior to smoking the “UBC” cigarette were similar (as would be expected in a well-controlled experimental design) to ratings prior to smoking both the “reduced nicotine” cigarettes, craving reduction would have been similar across all nicotine content descriptions. Thus, although statistically significant, this finding is not practically meaningful. Interestingly, reduction of craving due to intention or desire to smoke did not differ by nicotine content description. Participants’ intention/desire to smoke decreased overall, but the magnitude of this decrease was similar across all nicotine content descriptions.

These null results are consistent with findings of other dose description studies which found no effect of nicotine dose description, but did find an effect of actual dose, on craving reduction (Juliano & Brandon, 2002; Perkins et al., 2008). In these studies, regardless of what description participants received, those who were actually given nicotine had significantly reduced craving compared to those not given nicotine. Because
all participants in the present study received nicotine-containing cigarettes, and were also in a nicotine-deprived state, it is conceivable that the pharmacological effects of nicotine outweighed any potential bias of nicotine content description on craving reduction.

In the only study to assess a “reduced” (vs. no) nicotine content description effect on craving reduction, Joel (2013) also found no effect of nicotine content description. Participants rated identical denicotinized cigarettes labeled as having either “very low” and “average” nicotine content equally on measures of craving reduction. In contrast to the current study and other dose description studies, this finding is interesting because participants had non-pharmacologically active levels of nicotine content within the cigarettes they smoked, yet there was still no effect of description on craving reduction. Taken together with the findings of Juliano & Brandon (2002) and Perkins et al. (2008), these results suggest that actual nicotine dose has a much greater effect than nicotine dose/content description on acute craving reduction. Future studies should utilize a modified version of the balanced placebo design to compare gradations of nicotine content descriptions and actual dose on craving reduction. Studies of this design would be better suited to more definitely distinguish behavioral effects of reduced nicotine content descriptions from the pharmacologic effects of nicotine.

Withdrawal Findings.

Hypothesis 1.2. There will be a dose-dependent relationship between nicotine content description and withdrawal suppression (i.e., greater withdrawal suppression will be associated with the greatest nicotine content description).
There was no effect of nicotine content description on withdrawal suppression; all nicotine content descriptions produced similar withdrawal relief after smoking study-supplied cigarettes. Given the small estimated size for this null effect (i.e., $\text{partial } \eta^2 = 0.03$), it is possible that withdrawal suppression may differ by nicotine content description among a larger sample of smokers. However, this null finding is consistent with the results of other nicotine dose description studies utilizing larger sample sizes (Juliano & Brandon, 2002; Perkins et al., 2008, 2009). These studies found that regardless of nicotine dose description (e.g., told nicotine containing or told no nicotine) and actual nicotine dose (e.g., nicotine or denicotinized), participants experienced similar withdrawal suppression after smoking or using a nicotine nasal spray. Joel (2013) did not assess withdrawal as an outcome, so it is unclear if withdrawal relief would differ by nicotine content description during use of cigarettes with actual reduced nicotine content. However, the present study’s finding, taken together with the results of studies by Perkins et al. (2008, 2009) and Juliano and Brandon (2002), suggests that the behavioral act of smoking may be more important for acute withdrawal relief than both actual nicotine content and nicotine content description.

**Sensory effects of smoking.**

_Hypothesis 1.3. There will be a dose-response relationship between nicotine content description and sensory effects of smoking (i.e., positive ratings of sensory effects will be associated with the greatest nicotine content description)._  

Analyses found an overall effect of nicotine content description on sensory effects of smoking. When this effect was further explored among individual sensory effects,
participants rated the “LNC” and “VLNC” cigarettes as being weaker (in general), having weaker smoke, and being too mild in comparison to the “UBC” cigarette. There was no difference between the two “reduced” nicotine content descriptions on any of these sensory ratings. Interestingly, there were no differences by description on other potentially important sensory characteristics (e.g. satisfaction, taste, or aftertaste). These results are consistent with some studies finding a significant effect of nicotine dose but not description on these outcomes (Darredeau et al., 2013), yet inconsistent with others demonstrating a significant effect of description (Joel, 2013).

One possible interpretation of these findings might be that the pharmacological presence of nicotine affects ratings related to rewarding effects of smoking (e.g., satisfaction, liking), whereas non-pharmacological factors such as nicotine content affect sensory effects of smoking (e.g., taste). Because all study cigarettes contained sufficient nicotine content, this might explain why participants rated all study cigarettes similarly on measures more closely associated with reward (e.g., satisfaction, taste), but provided greater ratings of sensory characteristics (e.g., strength) for the cigarette with the greatest nicotine content description. Future studies which cross nicotine content description and actual nicotine content (i.e., studies similar to the previously mentioned BPD studies) are needed to further separate the effects of each on sensory effects of smoking. Additionally, studies are needed to determine which types of ratings are stronger predictors of long-term product acceptance. If sensory characteristics are found to be more important determinants of future cigarette use compared to rewarding characteristics, regulatory agencies may need to increase education about RNCs to alter smokers’ negative biases about these sensory effects.
**Summary of Aim 1 Findings**

Taken together, analyses found mixed effects of nicotine content description on subjective responses to smoking; nicotine content description affected some measures of craving (e.g., craving due to anticipation of negative affect relief) and some sensory aspects of smoking (e.g., harshness). However, nicotine content description did not affect withdrawal or other measures of craving (e.g., intention to smoke) and sensory characteristics (e.g., taste). After further exploring differences in craving reduction, this difference could not be attributed to nicotine content description effects; thus for practical purposes, there was no effect of nicotine content description on craving reduction. In conclusion, nicotine content description did not demonstrate overall dose-response effects on subjective responses to smoking. Because participants smoked their preferred brand during each experimental session, the absence of nicotine content description effects on subjective responses may have resulted from each study cigarette containing pharmacologically active levels of nicotine. Thus, although participants indicated that they believed they were using cigarettes with less nicotine than their preferred brand cigarette, these cigarettes still contained enough nicotine to ameliorate acute craving and withdrawal, and produced similar sensory effects when smoked. These results appear to suggest that negative subjective ratings given to RNCs in current trials are resultant from deficient nicotine content, not bias. However, future studies using methods similar to the balanced placebo design are needed to definitively make this conclusion.

**Aim 2: Examine nicotine content description effects on smoking behaviors.**
Overview. Overall, nicotine content description had little effect on smoking behaviors. Nicotine content description had no effect on smoking-induced CO boost, on most of the average topography measures (average interpuff interval, average puff duration) or on any of the composite topography measures (total puffs taken, total puff volume, total puff duration). The only smoking behavior that varied by nicotine content description was average puff volume, which did not follow a fully dose-dependent association with nicotine content description. Aim 2 findings are further discussed below by each specific smoking behavior construct.

Smoking topography.

Hypothesis 2.1. There will be a negative dose-response relationship between nicotine content description and smoking topography measures (i.e., greater measures of smoking topography will be associated with the lowest nicotine content description).

Among the subset of participants with complete and valid topography data (n = 16), there was a significant effect of nicotine content description on average puff volume, but not any other composite or average topography measures: average interpuff interval, average duration, total puffs taken, total puff count, total puff duration, or total puff volume. On average, smokers took deeper puffs when smoking the “UBC” cigarette compared to both the “LNC” and “VLNC” cigarettes.

These findings are largely consistent with the results of Joel (2013) demonstrating no difference between two identical denicotinized cigarettes labeled as "low" and "very low" nicotine on number of puffs taken, average puff duration, and average interpuff interval. However, contrary to our results demonstrating an effect of nicotine content
description on average – but not total – puff volume, Joel instead found a marginally significant effect ($p < 0.10$) of description on total – not average – puff volume. Because the present study manipulated nicotine content description while administering participants' preferred brand cigarettes, while Joel (2013) manipulated nicotine content description while administering denicotinized cigarettes, these findings provide no clear conclusions regarding whether attempts to initially compensate during use of RNCs result from deficient nicotine content or biases about reduced nicotine. A study which evaluates the interaction of nicotine content description x actual nicotine content – such as that offered by a balanced placebo design – is needed to make a more definitive conclusion regarding the true effects of reduced nicotine content descriptions and actual reduced nicotine content on smoking topography measures.

**CO boost.**

_Hypothesis 2.2._ There will be a negative dose-response relationship between nicotine content description and CO boost (i.e., greater CO boost will be associated with the lowest nicotine content description).

There was no difference in CO boost by nicotine content description; participants’ CO levels increased similarly after smoking each cigarette regardless of nicotine content description. As with results from withdrawal analyses, the small size of this null effect (i.e., $\eta_p^2 = 0.001$) might suggest that this result may not be representative of nicotine content description effects on CO boost in a larger sample of smokers. However, this finding is consistent with the results of Juliano & Brandon (2002) and Joel (2013) which also found similar CO boost among participants regardless of nicotine content.
Regardless of whether cigarettes were described as containing no or reduced nicotine— independent of actual nicotine content—this description appears to have no effect on CO boost after smoking. These results seem to indicate that as measured by CO boost, attempts to compensate during initial use are likely not the result of biases about RNCs. However, given that all study cigarettes contained sufficient nicotine content, it is also possible that participants did not feel the need to compensate while smoking study cigarettes as they would when using cigarettes of actual reduced nicotine content.

**Summary of Aim 2 Findings**

Overall, analyses found very little effect of nicotine content description on measures of smoking behavior; there was an effect of nicotine content description on average puff volume, but not on CO boost or any other measures of smoking topography. In conclusion, nicotine content description did not have an overall dose-response effect on smoking behaviors. These results are consistent with other dose-description studies, which overall have not demonstrated a clear effect of nicotine content description across multiple measures of smoking topography (Darredeau et al., 2013; Joel, 2013; Juliano & Brandon, 2002; Perkins et al., 2009).

In previous studies of RNCs, smokers have initially attempted to compensate (i.e., increase smoking behaviors) for reduced nicotine content within their cigarettes by increasing smoking topography (Strasser et al., 2007). However, smokers generally return to normal levels over time due to deficient nicotine content within the RNCs (Benowitz et al., 2012; Hatsukami et al., 2015). It is possible that initial compensation results from negative bias about RNCs, such that smokers may anticipate needing to engage in greater
smoking behaviors to achieve sufficient blood levels of nicotine. Given that all study participants smoked cigarettes of sufficient nicotine content, if bias were responsible for initial compensatory behaviors, participants would be expected to demonstrate at least some difference in topography measures by nicotine content description. Specifically, smoking topography measures during use of the “reduced nicotine” cigarettes should be greater than those during use of the “UBC” cigarette. However, results demonstrated either no description effect or the reverse effect, likely due to the sufficient nicotine content within the study-supplied cigarettes. These results suggest that the compensatory smoking behaviors observed during initial use of RNCs (Benowitz et al., 2012; Strasser et al., 2007) do not appear to be the result of bias.

**Covariate Influences on Aim 1 and 2 Findings**

To determine if nicotine content description effects on subjective ratings and smoking behaviors would remain above and beyond the influence of gender and nicotine dependence, all analyses for Aims 1 and 2 were replicated to first control for the gender, and then again to control for both gender and dependence (as measured by the FTND). Initial analyses found no nicotine content description effects on withdrawal suppression, CO boost, or composite topography measures. As such, it is not surprising that adding gender and dependence as covariates for these analyses did not alter original findings.

The addition of gender as a covariate removed the effect of nicotine content description on reduction of both global craving and craving due to anticipation of negative affect relief. Because gender groups were unequal (16 male vs. 8 female participants), it is possible that adding gender as a covariate to analyses of such a small
sample size simply reduced the ability of analyses to detect interaction effects on craving. The subsequent addition of dependence as a covariate did not alter these results. Given that dependence was correlated with robustly craving ratings (e.g., r's = 0.30-0.59) these results might suggest that although nicotine content description may affect craving reduction, this effect is relatively small compared to that of the influence of dependence. In other words, biases about using RNCs may have a slight effect on these cigarettes’ ability to reduce certain aspects of cigarette craving, but level of nicotine dependence may be a more important determinant of craving reduction.

Interestingly, the addition of gender as a covariate to analyses of sensory effects of smoking did not wash out any of the original nicotine content description effects. The inclusion of gender increased many of the effect sizes for these relationships, and nicotine content description effects became significant for a number of additional items (e.g., harshness, satisfaction from smoking, taste). Although the study sample was too small to fully explore gender effects, this is an important area for future study. If one gender is more likely to be biased toward cigarettes described as containing reduced nicotine, intervention efforts specifically targeting the biases of this gender may be needed to ensure consumer acceptance of RNCs prior to the implementation of a nicotine reduction policy. The addition of dependence as a covariate to the previous analysis removed the main multivariate main effect of nicotine content. Given that dependence was not correlated with sensory items, it is possible that controlling for both dependence and gender in a RM-MANOVA predicting 14 different outcomes caused this analysis to be too underpowered to adequately detect nicotine content description effects.
Similar to craving analyses, adding gender as a covariate to analyses of average topography measures removed the multivariate effect of nicotine content description on the combined measures, consequently removing the univariate effect of nicotine content description on average puff volume. Including nicotine dependence as a covariate did not alter these findings. Because gender groups were extremely unbalanced in topography analyses (10 male vs. 6 female), and because dependence was not correlated with topography measures (unlike craving), it is possible that the disappearance of nicotine content description effects is due to issues of sample size.

In summary, the robust associations of gender and nicotine dependence with many of the primary outcomes suggest that these are important covariates for analyses. However, given the study’s small overall sample size and the unequal numbers of male and female smokers included in analyses, the inclusion of these covariates seems to have reduced the ability of the analyses to detect the few small effects of nicotine content description on study outcomes. As such, any significant effects of nicotine description content were no longer significant after controlling for gender and dependence.

**Aim 3 Exploratory Findings**

**Aim 3: Assess initial RNC outcome expectancies about and willingness to use** RNCs, **and evaluate willingness and expectancies as potential moderators of the effects of nicotine content descriptions on subjective ratings and smoking behaviors.**

**Overview.** Few studies of RNCs have prospectively assessed smokers’ outcome expectancies related to using these products, or even their willingness to use these products. As such, these outcomes were assessed at baseline (i.e., before participants had
been exposed to study cigarettes), and were then explored as moderators of nicotine content description effects. In general, participants held more negative smoking outcome expectancies about RNCs compared to their own preferred brand cigarette. However, these expectancies did not appear to moderate nicotine content description effects (with the exception of average puff volume). Participants were generally willing to use RNCs in appropriate ways, and less willing to supplement RNC use with or exclusively use other types of tobacco products. Willingness to use RNCs also did not moderate nicotine content description effects on any outcomes.

**Willingness to use RNCs.**

_Hypothesis 3.1. Participants will, in general, express low willingness to engage in behaviors that promote positive use of RNCs, and will express high willingness to engage in behaviors to avoid use of RNCs._

Contrary to the proposed hypothesis, the vast majority of participants expressed at least some willingness to engage in behaviors encouraging appropriate use of RNCs, and expressed no willingness at all to engage in behaviors to avoid use of RNCs. Specifically, 93.9% of the sample expressed at least some willingness to use RNCs like their regular brand cigarettes, and 27.3% reported being strongly willing to do so. Additionally, 78.9% of the sample expressed at least some willingness to use RNCs to gradually quit smoking; 30.3% were strongly willing. Given that participants reported these responses at baseline, before even using the study cigarettes, these results are encouraging in that prior to receiving any sort of information about RNCs, participants reported being open to using
these products as intended. These results suggest that if a nicotine reduction policy were implemented, individuals would initially be willing to use RNCs in appropriate ways.

In general, participants expressed less willingness to supplement RNC use with other tobacco products, and less willingness to exclusively use these products instead of RNCs. Of note, participants were less willing to either supplement RNC use with or exclusively use nicotine replacement therapies (NRT; e.g., gum, patch) or other tobacco products (e.g., chew, snus, cigars). Although the majority of the sample indicated less willingness to supplement RNC use with, or exclusively use, e-cigarettes and roll-your-own tobacco, the proportion of participants endorsing these categories was much lower compared to NRT and other tobacco products. For example, 84.8% of participants indicated they were not willing at all to supplement RNCs with NRT, but only 57.6% indicated the same of e-cigarettes. These findings might suggest that if a nicotine reduction policy were implemented, e-cigarettes and roll-your-own tobacco would be the most likely contenders for alternative tobacco products, should smokers not accept RNCs.

Perhaps one of the more concerning findings was that 33.3% of the sample expressed at least some willingness to buy cigarettes with higher nicotine content from potentially illegal sources. Because willingness to perform a behavior may serve as a proxy for actually performing that behavior, this finding provides preliminary evidence that smokers are open to seeking out tobacco products through illegal means. Because a significant concern of regulatory efforts is the fueling of a black market of illegal, high-nicotine content products, more research is needed regarding smokers’ specific motivations and reasons for endorsing willingness for this option.


**RNC smoking outcome expectancies.**

_Hypothesis 3.2. Participants will have more negative smoking outcome expectancies for RNCs compared to their preferred cigarette brand._

In general, compared to their own preferred cigarette, participants provided more negative ratings of RNCs for smoking outcome expectancies related to rewarding and sensory aspects of smoking (e.g., liking, satisfaction) and more positive ratings for outcome expectancies related to health consequences of smoking (e.g., addiction, cancer). These findings are consistent with Joel (2013) also demonstrating that participants provided lower ratings for a “very low” nicotine vs. “average” nicotine cigarette on sensory and rewarding aspects of smoking, but also provided lower ratings for negative health consequences of smoking (e.g., the “very low” nicotine cigarette was rated lower than the “average” for causing lung cancer). Taken together, these findings are critical for regulatory efforts. Participants in these studies had no pre-existing knowledge of what RNCs were or how they differed from their current brand, yet the descriptions of “reduced” and “very low” nicotine implicitly conveyed worse sensory and rewarding effects of smoking, but also conveyed better health outcomes to participants. Regulatory efforts may need to consider increasing education about sensory and health effects of RNCs to encourage responsible use of these products.

**Willingness to use RNCs as a moderator of nicotine content description effects.**

_Hypotheses 3.3 - 3.7. Willingness will moderate nicotine content description effects on subjective and behavioral responses to smoking, such that smokers who are_
less (vs. more) willing to use RNCs will experience more robust dose-nicotine content description effects.

Contrary to the proposed hypothesis, willingness to use RNCs did not moderate the effect of nicotine content description on any subjective responses or smoking behaviors. We offer a few explanations for the lack of a moderating effect of willingness of nicotine dose description effects. First, the small size of the sample may have caused analyses to be too underpowered to detect the triple interaction effect of willingness x nicotine content description x time for craving, withdrawal, and CO analyses, and additionally too underpowered to examine the interaction of willingness x nicotine content description on multivariate outcomes (e.g., total and average topography measures, sensory characteristics). Examination of effect sizes provides support for this explanation, given that effect sizes for the various willingness interaction terms ranged from 0.002 to 0.01, although multivariate analyses seemed to have reasonable effects sizes (0.08 to 0.31).

Second, it is possible that the lack of variability in responses to the baseline questionnaire of willingness to use RNCs resulted in the creation of a composite willingness score that did not accurately capture the true construct of willingness to use RNCs. For example, several items assessing participants’ willingness to exclusively use alternative tobacco products instead of RNCs were included in the composite score, assuming that high willingness to exclusively use chew or snuff in place of RNCs conveys low willingness to use RNCs. However, because the majority of participants indicated that they were not at all willing to use many of these alternative tobacco products, this may indicate a lack of willingness to use these products in general,
regardless of whether RNCs were available or not. Thus, the inclusion of these items into the composite willingness measure may have resulted in a composite willingness measure reflecting lack of willingness to use other tobacco products, but not necessarily willingness to use RNCs.

Further, participants were asked about their willingness to engage in a number of specific behaviors related to RNC use (e.g., using RNCs to gradually quit, using alternative tobacco products instead of RNCs) as opposed to directly asking about general willingness to use a cigarette with reduced nicotine. As such, future studies may consider asking participants simply and directly if they would be willing to use RNCs, as opposed to how they would use RNCs if they became available.

RNC smoking outcome expectancies as a moderator of nicotine content description effects.

Hypotheses 3.8 - 3.12. RNC outcome expectancies will moderate nicotine content description effects on subjective and behavioral responses to smoking, such that smokers with negative (vs. positive/neutral) RNC outcome expectancies will experience more robust dose-response nicotine content description effects.

Analyses found that RNC outcome expectancies moderated nicotine content description effects for average topography measures only; specifically, participants who held negative RNC outcome expectancies displayed greater average puff volumes while smoking the “UBC” cigarette compared to puff volumes while smoking the “LNC” and “VLNC” cigarettes. As such, this finding partially confirms the proposed hypothesis, and further demonstrates that participants' expectancies about RNCs – prior to ever using
RNCs – can influence their subsequent responses to these products. Future studies should consider exploring the effects of specific outcome expectancies, as opposed to the general composite expectancies measure used in the study, to determine if they would be stronger moderators of nicotine content description effects.

**Regulatory Implications**

Although some methodological issues limit the results of this study, a number of study findings may have implications useful for informing future regulatory efforts. First, the absence of differences in participants' estimated cigarette nicotine content, and subjective and behavioral responses between the “LNC” and “VLNC” cigarettes suggests labeling reduced nicotine cigarettes as having “low” and “very low” nicotine content may not result in dramatic differences between consumer acceptance of either product. However, this warrants further exploration among a larger sample of smokers. If a nicotine reduction policy is implemented, one issue the FDA will need to consider is if and how to inform smokers of the gradual change in the nicotine content of their cigarettes. It was expected that smokers would be more likely to accept a cigarette described as having “low” versus “very low” nicotine content, given that the latter implies a more serious departure from the nicotine content of participants' normal brand. Yet study findings demonstrated that these vague but distinct descriptions resulted in only subtle differences between estimated nicotine content, and consequently, only subtle differences in initial subjective responses and smoking behaviors.

Second, the study’s overall findings suggest that reduced nicotine content descriptions have little effect on subjective and behavioral responses to smoking, perhaps
due to the fact that all cigarettes used contained pharmacologically sufficient nicotine content. Although this conclusion cannot be definitively reached given the small effect sizes of null findings, these results are aligned with those of prior dose description studies demonstrating that the pharmacological effects of nicotine had a greater effect on subjective responses to smoking than descriptions of receiving nicotine. Findings should be confirmed in future studies comparing the effects of reduced nicotine content descriptions on similar outcomes in which varying descriptions of content are provided for both nicotine-containing and reduced nicotine-containing cigarettes.

Third, the finding that participants provided more negative smoking outcome expectancies for RNCs compared to their preferred brand cigarette at baseline suggests that smokers may have already developed negative biases about these cigarettes prior to ever using them. It is important to note that at no point during the study were participants provided with any information regarding either the goals of a nicotine reduction policy or how RNCs might differ from commercially available cigarettes often perceived to contain less nicotine (e.g. "light" or "ultra-light" cigarettes). Thus, it is possible that participants' negative smoking outcome expectancies were shaped by pre-existing misinformation about cigarettes previously labeled as “light” and “ultra-light cigarettes,” as such labels imply these cigarettes are “healthier” and/or contain reduced levels of harmful cigarette constituents. These findings suggest that prior to implementing a federal nicotine reduction policy, the FDA may need to clearly explain to smokers how RNCs differ from “light/ultra-light” cigarettes, as well as educate smokers on the actual health consequences of using RNCs.
Finally, the observation that participants who held negative (vs. positive/neutral) smoking outcome expectancies about using RNCs took deeper average puffs when smoking the “UBC” cigarette compared to the “reduced nicotine” may also be of importance to regulatory effects. This finding implies that smokers holding negative smoking outcome expectancies for using RNCs are likely to dislike cigarettes described as having “reduced” nicotine content, regardless of the actual nicotine content of the cigarettes. This suggests that if a nicotine reduction policy is implemented, the FDA may need to increase education about RNCs and modify existing outcome expectancies to become more positive about using these cigarettes. A study of outcome expectancies regarding use of the nicotine patch by Fucito & Juliano (2007) provides an example of how such a strategy may be applied. In this study, smokers’ outcome expectancies about using the nicotine patch were manipulated prior to a quit attempt by providing some smokers with information about the positive benefits of using the patch and providing others with the standard instructions available for the patch. Those who received the benefits information reported greater positive expectancies about using the patch, and subsequently experienced increased positive mood and greater quitting during an abstinence period. Thus, it may be necessary for the FDA to change smokers’ expectancies about using RNCs prior to policy implementation, in order for smokers to react positively to and benefit from the use of these products.

Limitations

Although this dissertation's findings may have important regulatory implications, interpretations of findings must consider several caveats. First, and perhaps most
importantly, analyses of topography data were limited by equipment malfunction of the CReSS V3 topography device. Specifically, of the 72 conducted experimental sessions, the topography device failed to capture data entirely for 3 sessions (4.2%) and recorded questionable data (e.g., >70% aberrant puff volumes) for 7 sessions (9.7%). Because repeated measures analyses eliminated participants based on pairwise deletion, this resulted in eight of 24 participants (33%) being excluded from analyses of topography data. These issues were not unique to this study (Denlinger & Donny, personal communication; Strasser, personal communication; Pacek, personal communication), and are consistent with other recent topography studies (Norton, June, & O’Connor, 2014). The principal investigator repeatedly worked with the topography device manufacturer to resolve issues, but the device performed unreliably for the duration of the study.

Second, numerous analyses were conducted to explore study aims, and as such, multiple comparisons may have increased the rate of a Type I error occurring. Although pairwise comparisons used to explore significant main effects of nicotine content description were adjusted for multiple comparisons, this only occurred within a given outcome, not within aims. For example, pairwise comparisons used a Bonferroni adjustment to compare cigarette descriptions among the 14 individual sensory effect items; no adjustments for multiple comparisons were made for significance at the overall main effect level (e.g., no corrections were made for the overall effect of nicotine content on sensory effects vs. craving vs. withdrawal). However, this analytic strategy is consistent with, and in some cases, more conservative than similar dose description studies (Juliano & Brandon, 2002; Perkins et al., 2008, 2009). Additionally, many study
findings remained significant despite using a correction as severe as the Bonferroni adjustment.

Third, difficulties in recruiting and retaining female participants limited adequate exploration of gender differences in nicotine content description effects on study outcomes. Because men comprised the majority (66.7%) of the sample, findings are likely more representative of nicotine content description effects on male smokers’ subjective and behavioral responses to smoking. Additionally, difficulties with recruiting female smokers may be indicative of selection bias; female participants who participated in the study may not be representative of the general female smoking population. Future studies sufficiently powered to explore gender differences in nicotine content description effects are needed to conclusively determine if male and female smokers vary in responses to cigarettes described as having reduced nicotine content.

Fourth, although every effort was made to keep both research staff and participants blinded to the nicotine content of the study-supplied cigarettes, the principal investigator – who conducted 66% of the 72 of the experimental sessions – was aware of actual nicotine content. Thus, the study was not truly double blind, and it is possible that the data collected during sessions run by the principal investigator may be biased. Statistical analyses were not powered to empirically test whether results from sessions conducted by the principal investigator differed from the results of those conducted by other study staff, but examination of the overall trends by research staff member suggests that participants' responses across sessions did not differ by experimenter. However, the possibility must be considered that participants' responses were influenced to some extent by the bias of the principal investigator.
Fifth, because questions about willingness to use RNCs were assessed in an environment in which participants were relatively unfamiliar with RNCs, study findings may not be representative of smokers’ willingness to use RNCs in an environment in which these products are available and marketed to consumers. If a nicotine reduction policy is implemented, it is likely that the regulatory agencies will disseminate a great deal of information to increase education about the potential benefits of these products. This information dissemination may then result in dramatic differences between the results of this study and willingness to use RNCs during policy implementation. However, the findings of this study remain nonetheless important for assessing initial willingness to engage in a variety of behaviors related to using RNCs independent of any pre-existing knowledge about these products.

Finally, given that this study required participants to smoke \( \geq 5 \) cigarettes per day, findings may not generalize to light or non-daily smokers. Although daily and nondaily smokers may differ in subjective/behavioral responses to effects of nicotine content descriptions, it is difficult to biochemically verify smoking status and distinguish cigarette use from abstinence among these smokers. Results may also not generalize to smokers of cigarettes that were either unblindable (e.g., American Spirit) or incompatible with the topography device (e.g., “roll-your-own”). Because all smokers will be affected by a federal nicotine reduction policy, future studies may benefit from examining these aims using a wider variety of cigarette smokers, or using a different topography device which can estimate the smoking behaviors of “roll-your-own” cigarette smokers.
Future Directions

To improve upon the limitations of the current study, and to fully integrate study findings with the extant literature on nicotine dose/content description effects, there is a need for a future laboratory study using a 3 x 3 balanced placebo design to cross both actual nicotine content and nicotine content description. In this type of study, an adequate sample of female and male smokers would be randomly assigned to one of nine groups based on nicotine content description (told usual vs. told very low nicotine vs. told no nicotine) and actual nicotine content (given usual vs. reduced vs. lowest possible nicotine content). Following a design similar to this dissertation, participants would abstain for 12-h before a single laboratory session, in which they would provide pre-cigarette assessments of subjective responses, smoke a cigarette through a topography device, and then provide-post-cigarette assessments of subjective responses. This type of study would allow for the separation of nicotine's pharmacological effects from the effects of nicotine content description on subjective responses and smoking behaviors. Additionally, this study should re-examine if smoking outcome expectancies regarding RNC use or willingness to use RNCs moderate these effects among a larger sample of smokers.

Conclusions

In summary, the results of this dissertation have demonstrated that describing a cigarette as containing reduced nicotine content may result in differences in only some subjective and behavioral responses to smoking that cigarette when compared with smokers’ usual cigarette brand. Specifically, cigarettes described as containing “low” and “very low” nicotine content were smoked with shallower puffs, and were rated as being
weaker, milder, and having weaker smoke than a cigarette described as containing normal nicotine content. However, given that these effects disappeared after controlling for gender and dependence, this suggests that pragmatically, these effects are small and perhaps unlikely to ultimately influence long-term consumer acceptance of RNCs. Additionally, participants' willingness to use RNCs did not moderate nicotine content description effects, but RNC outcome expectancies did moderate the effect of nicotine content description on average puff volume; this effect was only experienced among smokers with negative (vs. positive/neutral) RNC outcome expectancies. Findings suggest that although the negative ratings given to RNCs may partially be due to descriptions about "reduced" nicotine content, these differences are more likely the result of deficient nicotine levels with RNCS although this warrants further investigation. Additionally, results suggest that regulatory agencies may need to increase education about RNCs prior to implementation of a nicotine reduction strategy in order to modify pre-existing biases and expectancies about RNCs.
References


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Are you a smoker?

The Smoking & Health Behavior Research Laboratory at Penn State is currently seeking healthy smokers to participate in a research study evaluating responses to cigarettes with different levels of nicotine. This is not a quit smoking study.

You may be eligible if you:

- Are at least 18 years old
- Smoke cigarettes daily
- Are not pregnant (if female)

You will be asked to come into our laboratory for a total of four short visits where you will smoke different types of cigarettes through a device that measures your smoking behaviors. After smoking, you will provide ratings of the cigarettes. Participants who complete the entire study will receive up to $100.

For more information, contact the Smoking & Health Behavior Research Laboratory at 814-865-8442 or at nicotinestudy@psu.edu

This study is under the direction of Melissa Mercincavage, M.S., and Steven A. Branstetter, Ph.D. (Biobehavioral Health; 814-865-7793)
A2. Telephone Eligibility Screen

Interviewer initials: __________
Phone verbal consent date & time: __________

RNC Study Telephone Eligibility Screen

Comments:

Subject Name: ________________ Daytime Phone#: ______________________
Gender: M F Age: ________
Where did you hear about our study? ______________________________________________________________________________

First I will ask you some questions about your smoking:
1. How many cigarettes a day do you smoke (specific #)? _______________ >>>If <5, exclude.
2. How long have you been smoking at your current rate? ____________ >>>If <6 months, exclude.
3. Have your smoking habits changed in any way over the past 12 months (change brands or smoke more or less)? If yes, describe: YES NO
   >>>Exclude as needed based on smoking at least 5 CPD for at least 6 months (i.e., if participant has been smoking 10 CPD for 2 months and only 1 CPD for the previous 4 months, exclude).
4. Are you at all interested in quitting smoking? YES NO
   If yes: Do you have a firm quit date? YES NO
   Are you planning to quit smoking in the next month? YES NO
   >>>If participant responds YES to last question or indicates quit date in next 30 days, exclude from study.
5. What brand of cigarettes do you smoke? ______________________________
   >>>If participant rolls own cigs or smokes crushable cigs, exclude. Otherwise collect cigarette information to compare against cigarettes to be brought in for baseline session.

   Strength: Full flavor Light Ultra-light Filter: Filtered Unfiltered
   Length: Reg (70) Kings (80-85) Long (100) Extra Long (120) Flavor: Menthol Non-menthol

Now I have some questions about your overall health:
1. (women only) Are you currently pregnant or trying to become pregnant? YES NO
2. Do you see a doctor regularly for a specific medical problem? (Current prescriptions?) YES NO
3. Have you been told by a doctor that you have high blood pressure or heart disease? YES NO
4. Have you been told by a doctor or are currently diagnosed with diabetes? YES NO
5. Do you have any other health or orthopedic problems? Is there anything special medically about your heart or lungs, live or kidney, or thyroid? YES NO
6. Have you ever had asthma? YES NO
7. Are you currently taking any medications (e.g., prescriptions, OTC, birth control, vitamins, herbal supplements)?

_______________________________________ YES NO

8. Do you keep any medications around the house for use as needed?

_______________________________________ YES NO

>>>If participant responds YES to any of questions 1-6, exclude. Exclude as needed based on medication answers (e.g., if taking BP meds despite saying "NO" to #3, exclude).

If you qualify for this study, are there certain days or certain times of the day that would be more convenient for you to come in for sessions?

AM M _______ T _______ W _______ H _______ F _______

PM M _______ T _______ W _______ H _______ F _______

How would you get here? (e.g., bus, car, walk) ______________________

Would it be okay to say that we’re calling from the Smoking & Health Behavior Research Lab if we need to leave messages for you at the phone number you gave? YES NO

If you don’t meet the criteria for this study, would it be okay for us to contact you about future studies? YES NO
A3. Text Used to Contact Participants from Smoking Study Databases

Hello, {insert name}. I am contacting you on behalf of the Smoking & Health Behavior Research Laboratory at Penn State because you recently completed a smoking study on campus and had indicated that you would like to be contacted about future opportunities. We are now recruiting for a new study that may be of interest to you.

Our current study is evaluating how smokers respond to smoking cigarettes which contain different levels of nicotine. During the study period you would come into our laboratory in Chandlee Laboratory on Penn State’s campus for four visits; a baseline visit lasting about an hour and 3 experimental sessions each lasting no more than half an hour. Prior to each of the three experimental sessions, you will be asked to stop smoking 12 hours before your scheduled appointment time. During each experimental session, you will be asked to smoke as much or as little as you like of a single, study-supplied cigarette through an electronic device which will measure how you smoke. You will also be asked to fill out some forms asking about your smoking behaviors and your ratings of the cigarettes you smoke.

If this sounds like a study you may be interested in, please contact the Smoking & Health Behavior Research Laboratory at 814-865-8442 or at nicotinestudy@psu.edu.

Thank you for your time,

{insert name of person at SHBRL contacting the participant}
A4. Female-Specific Flyer and Website Advertisement

Are you a female smoker?

The Smoking & Health Behavior Research Laboratory at Penn State is currently seeking healthy female smokers to participate in a research study evaluating responses to cigarettes with different levels of nicotine. This is not a quit smoking study.

You may be eligible if you:
Are at least 18 years old
Smoke cigarettes daily
Are not pregnant

You will be asked to come into our laboratory for a total of four short visits where you will smoke different types of cigarettes through a device that measures your smoking behaviors. After smoking, you will provide ratings of the cigarettes. Participants who complete the entire study will receive up to $100.

For more information, contact the Smoking & Health Behavior Research Laboratory at 814-865-8442 or at nicotinestudy@psu.edu

This study is under the direction of Melissa Mercincavage, M.S., and Steven A. Branstetter, Ph.D. (Biobehavioral Health; 814-865-7793)
A5. Consent Form

CONSENT FOR RESEARCH
The Pennsylvania State University

Title of Project: Behavioral and Subjective Responses to Differences in Cigarette Nicotine Content

Principal Investigator: Melissa Mercincavage, M.S.

Address: 219 Biobehavioral Health Building
University Park, PA 16802

Telephone Number: (814) 865-8442

Advisor: Steven A. Branstetter, Ph.D.

Advisor Telephone Number: (814) 865-7793

Subject's Printed Name: ____________________________

We are asking you to be in a research study. This form gives you information about the research. Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you. Please ask questions about anything that is unclear to you and take your time to make your choice.

1. Why is this research study being done?

We are asking you to be in this research because you have expressed interest in participating in this study and because you qualified for participation during an initial telephone interview.

This research is being done to find out how smokers react to different levels of nicotine contained in cigarettes. We will measure your evaluation of the cigarettes you smoke using a variety of questionnaires, and will use an electronic smoking topography device to measure how you smoke the cigarettes (e.g., how deeply you inhale, how many puffs you take). Approximately 50 people will take part in this research study conducted at Penn State’s University Park campus.

2. What will happen in this research study?

Today’s Session (Baseline): Visit #1

Today’s initial session will be scheduled between the hours of 9 a.m. and 7 p.m. and will take place at the Smoking Behavior Research Laboratory in 308 Chandlee Laboratory at the Pennsylvania State University. This session will last approximately 1 hour. You will be asked to smoke as you normally would prior to coming into the laboratory for this session.

The procedure for this session is as follows:

1. You will complete this consent form.
2. You will provide an expired air carbon monoxide sample by breathing into an electronic device.
3. (If female) You will provide a urine sample to be tested for pregnancy.
4. You will fill out several questionnaires which will ask you to provide information about your demographics, smoking and health history, and attitudes about smoking and other health
behaviors to determine your eligibility to continue in the research study. You will be able to skip any questions that you prefer to not answer (although this may affect your eligibility for continuing in the research study).

5. At the end of the baseline session, if you are eligible to continue in the research study, you will schedule your first experimental session.

**Experimental Sessions: Visits #2-4**

If you are eligible to participate in this study, you will next be asked to return to 308 Chandlee for three separate half-hour visits. These visits will be scheduled on days convenient to you, and will generally be scheduled between the hours of 9 a.m. and noon. You will be required to stop smoking 12 hours before each of these visits. If you do not abstain from smoking overnight, your visit will be rescheduled for the following day.

The procedure for the experimental sessions is as follows:

1. You will stop smoking 12 hours before your scheduled appointment time.
2. You will arrive at 308 Chandlee Laboratory at your scheduled appointment time.
3. You will provide a carbon monoxide sample to verify that you have abstained from smoking overnight. If you have not abstained from smoking, your experimental session will be rescheduled for the following day. If female, you will also provide a urine sample to be test for pregnancy at this time.
4. You will complete a series of computerized questionnaires which will ask you about your current cigarette craving, withdrawal, and mood. You will be able to skip any questions that you prefer to not answer.
5. You will smoke a study-provided cigarette through a device which will measure your smoking behaviors. You will not know what type of cigarette you will smoke.
6. You will fill out computerized questionnaires asking you to rate the cigarette you smoked.
7. You will complete final computerized questionnaires assessing your cigarette craving, withdrawal, and mood.
8. A researcher will schedule your next experimental session.
9. Upon completing your final session, you will be compensated for your time.

3. **What are the risks and possible discomforts from being in this research study?**

There is very little risk to you in participating in this study. All the questionnaires, measures, and data collection methods are well-established and considered routine. However, there may be some minor and temporary discomforts to you while participating in this study:

a) There is a chance that you may experience mild symptoms of nicotine withdrawal when asked to refrain from smoking overnight prior to the experimental study sessions. These symptoms may include irritability, fatigue, nausea, and difficulty concentrating. These symptoms are expected to be mild and should subside once you resume smoking during and after the experimental study sessions.

b) There is a chance you may feel uneasy providing answers to certain questionnaire questions. You are allowed to skip over any questions that you feel uncomfortable, and you are also allowed to withdraw from the study at any time, for any reason, without repercussions.

c) There is a risk of loss of confidentiality if your medical information or your identity are obtained by someone other than the investigators and trained research staff. Several precautions have been taken to prevent this from happening.

d) Among female participants using oral contraceptives, smoking may increase your risk of cardiovascular disease, stroke, and/or blood clots. However, given that the maximum number of cigarettes this study would require you to smoke (3 cigarettes total) across the
entire multi-session study is less than the minimum number of cigarettes you smoke in a day, this study confers no additional risk for oral contraceptive users.

4. **What are the possible benefits from being in this research study?**

4a. **What are the possible benefits to you?**

You are not expected to receive any direct benefits from your participation in this study.

4b. **What are the possible benefits to others?**

It is hoped that your participation will benefit society by providing data that may be used to inform policy decisions regarding nicotine regulation. By extension, these findings may also help to determine if a widespread, nicotine reduction strategy will be feasible and effective way of decreasing cigarette use.

5. **What other options are available instead of being in this research study?**

Because this study is designed to help us understand how smokers evaluate cigarettes of varying nicotine content, there are no alternative procedures that can be used to measure smoking behaviors or self-reported evaluations of cigarettes smoked. You may choose to end your participation in this research at any time.

6. **How long will you take part in this research study?**

If you agree to take part, it will take you about 2.5 hours total to complete this research study. After today’s session, you will be asked to return to the research laboratory 3 times. Today’s baseline session is expected to last 1 hour, while the next 3 experimental sessions should each last no more than 30 minutes.

7. **How will your privacy and confidentiality be protected if you decide to take part in this research study?**

Efforts will be made to limit the use and sharing of your personal research information to people who have a need to review this information.

- All data files will be coded with a unique ID number and all names or other personal identifiable information will be removed.
- Any documents containing personal identifiable information will be kept under lock and key in the Smoking & Health Behavior Research Lab, which only Ms. Mercincavage and Dr. Branstetter will have access to.
- Computerized questionnaire data will be stored and secured on a laptop unconnected to external networks in a password protected file.
- In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

We will do our best to keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people may find out about your participation in this research study. For example, the following people/groups may check and copy records about this research.

- The Office for Human Research Protections in the U. S. Department of Health and Human Services
- The Institutional Review Board (a committee that reviews and approves research studies) and
- The Office for Research Protections.
Some of these records could contain information that personally identifies you. Reasonable efforts will be made to keep the personal information in your research record private. However, absolute confidentiality cannot be guaranteed.

9. **Will you be paid to take part in this research study?**

You will be paid at a rate of $10/hour for participation in the four study sessions, including the baseline session. Additionally, you will receive $15/session for abstaining overnight for each of the three half-hour experimental sessions. Broken down by each session, you would earn:

- $10 for completing today's 1 hour baseline session
- $20 for completing the first half-hour experimental session ($5 for session completion, $15 for abstaining from smoking overnight)
- $20 for completing the second half-hour experimental session ($5 for session completion, $15 for abstaining from smoking overnight)
- $20 for completing the third half-hour experimental session ($5 for session completion, $15 for abstaining from smoking overnight)
- $30 bonus for completing the entire study

If you complete all four sessions, you will receive an additional $30, for a total compensation of $100. In the event that your participation is discontinued by either you or the investigator prior to the last session, you will be paid only the $10/hour rate for completed sessions. You will not receive the additional $30 bonus.

10. **What are your rights if you take part in this research study?**

Taking part in this research study is voluntary.

- You do not have to be in this research.
- If you choose to be in this research, you have the right to stop at any time.
- If you decide not to be in this research or if you decide to stop at a later date, there will be no penalty or loss of benefits to which you are entitled.

If you decide to leave the research, **you will be compensated for your participation to the point at which you terminate your participation.** If you decide to leave the research, contact the investigator so that the investigator can provide you with compensation.

Researchers and study staff can remove you from the research study without your approval. Possible reasons for removal include repeated failure to comply with study protocol (e.g., repeatedly not abstaining from smoking prior to experimental sessions), mistreatment of study staff, etc.

11. **If you have questions or concerns about this research study, whom should you call?**

Please call the head of the research study (principal investigator), Melissa Mercincavage, at (814) 865-8442 if you:

- Have questions, complaints or concerns about the research.
- Believe you may have been harmed by being in the research study.

You may also contact the Office for Research Protections at (814) 865-1775, ORProtections@psu.edu if you:

- Have questions regarding your rights as a person in a research study.
- Have concerns or general questions about the research.
- You may also call this number if you cannot reach the research team or wish to talk to someone else about any concerns related to the research.
INFORMED CONSENT AND AUTHORIZATION TO TAKE PART IN RESEARCH

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the research to the subject or subject representative and have answered any questions he/she has about the research.

Signature of person who explained this research   Date   Time   Printed Name
(Only approved investigators for this research may explain the research and obtain informed consent.)

Signature of Person Giving Informed Consent and Authorization

Before making the decision about being in this research you should have:
- Discussed this research study with an investigator,
- Read the information in this form, and
- Had the opportunity to ask any questions you may have.

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Signature of Subject

By signing this consent form, you indicate that you voluntarily choose to be in this research and agree to allow your information to be used and shared as described above.

Signature of Subject   Date   Time   Printed Name
A6. Study Description/Telephone Screen Consent Script

Thank you for calling about our research studies at the Smoking & Health Behavior Research Laboratory. My name is {say name} and before I can determine if you are eligible for the study, I will need to tell you a little more about the details of this study.

This research is evaluating how smokers respond to smoking cigarettes which contain different levels of nicotine. During the study period you would come into our laboratory in Chandlee Laboratory on Penn State’s campus for four visits; a baseline visit lasting about an hour and 3 experimental sessions each lasting no more than half an hour. Prior to each of the three experimental sessions, you will be asked to stop smoking 12 hours before your scheduled appointment time. During each experimental session, you will be asked to smoke as much or as little as you like of a single, study-supplied cigarette through an electronic device which will measure how you smoke. You will also be asked to fill out some forms asking about your smoking behaviors and your ratings of the cigarettes you smoke.

Does this sound like a study you might be interested in? {answer any questions participants may have about study protocol at this time}

{If no}: Okay, thank you for calling.

{If yes}: Okay. In order to see if you qualify, we need to get some information from you. I would like to ask you some questions now about your smoking and general health. These questions should take about 10 minutes.

There is a possibility that some of these questions may make you uncomfortable or distressed; if so, please let me know. You don’t have to answer those questions if you don’t want to. You also need to understand that all information that I receive from you by phone, including your name and any other identifying information will be strictly confidential and will be kept under lock and key. The purpose of these questions is only to determine whether you are eligible for this study. If you are eligible, you will be asked to come into the lab for a brief information session, at which you will learn more about the study and sign consent forms. Remember, your participation is voluntary; you do not have to complete these questions.

Do I have your permission to ask you these questions?

{If no}: Okay, thank you anyway for calling.

{If yes, continue on to screening questions from Telephone Eligibility Screen document}
A7. Post-Study Debriefing Statement

{To be read to participants at the conclusion of the entire study}:

Research staff: “Hello, my name is {insert name} and I work in the Smoking and Health Behavior Research Laboratory at Penn State. About {insert time frame since participant completed study} ago you completed a study examining how smokers react to cigarettes with different nicotine content. I am calling because the purpose of the study you just completed was not fully divulged to you prior to your participation.

During this study, you had the opportunity to smoke as much or as little as you wanted of three study-provided cigarettes, and then provided ratings of these cigarettes. You were told that these cigarettes were made by the manufacturer of your own brand, but that the cigarettes contained different amounts of nicotine content. Although you were given specific information about the amount of nicotine in these cigarettes prior to smoking them, in reality, these cigarettes were actually your own brand of cigarette. When you entered the study, you were asked to show us your preferred brand of cigarette. We recorded this information and then purchased the same brand of cigarette to be used in all of your study sessions. The reason we did not disclose this information to you is because we were interested in how your specific beliefs about nicotine content affected the way you smoked and rated the cigarette.

If you feel a need to speak to a professional concerning any uncomfortable feelings from your participation in this research, you may contact either Melissa Mercincavage or Dr. Steven Branstetter. Their contact information can be found on the first page of the consent form you signed for the study, but I can provide you with it again if necessary.

Do you have any questions about your participation today?”

{If individual has questions, provide answers}

{If individual does not have questions or after questions have been answered}:

“Thank you for your time and for volunteering for our study.”
A8. Script to Invite Prospective Participants Into Study

“This study examines the effects of different levels of nicotine content on smoking behaviors and ratings. It involves 4 sessions at our lab in Chandlee Laboratory on Penn State’s campus. The first initial baseline session will last about an hour, and then each of the three following sessions will be about a half hour long. You will have to stop smoking overnight (12 hours) before most sessions, except the first one. For the first session, you must smoke normally and must bring in a pack of your preferred cigarette brand. Later during that first session, you’ll fill out several screening forms. Females will also be required to provide a urine sample to be tested for pregnancy. We will then schedule the first of 3 experimental sessions, again lasting approximately a half hour each.

During the 3 experimental sessions you may be asked to smoke a single, study-supplied cigarette that will contain a different amount of nicotine. The most nicotine you would ever receive at one time is the amount found in an average, commercially available cigarette. You will have to stop smoking for 12 hours prior to all three of the experimental sessions. We will take an air sample to confirm that you stopped smoking as required. The main things you’ll do while you’re here are smoke a cigarette through an electronic device which measures your smoking behaviors, and fill out some short forms about how you think and feel about the cigarette you smoked.

You’ll be paid $100 for following all instructions and completing the 4 sessions of this study, involving about 2.5 hours of your time. We’ll give you your payment at the end of your final session. Does that sound like something you might be interested in?

{If interested, schedule appointment. Remind to bring pack of preferred cigarettes and to smoke normally prior to coming in for the session. The day before their appointment, participants will also receive a reminder call (or e-mail) to smoke normally and to bring cigarette pack. Inform participant of where our lab is located and ask if they have any other questions.}
Appendix B. Baseline Measures

B1. Demographic Questionnaire

1. Please circle your gender:  Male  Female

2. Please circle your ethnic status (circle as many as apply):

   Race  Race if Hispanic
   1 White  9 Hispanic/Latino only
   2 Black  10 + White
   3 Asian/Indian  11 + Black
   4 Native Indian/Alaskan Native  12 + Asian/Indian
   5 Native Hawaiian/Pacific Islander  13 + Native American/Alaskan Native
   6 Hispanic  14 + Native Hawaiian/Pacific Islander
   7 More than one race  15 + More than two races
   8 Unknown/Other  16 + Unknown

3. How old are you? ____________________

4. Please circle your highest level of education (circle one):

   1. <7th grade  Academic Grade Level if Partial College
   2. Junior High (9th grade)  1. Freshman (Grade 13)
   3. Partial High School  2. Sophomore (Grade 14)
   4. High School Graduate  3. Junior (Grade 15)
   5. Partial College (at least one year or specialized technical training)  4. Senior (Grade 16)
   6. College or University Graduate  5. Other: __________
   7. Graduate or Professional Training

5. Please circle your current marital status (circle one):

   1. Single  4. Separated
   2. Married  5. Divorced
   3. Partnered  6. Widowed

6. What is your current occupation? ____________________
B2. Smoking, Drug Use, and Health History Questionnaire

Please tell us about the types of tobacco you use by filling out the table:

<table>
<thead>
<tr>
<th>Have you ever used this product?</th>
<th>Cigarettes</th>
<th>Chew</th>
<th>Tobacco &amp; Ash/Snuff</th>
<th>Pipe</th>
<th>Cigar</th>
<th>Electronic cigarettes</th>
<th>Hookah, Shisha</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
</tr>
<tr>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
</tr>
<tr>
<td>How much tobacco do you currently use?</td>
<td>___ per day</td>
<td>___ cans per week</td>
<td>___ x a day/week/month/year</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
</tr>
<tr>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
</tr>
<tr>
<td>How old were you when you first tried this product?</td>
<td>___ years old</td>
<td>___ years old</td>
<td>___ years old</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
</tr>
<tr>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
</tr>
<tr>
<td>How old were you when you first started using regularly?</td>
<td>___ years old</td>
<td>___ years old</td>
<td>___ years old</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
</tr>
<tr>
<td>☐ No</td>
<td>☐ Yes</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
<td>☐ No</td>
</tr>
</tbody>
</table>

1. Are you planning to stop using tobacco? (Please check only one)
   ☐ Yes, I’ve already stopped
   ☐ Yes, within the next 6 months.
   ☐ Yes, plan to stop today
   ☐ Not sure
   ☐ Yes, in the next 30 days.
   ☐ No, I’m not planning to stop for good

2. Are you currently pregnant?
   ☐ No
   ☐ Yes

3. Have you ever had or currently have any of the following? (Check all that apply)
   ☐ Seizures
   ☐ Peptic Ulcer Disease
   ☐ Peripheral vascular disease
   ☐ Head injury
   ☐ Diabetes
   ☐ Coronary artery disease
   ☐ Shortness of breath
   ☐ Eating disorders
   ☐ Skin allergy or sensitivities
   ☐ Stroke
   ☐ Cancer
   ☐ Alcohol withdrawal
   ☐ Emphysema or chronic bronchitis
   ☐ Asthma
   ☐ High blood pressure
   ☐ Cough

4. Describe any current medical problems or physical symptoms you are having:
   _______
5. List any allergies you have:

6. List all medications you are taking, including reason for use and how often:

7. Do you have a history of depression?  ☐ Yes  ☐ No

8. Do you have a history of anxiety?  ☐ Yes  ☐ No

9. Have you ever used alcohol?  ☐ Yes  ☐ No
   
   *If Yes:* Do you currently use Alcohol?  ☐ Yes  ☐ No
   
   How many drinks per week on average do you have? (one drink = one beer, one glass of wine, one shot alcohol) # Drinks ______a week

10. Have you received treatment for alcohol or other drug dependency?  ☐ Yes  ☐ No
   
   *If Yes:* Are you currently receiving treatment for this condition?  ☐ Yes  ☐ No
   
   Have you been sober and/or drug free for a year or more?  ☐ Yes  ☐ No

11. Have you tried to stop using tobacco before today? …if “No” please go to question # 8  ☐ Yes  ☐ No

12. What is your main reason for wanting to stop using tobacco? *(Check all that apply)*
   ☐ Health Reasons  ☐ To Save Money  ☐ To be a Positive Role Model
   ☐ Live Longer  ☐ Protect the health of others  ☐ Other(s):______________________

13. When do you use tobacco? *(Check all that apply)*
   ☐ When feeling stressed  ☐ When wanting to cheer  ☐ When drinking coffee, tea or soda
   up
When feeling anxious ☐  When bored ☐  When wanting something in your mouth ☐
After meals ☐  When At work ☐  When hunting or fishing ☐
When relaxing ☐  When drinking ☐  When around other users ☐

14. Does anyone in your family have a tobacco-related disease? ☐ No ☐ Yes, what disease(s) ________________________________

15. What is the biggest obstacle you face in stopping tobacco use?
________________________________________________________

16. Are you under a lot of stress now? ☐ Yes ☐ No
If yes, from what? ________________________________________

Please tell us about your current and/or previous drug use by filling out the table:

<table>
<thead>
<tr>
<th></th>
<th>Marijuana (mushrooms)</th>
<th>Psilocybin (mushrooms)</th>
<th>Ecstasy (Molly)</th>
<th>Amphetamines</th>
<th>Cocaine</th>
<th>Opiates (heroin, oxycontin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you ever used this product?</td>
<td>☐ Yes ☐ No</td>
<td>☐ Yes ☐ No</td>
<td>☐ Yes ☐ No</td>
<td>☐ Yes ☐ No</td>
<td>☐ Yes ☐ No</td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>How much do you currently use?</td>
<td>___ x a day/week/month/year</td>
<td>___ x a day/week/month/year</td>
<td>___ x a day/week/month/year</td>
<td>___ x a day/week/month/year</td>
<td>___ x a day/week/month/year</td>
<td>___ x a day/week/month/year</td>
</tr>
<tr>
<td>How old were you when you first tried this product?</td>
<td>___ years old</td>
<td>___ years old</td>
<td>___ years old</td>
<td>___ years old</td>
<td>___ years old</td>
<td>___ years old</td>
</tr>
<tr>
<td>How old were you when you first started using regularly?</td>
<td>___ years old</td>
<td>___ years old</td>
<td>___ years old</td>
<td>___ years old</td>
<td>___ years old</td>
<td>___ years old</td>
</tr>
<tr>
<td></td>
<td>☐ Don’t use regularly</td>
<td>☐ Don’t use regularly</td>
<td>☐ Don’t use regularly</td>
<td>☐ Don’t use regularly</td>
<td>☐ Don’t use regularly</td>
<td>☐ Don’t use regularly</td>
</tr>
</tbody>
</table>
B3. Willingness to use RNCs Questionnaire

Sometimes people don’t make specific plans to engage in certain behaviors, but they are open or willing. If reduced nicotine cigarettes became available today, how willing would you be to do the following behaviors in the next 30 days?

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Use reduced nicotine cigarettes like I smoke my current brand</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. Use reduced nicotine cigarettes but smoke more cigarettes/day</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. Use reduced nicotine cigarettes to gradually quit smoking</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. Quit smoking immediately instead of using reduced nicotine cigarettes</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. Supplement using reduced nicotine cigarettes with e-cigarettes</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6. Supplement using reduced nicotine cigarettes with other tobacco products (chewing tobacco, cigars)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7. Supplement using reduced nicotine cigarettes with nicotine replacement therapy (gum, patch, lozenge)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8. Supplement using reduced nicotine cigarettes with roll-your-own cigarettes</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>9. Use e-cigarettes exclusively or instead of using reduced nicotine cigarettes</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>10. Use other tobacco products (chewing tobacco, cigars) exclusively or instead of using reduced nicotine cigarettes</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>11. Use nicotine replacement therapy (gum, patch, lozenge) exclusively or instead of using reduced nicotine cigarettes</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>12. Use roll-your-own cigarettes instead of using reduced nicotine cigarettes</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>13. Buy cigarettes with higher nicotine content from other, potentially illicit sources</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
### B4. Questionnaire of Smoking Outcome Expectancies

The next set of questions will ask you about your preferred brand/type of cigarette:

I believe smoking my preferred brand/type of cigarette…

<table>
<thead>
<tr>
<th>Perception</th>
<th>Strongly disagree</th>
<th>Moderately disagree</th>
<th>Neither disagree nor agree</th>
<th>Moderately agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is satisfying.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Tastes good.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Provides enjoyable sensations in my throat and chest.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Calms me down.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Makes me feel more awake.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Makes me feel less irritable.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Helps me concentrate.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Reduces my hunger for food.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Makes me dizzy.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Makes me nauseous.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Relieves my craving for a cigarette.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Is enjoyable.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Is addictive.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Is safe.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Is healthy.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Increases my risk of having a cardiovascular issue (heart attack, heart disease).</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Increases my chance of developing lung cancer/disease.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Helps me control my weight.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
The next set of questions will ask you about reduced nicotine cigarettes:

Compared to my usual brand/type of cigarette, I believe smoking a reduced nicotine cigarette will…

<table>
<thead>
<tr>
<th></th>
<th>Strongly disagree</th>
<th>Moderately disagree</th>
<th>Neither disagree nor agree</th>
<th>Moderately agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is satisfying.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Tastes good.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Provides enjoyable sensations in my throat and chest.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Calms me down.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Makes me feel more awake.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Makes me feel less irritable.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Helps me concentrate.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Reduces my hunger for food.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Makes me dizzy.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Makes me nauseous.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Relieves my craving for a cigarette.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Is enjoyable.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Is addictive.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Is safe.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Is healthy.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Increases my risk of having a cardiovascular issue (heart attack, heart disease).</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Increases my chance of developing lung cancer/disease.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Helps me control my weight.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
B5. Fagerstrom Test for Nicotine Dependence (FTND)

INSTRUCTIONS: For each question, circle the correct answer.

1. How soon after you wake up do you smoke your first cigarette?
   a) Within 5 minutes
   b) Within 6-30 minutes
   c) Within 31-60 minutes
   d) After 60 minutes

2. Do you find it difficult to refrain from smoking in places where it is forbidden (e.g., in church, at the library, in cinema, etc)?
   a) Yes
   b) No

3. Which cigarette would you hate most to give up?
   a) The first one in the morning
   b) Any other

4. How many cigarettes per day do you smoke?
   a) 10 or less
   b) 11-20
   c) 21-30
   d) 31 or more

5. Do you smoke more during the first hours after waking than during the rest of the day?
   a) Yes
   b) No

6. Do you smoke even when you are ill enough to be in bed most of the day?
   a) Yes
   b) No
### B6. Hooked on Nicotine Checklist (HONC)

<table>
<thead>
<tr>
<th></th>
<th>Question</th>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Have you ever tried to quit smoking, but couldn’t?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Do you smoke now because it is really hard to quit?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Have you ever felt like you were addicted to tobacco?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Do you ever have strong cravings to smoke?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Have you ever felt like you really needed a cigarette?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Is it hard to keep from smoking in places where you are not supposed to?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

When you haven’t used tobacco for a while … OR
When you tried to stop smoking....

<table>
<thead>
<tr>
<th></th>
<th>Question</th>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Did you find it hard to concentrate because you couldn't smoke?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Did you feel more irritable because you couldn't smoke?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Did you feel a strong need or urge to smoke?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Did you feel nervous, restless or anxious because you couldn't</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
B7. Wisconsin Inventory of Smoking Dependence Motives (WISDM-68)

Below are a series of statements about cigarette smoking. Please rate your level of agreement for each using the following scale:

Not true of Me At All Extremely True of Me

1. I enjoy the taste of cigarettes most of the time. 1 2 3 4 5 6 7
2. Smoking keeps me from gaining weight. 1 2 3 4 5 6 7
3. Smoking makes a good mood better. 1 2 3 4 5 6 7
4. If I always smoke in a certain place it is hard to be there and not smoke. 1 2 3 4 5 6 7
5. I often smoke without thinking about it. 1 2 3 4 5 6 7
6. Cigarettes control me. 1 2 3 4 5 6 7
7. Smoking a cigarette improves my mood. 1 2 3 4 5 6 7
8. Smoking makes me feel content. 1 2 3 4 5 6 7
9. I usually want to smoke right after I wake up. 1 2 3 4 5 6 7
10. Very few things give me pleasure each day like cigarettes. 1 2 3 4 5 6 7
11. It’s hard to ignore an urge to smoke. 1 2 3 4 5 6 7
12. The flavor of a cigarette is pleasing. 1 2 3 4 5 6 7
13. I smoke when I really need to concentrate. 1 2 3 4 5 6 7
14. I can only go a couple hours between cigarettes. 1 2 3 4 5 6 7
15. I frequently smoke to keep my mind focused. 1 2 3 4 5 6 7
16. I rely upon smoking to control my hunger and eating. 1 2 3 4 5 6 7
17. My life is full of reminders to smoke. 1 2 3 4 5 6 7
18. Smoking helps me feel better in seconds. 1 2 3 4 5 6 7
19. I smoke without deciding to. 1 2 3 4 5 6 7
20. Cigarettes keep me company, like a close friend. 1 2 3 4 5 6 7
21. Few things would be able to replace smoking in my life. 1 2 3 4 5 6 7
22. I’m around smokers much of the time. 1 2 3 4 5 6 7
23. There are particular sights and smells that trigger strong urges to smoke. 1 2 3 4 5 6 7
24. Smoking helps me stay focused. 1 2 3 4 5 6 7
25. Smoking helps me deal with stress. 1 2 3 4 5 6 7
26. I frequently light cigarettes without thinking about it. 1 2 3 4 5 6 7
27. Most of my daily cigarettes taste good. 1 2 3 4 5 6 7
28. Sometimes I feel like cigarettes rule my life. 1 2 3 4 5 6 7
29. I frequently crave cigarettes. 1 2 3 4 5 6 7
30. Most of the people I spend time with are smokers. 1 2 3 4 5 6 7
31. Weight control is a major reason that I smoke. 1 2 3 4 5 6 7
32. I usually feel much better after a cigarette. 1 2 3 4 5 6 7
33. Some of the cigarettes I smoke taste great. 1 2 3 4 5 6 7
34. I’m really hooked on cigarettes. 1 2 3 4 5 6 7
35. Smoking is the fastest way to reward myself. 1 2 3 4 5 6 7
36. Sometimes I feel like cigarettes are my best friends. 1 2 3 4 5 6 7
37. My urges to smoke keep getting stronger if I don’t smoke. 1 2 3 4 5 6 7
38. I would continue smoking, even if it meant I could spend less time on my hobbies and other interests. 1 2 3 4 5 6 7
39. My concentration is improved after smoking a cigarette. 1 2 3 4 5 6 7
40. Seeing someone smoke makes me really want a cigarette.  
41. I find myself reaching for cigarettes without thinking about it.  
42. I crave cigarettes at certain times of day.  
43. I would feel alone without my cigarettes.  
44. A lot of my friends or family smoke.  
45. Smoking brings me a lot of pleasure.  
46. Cigarettes are about the only things that can give me a lift when I need it.  
47. Other smokers would consider me a heavy smoker.  
48. I feel a strong bond with my cigarettes.  
49. It would take a pretty serious medical problem to make me quit smoking.  
50. When I haven’t been able to smoke for a few hours, the craving gets intolerable.  
51. When I do certain things I know I’m going to smoke.  
52. Most of my friends and acquaintances smoke.  
53. I love the feel of inhaling the smoke into my mouth.  
54. I smoke within the first 30 minutes of awakening in the morning.  
55. Sometimes I’m not aware that I’m smoking.  
56. I’m worried that if I quit smoking I’ll gain weight.  
57. Smoking helps me think better.  
58. Smoking really helps me feel better if I’ve been feeling down.  
59. Some things are very hard to do without smoking.  
60. Smoking makes me feel good.  
61. Smoking keeps me from overeating.  
62. My smoking is out of control.  
63. I consider myself a heavy smoker.  
64. Even when I feel good, smoking helps me feel better.  
65. I reach for cigarettes when I feel irritable.  
66. I enjoy the sensations of a long, slow exhalation of smoke.  
67. Giving up cigarettes would be like losing a good friend.  
68. Smoking is the easiest way to give myself a lift.
Appendix C. Experimental Session Measures

C1. Brief Questionnaire of Smoking Urges (QSU-Brief)
Consider how you are feeling RIGHT NOW. Place a vertical line at the point that best indicates how you currently feel.

1. I have a desire for a cigarette right now.
   | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - |
   Do not agree | Moderately agree | Strongly agree

2. Nothing would be better than smoking a cigarette right now.
   | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - |
   Do not agree | Moderately agree | Strongly agree

3. If it were possible, I probably would smoke now.
   | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - |
   Do not agree | Moderately agree | Strongly agree

4. I could control things better right now if I could smoke.
   | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - |
   Do not agree | Moderately agree | Strongly agree

5. All I want right now is a cigarette.
   | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - |
   Do not agree | Moderately agree | Strongly agree

6. I have an urge for a cigarette.
   | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - |
   Do not agree | Moderately agree | Strongly agree

7. A cigarette would taste good now.
   | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - |
   Do not agree | Moderately agree | Strongly agree

8. I would do almost anything for a cigarette now.
   | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - |
   Do not agree | Moderately agree | Strongly agree

9. Smoking would make me less depressed.
   | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - |
   Do not agree | Moderately agree | Strongly agree

10. I am going to smoke as soon as possible.
    | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - | - - - - |
    Do not agree | Moderately agree | Strongly agree
### C2. Minnesota Nicotine Withdrawal Scale Revised (MNWS)

Please rate yourself as you are feeling RIGHT NOW. Place a vertical line at the point that best indicates how you currently feel.

**Angry, irritable, frustrated**

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Slight</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
</table>

**Anxious, nervous**

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Slight</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
</table>

**Depressed mood, sad**

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Slight</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
</table>

**Desire or craving to smoke**

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Slight</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
</table>

**Difficulty concentrating**

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Slight</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
</table>

**Increased appetite, hungry, weight gain**

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Slight</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
</table>

**Insomnia, sleep problems, awakening at night**

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Slight</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
</table>

**Restless**

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Slight</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
</table>

**Impatient**

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Slight</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
</table>

**Constipation**

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Slight</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
<td>Slight</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>------------------</td>
<td>------</td>
<td>--------</td>
<td>------</td>
<td>----------</td>
<td>--------</td>
</tr>
<tr>
<td><strong>Dizziness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Coughing</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dreaming or nightmares</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nausea</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sore throat</strong></td>
<td></td>
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</tbody>
</table>
### C3. Visual Analog Scale of Subjective Ratings of Smoking Reward

Please place a vertical line at the location that best represents your rating of the cigarette for each characteristic:

<p>| | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. <strong>Strength</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Very weak</td>
<td></td>
<td>Very strong</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. <strong>Harshness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Very mild</td>
<td></td>
<td>Very harsh</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. <strong>Heat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No heat</td>
<td></td>
<td>Very hot</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. <strong>Draw</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Easy</td>
<td></td>
<td>Difficult</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. <strong>Taste</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bad</td>
<td></td>
<td>Good</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>6. <strong>Satisfaction from smoking</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unsatisfying</td>
<td></td>
<td>Satisfying</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. <strong>Burn rate</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Burned</td>
<td></td>
<td>Did not burn too fast in too few puffs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. <strong>Taste (mildness)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mild taste</td>
<td></td>
<td>Not mild taste</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. <strong>Too mild</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>It was too mild for me</td>
<td></td>
<td>It was not too mild for me</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. <strong>Harshness of smoke</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Smoke seemed too harsh</td>
<td></td>
<td>Smoke did not seem too harsh</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. <strong>After taste</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Did not leave a good aftertaste in my mouth</td>
<td></td>
<td>Left a good aftertaste in my mouth</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. <strong>Staleness</strong></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Somehow it seemed stale</td>
<td></td>
<td>Somehow it did not seem stale</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. <strong>Strength of smoke</strong></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Smoke seemed very weak</td>
<td></td>
<td>Smoke seemed very strong</td>
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<td></td>
</tr>
<tr>
<td>14. <strong>Smoke smell</strong></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unpleasant</td>
<td></td>
<td>Pleasant</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
C4. Estimated Nicotine Content Questionnaire

1. How much NICOTINE do you think your usual brand cigarette contains?

   | - - - | - - - | - - - | - - - | - - - | - - - | - - - | - - - | - - - | - - - |
   None                                                                   Very Much

2. How much NICOTINE do you think the cigarette you just smoked contains?

   | - - - | - - - | - - - | - - - | - - - | - - - | - - - | - - - | - - - | - - - |
   None                                                                   Very Much
## C5. Carbon Monoxide Data Collection Sheet

<table>
<thead>
<tr>
<th>Sample</th>
<th>Date sample obtained</th>
<th>Time sample obtained</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experimental Session 1</td>
<td>Pre-cigarette</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Post-cigarette</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experimental Session 2</td>
<td>Pre-cigarette</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Post-cigarette</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experimental Session 3</td>
<td>Pre-cigarette</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-cigarette</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
MELISSA MERCINCAVAGE
Vita

EDUCATION

Ph.D. Biobehavioral Health, 2015 (expected)
The Pennsylvania State University, University Park, PA
M.S. Biobehavioral Health, 2012
The Pennsylvania State University, University Park, PA
B.S. Psychology (with Honors), 2008
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AWARDS AND HONORS

2013 TL1 Career Development Award, Clinical and Translational Science Institute, The Pennsylvania State University
2013 Graduate Teaching Excellence Award, Department of Biobehavioral Health, The Pennsylvania State University
2010 Robert E. Graham Fellowship Award, College of Health and Human Development, The Pennsylvania State University

SELECTED PUBLICATIONS