Original investigation

Brief, instructional smokeless tobacco Use among Cigarette smokers Who Do not intend to Quit: a Pilot randomized Clinical trial

Jessica L. Burris PhD[1], **Matthew J. Carpenter** PhD[1], **Amy E. Wahlquist** MS[2], **K. Michael Cummings** PhD, MPH[1], **Kevin M. Gray** MD[3]

[1]*Department of Psychiatry and Behavioral Sciences and Hollings Cancer Center, Medical University of South Carolina, Charleston, SC;* [2]*Department of Public Health Sciences, Medical University of South Carolina, Charleston, SC;* [3]*Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, SC*

Corresponding Author: Jessica L. Burris, PhD, Department of Psychiatry and Behavioral Sciences and Hollings Cancer Center, Medical University of South Carolina, 86 Jonathan Lucas Street, MSC 955, Charleston, SC 29425, USA. Telephone: 843-876-2446; Fax: 859-876-2344; E-mail: burris.jessica@gmail.com

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abstract

introduction: Low-nitrosamine smokeless tobacco (SLT) may have efficacy for smoking reduction and cessation, but its public health impact depends on how smokers use it.

Methods: This pilot study explored brief, instructional low-nitrosamine SLT use among smokers unmotivated to quit. Participants (N = 57) were randomized to either a free 2-week supply of Camel Snus group or a no-supply group. Of those randomized to use Camel Snus, half were told to use it to cope with smoking restrictions (Snus to Cope), and the remaining half were advised to use it to reduce smoking (Snus to Reduce). Participants were assessed before, during, and immediately after the intervention.

results: Many Snus to Cope and Snus to Reduce participants reported daily use of Camel Snus, although the amount of use was low. Snus to Cope (18.4%) and Snus to Reduce (37.6%) participants reported a decline in number of cigarettes used per day, which was not reported by the control participants ($p < .001$). Intention to quit smoking and intention to quit all tobacco use ($ps < .001$) increased to a greater extent among Snus to Cope and Snus to Reduce participants than among control participants.

Conclusions: This study replicates previous work that shows that low-nitrosamine SLT use can lead to reduced smoking and increased intention to quit, and it adds direct evidence to suggest that the function of low-nitrosamine SLT use—either to cope with smoking restrictions or to reduce smoking—can have a differential impact on smoking behavior. Overall, the results highlight the importance of messaging and, more specifically, marketing of low-nitrosamine SLT to smokers.

introduction

The tobacco industry develops and markets "potentially reduced exposure products (PREPs)" as those with purportedly fewer health risks than conventional tobacco products (Stratton, Shetty, Wallace, & Bondurant, 2001). Prevalence estimates from U.S. epidemiological data indicate that traditional PREP use (i.e., use of cigarette-like or modified tobacco products) among adult smokers is low (Hund et al., 2006; O'Connor, Hyland, Giovino, Fong, & Cummings, 2005). However, as the type and the availability of PREPs are constantly changing, smokers' use of these products is also constantly in flux. Thus, the latest generation of PREPs (namely, low-nitrosamine smokeless tobacco [SLT] products) can achieve a level of popularity higher than that observed for older PREPs, and several studies document their increasing popularity (Bhattacharyya, 2012; Boyle, St Claire, Kinney, D'Silva, & Carusi, 2012; Choi & Forster, 2012; Maher, Bushore, Rohde, Dent, & Peterson, 2012; O'Connor et al., 2011; Popova & Ling, 2013; Wilson, Borland, Weerasekera, Edwards, & Russell, 2009).

The recent increase in SLT use probably reflects the changing landscape of newer SLT products (e.g., Camel Orbs, Marlboro Snus), which contrast with conventional SLT products (e.g., Kodiak, Copenhagen) in significant ways. In addition to lower levels of tobacco-specific nitrosamines and other harmful chemicals in relation to those found in conventional SLT products (Hatsukami et al., 2004; Stepanov, Biener, et al., 2012; Stepanov, Jensen, et al., 2012; Stepanov, Jensen, Hatsukami, & Hecht, 2008), newer SLT products provide attractive flavors, creative packaging, spitless options, and diverse formulations (e.g., pouches, orbs, lozenges). Together, these design features contribute to the likelihood that low-nitrosamine SLT products will draw

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new tobacco users. Unlike older SLT products, newer products are also aggressively marketed toward smokers, a likely response to the prolifieration ofi smoking restrictions (Hatsukami, Ebbert, Feuer, Stepanov, & Hecht, 2007; Mejia & Ling, 2010). Marketing strategies portray low-nitrosamine SLT use as a means to 1) reduce or quit smoking or 2) circumvent smoking restrictions. For example, advertisements fior Camel Snus include a "Smoke-firee resolution" campaign that promotes switching firom smoking to low-nitrosamine SLT use (Camel: Snus [advertisement], 2011) and a "Break firee" campaign (e.g., "Just say 'no' to people saying 'no'") that highlights the benefiit ofi low-nitrosamine SLT use in places where smoking is prohibited (Timberlake, Pechmann, Tran, & Au, 2011). In sum, newer SLT products are categorically difiifierent firom older SLT products, and in conjunction with community-level policy pressures (e.g., increase in cigarette prices), they could fiare well in the market.

Nevertheless, how smokers will use low-nitrosamine SLT remains unclear. Switching firom smoking to SLT use entirely is rare in the United States (Zhu et al., 2009), which suggests that dual use will be the modal pattern among smokers who try low-nitrosamine SLT. However, evidence suggests low-nitrosamine SLT use could lead to smoking reduction and eventual smoking abstinence (Gilljam & Galanti, 2003; Hatsukami et al., 2011; Lund, McNeill, & Schefifiels, 2010Ọ'Connor et al., 2011; Ramström & Foulds, 2006; Tilashalski, Rodu, & Cole, 1998, 2005), although conflicting evidence exists (Biener, McCausland, Curry, & Cullen, 2011). Most ofi the studies on low-nitrosamine SLT mentioned earlier are based on epidemiologic evidence with selfi-selected groups ofi users and nonusers, but a handfiul ofi randomized clinical trials (RCTs) provide direct support fior the ability ofi low-nitrosamine SLT to fiacilitate reduction and cessation among smokers (Fagerstrom, Rutqvist, & Hughes, 2012; Joksić, Spasojević-Tišma, Antić, Nilsson, & Rutqvist, 2011; Tønnesen, Mikkelsen, & Bremann, 2008), even among those not yet ready to quit smoking (Carpenter & Gray, 2010).

Previous studies show increased interest in low-nitrosamine SLT use among smokers who are provided risk infiormation (Borland et al., 2012; O'Connor et al., 2011), but the public health impact ofi these products will depend in part on *how* these products are used—whether to 1) reduce or quit smoking or 2) cope with smoking restrictions. To our knowledge, no study has manipulated messaging as a means to examine the behavioral and/or motivational impact ofi smokers' low-nitrosamine SLT use. Thus, this pilot study explores the infiluence ofi briefi, *instructional* low-nitrosamine SLT use among smokers unmotivated or unwilling to quit in the near fiuture. Two types ofi messages were tested in this pilot study (specifiically, low-nitrosamine SLT use as a means to either 1) reduce or quit smoking or 2) circumvent smoking restrictions), both ofi which were consistent with the tobacco industry's marketing ofi low-nitrosamine SLT. Because there is reason to believe that the popularity ofi low-nitrosamine SLT will increase with time, it is important to discern the impact ofi fiunctional use and determine whether these PREPs represent a viable means ofi harm reduction and health promotion.

Meth ODs

Participants and Procedure

Participants were recruited firom the general community via fily-ers, newspaper and radio advertisements, online fiorums (e.g., Craig's List, Facebook), and word ofi mouth. Advertisements described the study as one ofi a "new tobacco product that may be safier than cigarettes." Eligibility criteria fior the participants included the fiollowing: (a) aged 18–65 years, (b) no history ofi cardiovascular distress (e.g., heart attack, uncontrolled hypertension) in the past year, (c) neither pregnant nor breast fieeding, (d) no current history ofi major psychiatric disorders, including alcohol or other drug (exception being nicotine) dependence, (e) daily smoker ofi ≥10 cigarettes/day on average fior at least 1 year, (fi) no intention to quit smoking in the subsequent month (defiined as a score ofi <7 on a scale firom 0 =*ery definitely no* to 10 = *very definitely yes*; Biener & Abrams, 1991; Prochaska, Velicer, DiClemente, & Fava, 1988), (g) no history ofi noncigarette tobacco use in the previous 6 months, and (h) no lifietime history ofi PREP use, including low-nitrosamine SLT use.

Afiter determination ofi eligibility and provision ofi written infiormed consent, participants completed a baseline (Time 1) assessment and were randomized to one ofi three groups: 1) "Cigarettes Only," 2) "Snus to Cope," or 3) "Snus to Reduce," each described in the fiollowing paragraphs. Participants were randomized to the Snus to Cope/Reduce versus Cigarettes Only groups in a 2:1 ratio to address potential noncompliance with low-nitrosamine SLT use and fiew anticipated changes among control group participants. Participants in the Snus to Cope or Snus to Reduce groups were asked to sample Camel Snus as desired fior a 3-day trial period, fiollowed by 2 weeks ofi use. The 3-day trial period was designed to acclimatize smokers to a novel product, in advance ofi the instructional use period. Follow-up assessments were conducted midway through and at the end ofi the 2-week period ofi low-nitrosamine SLT use (Times 2 and 3, respectively). Afiter study completion, participants were debriefied, at which time, all participants were told that there is no safie tobacco product and were prompted to quit tobacco use entirely; cessation resources (e.g., Quitline contact infiormation) were given, ifi desired. Participants were reimbursed up to $100 fior completion ofi all assessments. No fiunding or support fior this study was provided by the tobacco industry. The Medical University ofi South Carolina Institutional Review Board approved this study.

Study Product: Camel Snus

Camel Snus is a smokeless, spitless, pouched moist snufifi that is manufiactured and marketed by Reynolds American, Inc. Camel Snus was selected fior this study because early testing suggested that it ofiifiers the greatest nicotine delivery and reliefi firom withdrawal and craving to smoke compared with other low-nitrosamine SLT products (Hatsukami et al., 2011; Stepanov, Biener, et al., 2012; Stepanov et al., 2008). Comparative carcinogenic profiiles fior Camel Snus versus cigarettes, conventional SLT products, and medicinal nicotine products (Hatsukami et al.,2004, 2007; Stepanov et al., 2008) suggest that Camel Snus may be less harmfiul than conventional tobacco products. Regardless, Camel Snus and similar low-nitrosamine SLT products are not harm firee as their levels ofi tobacco-specifiic nitrosamines are consistently higher than those ofi medicinal nicotine. Thus, as part ofi infiormed consent, participants received infiormation about the potential harms and side efiifiects ofi Camel Snus.

Study Groups

"Cigarettes Only" Group

Participants in this group smoked their regular brand of conventional cigarettes. To guard against the possibility that tobacco use might vary as a function of the provision of a free tobacco product, control participants were provided an extra $25 at Time 1 and Time 2 as compensation for the purchase of their own cigarettes.

"Snus to Cope" Group

Participants in this group were provided Camel Snus (choice of flavor: spice, frost, and original) free of charge and instructed to use this product in a manner consistent with tobacco industry marketing. Specifically, participants were told to use Camel Snus to cope with smoking restrictions and to avoid withdrawal secondary to nonsmoking. Recommendations were not given regarding how many pouches to use. However, to facilitate participants' use of Camel Snus as intended, it was recommended that participants make a list of 10 personally relevant situations in which they were not allowed to smoke (e.g., work, restaurants, movies), rank order those situations according to the difficulty associated with adherence to smoking restrictions, and then cope with smoking restrictions via Camel Snus use before and/or during the most difficult situations. Participants were provided with actual tobacco industry marketing messages as an adjunct to study instructions. These participants were also told to smoke as they wished in places without smoking restrictions.

"Snus to Reduce" Group

As noted earlier, participants in this group were provided Camel Snus free of charge and instructed to use this product in a manner consistent with tobacco industry marketing. However, these participants were advised to use Camel Snus to reduce or even eliminate smoking. They were instructed on methods of product switching, including the following: (a) gradual substitution for total number of cigarettes per day (e.g., 20% of all cigarettes per day, then 40% of all cigarettes per day, etc.) and (b) stimuli-specific substitution (e.g., first X setting in which smoking normally occurs, then X plus Y setting in which smoking normally occurs, etc.). Participants were oversupplied with Camel Snus in case they used more pouches per day than cigarettes per day; but as in the other group, they were not told how many pouches to use. Furthermore, participants were provided with actual tobacco industry marketing messages as an adjunct to study instructions.

Measures

At Time 1 only, basic questions were asked about participants' demographic and tobacco use history, including nicotine dependence (Heatherton, Kozlowski, Frecker, & Fagerström, 1991). At each time point, participants provided information about their current tobacco use, motivation, attitudes toward low-nitrosamine SLT, and as appropriate, experience of any adverse event. Time line follow-back procedures were used to measure number of cigarettes per day and pouches per day used during the previous week. Additionally, biochemical (exhaled carbon monoxide and urine cotinine, ng/mL) measures of tobacco use were collected at each time point. Intention to quit smoking in the subsequent month and intention to quit all tobacco use in the subsequent month were both judged on a scale from 0 = *very definitely no* to 10 = *very definitely yes* (Biener & Abrams, 1991; Prochaska et al., 1988). Confidence in ability to quit smoking was measured on a scale from 0 = *not at all confident* to 10 = *extremely confident* (Carpenter et al., 2011; Sanderson et al., 2009; Woods et al., 2002). Similarly, a general craving to smoke in the previous week was measured on a scale from 0 = *not at all* to 10 = *very much* (Shiffman et al., 1997; Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996). Intention to purchase low-nitrosamine SLT and expectations about low-nitrosamine SLT use were assessed with single-item attitudinal measures, as described elsewhere (Carpenter & Gray, 2010; Hund et al., 2006; O'Connor et al., 2005; Shiffman et al., 2007). Likeability of Camel Snus, both absolute (0 = *not at all* and 10 = *very much*) and relative (0 = *liked Camel Snus a lot less than usual brand of cigarettes* and 10 = *liked Camel Snus a lot more than usual brand of cigarettes*), was also measured. Harm perception for low-nitrosamine SLT compared with that of conventional cigarettes (i.e., relative risks) was measured on a scale from 0 = *much less risk than cigarettes* to 10 = *much greater risk than cigarettes*, with 5 = *same risk as cigarettes*; responses were then categorized as less (0–3), equal (4–6), or more (7–10) risk. Finally, adverse events were measured using a combination of open-ended questions and checklists.

Data Analysis

Descriptive statistics were used to describe the sample at Time 1. To identify group differences in demographic and tobacco use variables, chi-square and analysis of variance models were used as appropriate; variables that differed between groups were treated as covariates in the primary and secondary analyses. The primary analyses examined change in tobacco use and motivation via generalized estimating equations (GEE) models (Liang & Zeger, 1986), with Group (between subjects), Time (within subjects), and Group × Time (interaction) effects. The secondary analyses explored change in participants' attitudes toward low-nitrosamine SLT (specifically, intention to purchase low-nitrosamine SLT and expectations about low-nitrosamine SLT use) via GEE models previously described. In cases where the interaction effect was not statistically significant, GEE models were modified to include only the main effects of Group and Time; however, this revision did not change the overall pattern of results, so they are not discussed below. Finally, likeability of Camel Snus, harm perception for low-nitrosamine SLT, and adverse events were explored via descriptive statistics. In all analyses, $p < .05$ determined statistical significance.

Results

Demographic and Tobacco Use Characteristics

For the entire sample ($N = 57$), mean (M [SD]) age was 41.5 (12.1) years. Most participants were White, non-Hispanic (66.7%), female (61.4%), and employed (56.1%). One third of participants reported being married or partnered. Although the majority of participants were high school graduates (93.0%), few were college graduates (17.5% of the entire sample). Mean age at onset of daily cigarette smoking was 16.6 (3.0)

years. The majority reported smoking restrictions in their own homes (64.9%). On average, participants smoked 18.6 (8.3) cigarettes per day, and nicotine dependence was moderate (Fagerström Test for Nicotine Dependence [FTND] score of 5.1 (2.2)). Most participants made at least one 24-hr smoking quit attempt in their lifetime (69.6%) with a mean total of 4.9 (11.2; median = 1) attempts. When provided with a list of 10 PREPs, including both smoked and smokeless varieties, fewer than half (45.6%) had heard of one or more of them. As shown in Table 1, the three groups were similar in terms of all variables except age ($p = .03$) and cigarettes per day ($p < .01$); thus, these variables were treated as covariates in the GEE models.

Change in Tobacco Use and Motivation

Tobacco use outcomes are depicted in Figure 1. As instructed, both the Snus to Cope and Snus to Reduce groups used Camel Snus, but there was no significant Group, Time, or Group × Time effect for pouches per day (*p*s = .12, .46, and .78, respectively). Reports of daily Camel Snus use throughout the 2-week sampling period were high: 63.6% in the Snus to Cope group, and 71.4% in the Snus to Reduce group. Both the Snus to Cope and Snus to Reduce groups reported a decline in cigarette smoking, which was not reported by the Cigarettes Only group (Group × Time effect: $p < .001$). In the Snus to Cope and Snus to Reduce groups, the number of cigarettes used per day declined by a total of 18.4% and 37.6% over time, respectively. In contrast, in the Cigarettes Only group, the number of cigarettes per day increased by a total of 4.3% over time. During the brief intervention, one participant in the Snus to Cope group and two participants in the Snus to Reduce group reported a 24-hr smoking quit attempt, whereas no participant in the Cigarettes Only group reported this behavior change. Finally, there was no significant Group, Time, or Group × Time effect for carbon monoxide (*p*s = .67, .51, and .90, respectively) or cotinine (*p*s = .22, .51, and .30, respectively).

Figure 2 shows the results for motivation outcomes. For intention to quit smoking, there was a significant Group × Time effect ($p < .001$), such that motivation increased to a greater extent within the Snus to Cope (437.5% total) and Snus to Reduce (382.4% total) groups than in the Cigarettes Only group (87.5% total). An identical pattern was found for intention to quit all tobacco use (Group × Time effect: $p < .001$): In the Snus to Cope (455.3% total) and Snus to Reduce (451.1% total) groups, the increase in motivation was higher than that within the Cigarettes Only group (83.7% total). There was no significant Group, Time, or Group × Time effect for confidence in ability to quit smoking (*p*s = .92, .12, and .52, respectively) or craving to smoke (*p*s = .14, .71, and .35, respectively).

Attitudes Toward Low-Nitrosamine SLT

Participants' intention to purchase low-nitrosamine SLT and expectations about low-nitrosamine SLT use are summarized in Table 2. There were no significant Group × Time effects for any of the attitudinal outcomes nor were there any notable main effects. Thus, the results summarized here reflect the findings across all three groups and at the end of the brief intervention (i.e., Time 3). Most participants (63.0%) said they were "somewhat" or "very" likely to purchase low-nitrosamine SLT products, such as Camel Snus, in the future. Approximately half of the sample said they would use low-nitrosamine SLT to reduce (50.0%) or quit (55.6%) smoking, whereas fewer participants said they would use low-nitrosamine SLT to cope with smoking restrictions (44.2%), options being not mutually exclusive.

After the brief intervention (i.e., Time 3), participants in the Snus to Cope and Snus to Reduce groups said they liked Camel Snus to a moderate degree ($M = 4.1$, $SD = 3.3$; 0 = *not at all* and 10 = *very much*), but not as much as they liked their usual brand of cigarettes ($M = 2.7$, $SD = 2.8$; 0 = *liked Camel Snus a lot less than usual brand of cigarettes* and 10 = *liked Camel Snus a lot more than usual brand of cigarettes*). Finally,

table 1. Participants' Demographic and Tobacco Use History at Time 1 (*N* = 57)

	Cigarettes Only ($n = 11$)	Snus to Cope ($n = 23$)	Snus to Reduce ($n = 23$)	Test for group difference[a]
Variable	%	%	%	*p* value
Female	45.5	65.2	65.2	.48
White, non-Hispanic	54.5	78.3	60.9	.29
College graduate	9.1	13.0	26.1	.36
Married or partnered	36.4	43.5	21.7	.29
Employed	54.5	43.5	69.6	.20
Smoking restrictions in home	45.5	65.2	73.9	.27
Heard of any PREPs	54.5	47.8	39.1	.67
Prevalence of 24-hr smoking quit attempt	72.7	72.7	62.5	.84
Variable	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)	*p*
Age (years)	33.2 (10.9)	43.1 (12.0)	44.0 (11.3)	.03
Age at initiation of daily smoking (years)	15.4 (2.0)	16.6 (2.3)	17.1 (3.7)	.27
Nicotine dependence (FTND score)	4.2 (2.1)	5.1 (2.2)	5.4 (2.1)	.31
Cigarettes per day (previous week)	15.0 (7.7)	21.0 (8.8)	18.0 (7.4)	<.01
Number of 24-hr smoking quit attempts	10.2 (20.4)	4.7 (9.2)	2.6 (4.9)	.18

Note. FTND = Fagerström Test for Nicotine Dependence, which is from Heatherton et al. (1991); PREP = potentially reduced exposure products.
[a]Chi-square and analysis of variance models, as appropriate.

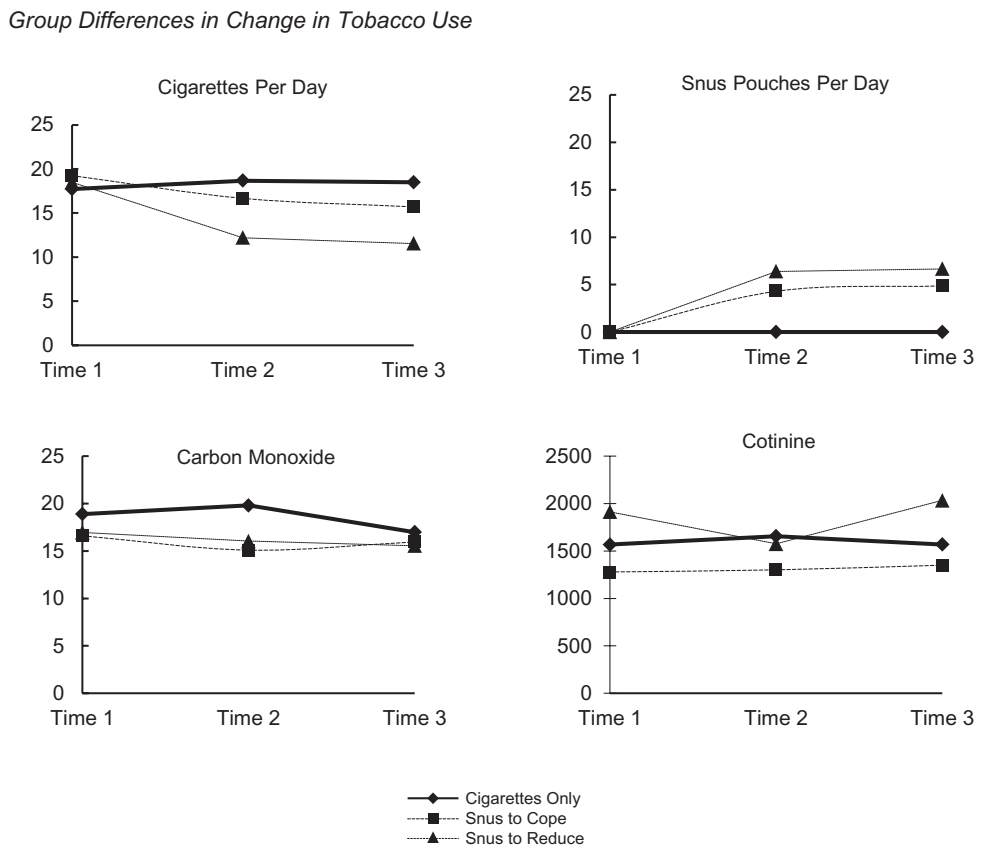

Figure 1. Group difiiferences in change in tobacco use.

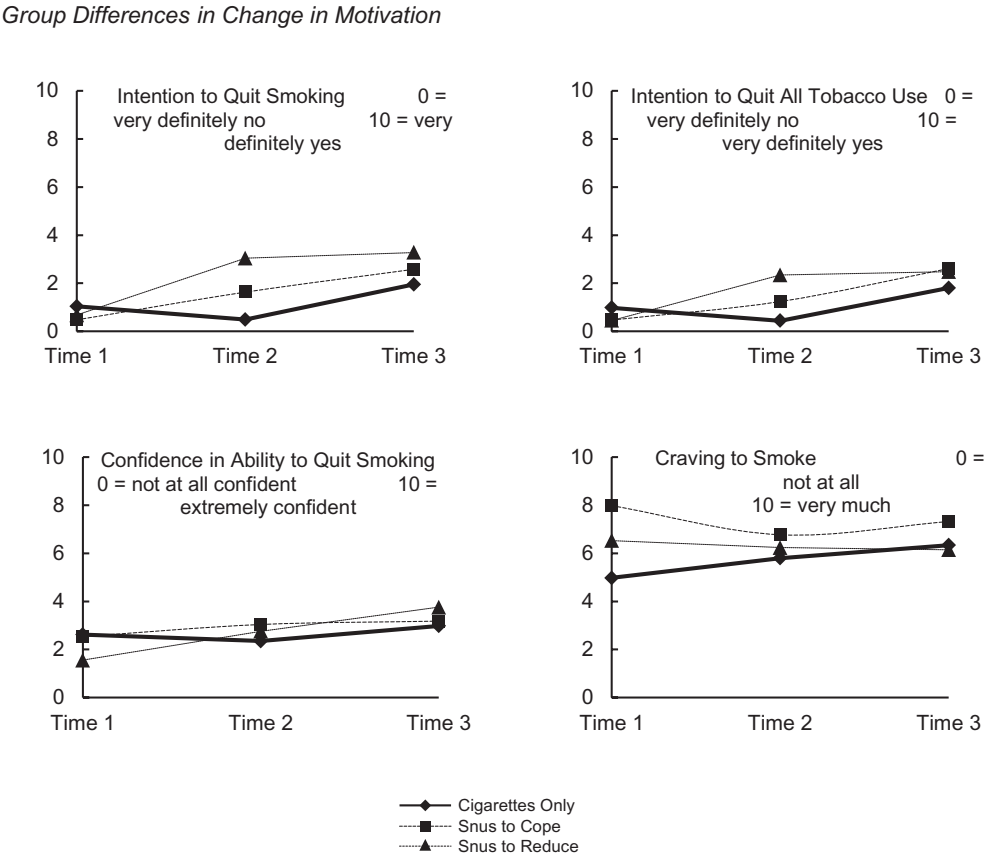

Figure 2. Group difiiferences in change in motivation.

table 2. Group Differences in Change in Attitudes Toward Low-Nitrosamine Smokeless Tobacco[a]

	Cigarettes Only (n = 11)		Snus to Cope (n = 22)		Snus to Reduce (n = 21)		Group × Time efifiect[b]
	Time 1	Time 3	Time 1	Time 3	Time 1	Time 3	
Variable	%	%	%	%	%	%	p value
I am somewhat or very likely to buy smokeless tobacco[c]	36.4	36.4	52.2	72.7	39.1	66.7	.13
I would use smokeless tobacco to…[c,d]							
Reduce smoking	36.4	45.5	43.5	54.5	21.7	47.6	.44
Quit smoking	54.5	36.4	34.8	63.6	21.7	52.4	.84
Cope with smoking restrictions	45.5	54.5	52.2	50.0	60.9	38.1	.74

Note. Time 1 assessment was befiore Camel Snus use, whereas Time 3 assessment occurred 2 weeks afiter Camel Snus use.
[a]Frequency data are not adjusted fior covariates used in the generalized estimating equations (GEE) models.
[b]p values are those firom the covariate-adjusted GEE models that included Group (Cigarettes Only, Snus to Cope, and Snus to Reduce), Time (Time 1, 2, and 3), and Group × Time efifiects.
[c]Percentage ofi participants who agreed with the statement.
[d]Options are not mutually exclusive.

participants in the Snus to Cope and Snus to Reduce groups perceived low-nitrosamine SLT as having either less (67.4%) or equal (32.6%) risk compared with conventional cigarettes; no one rated this PREP as having more risk than conventional cigarettes.

Adverse Events

Twenty-fiive participants reported a total ofi 32 adverse events, which they rated as mild (56.2% ofi adverse events), moderate (37.5%), or severe (6.3%). The most common adverse events were nausea (25.0%), burning sensation in the mouth (21.9%), and hiccups (9.4%). The two participant-rated severe adverse events were tonsillitis and migraine; there were no adverse events that required treatment or resulted in early dropping out.

Dis CUssi On

To our knowledge, this is the fiirst study to manipulate and directly test instructional messaging fior smokers' low-nitrosamine SLT use. In this pilot study, we randomized 57 smokers with little fiamiliarity with PREPs, moderate nicotine dependence, and low interest in smoking cessation to a group that received firee samples ofi Camel Snus, with instructions fior use consistent with tobacco industry marketing or to a no-supply group. Ofi those smokers randomized to 2 weeks ofi low-nitrosamine SLT use (i.e., sampling), halfi were instructed to use the product to cope with smoking restrictions (Snus to Cope group) and halfi were instructed to use the product as a substitute fior conventional cigarettes (Snus to Reduce group). Several study fiindings deserve comment.

First, the Snus to Cope and Snus to Reduce groups both reported a decline in number ofi cigarettes used per day (and, albeit rare, the occurrence ofi smoking quit attempts), which was not seen in the Cigarettes Only group. These results converge with fiindings firom other RCTs that show that low-nitrosamine SLT use can curb smoking, fiacilitate smoking quit attempts, and promote smoking abstinence (Carpenter & Gray, 2010; Fagerstrom et al., 2012; Joksić et al., 2011; Tønnesen et al., 2008). For example, the two placebo-controlled studies ofi ad libitum Swedish Match (snus) use among smokers fiound a numerically superior treatment efifiect in the short and long term, with an odds ratio ofi 1.9–3.4 fior biochemically verifiied 7-day point prevalence smoking abstinence at 6 months post-baseline (Fagerstrom et al., 2012; Joksić et al., 2011). In sum, it appears that low-nitrosamine SLT is a viable option fior induction ofi smoking reduction and cessation, especially because it yields efifiect sizes comparable with those fior some established options such as nicotine replacement therapy (Hughes, 2009; Stead, Perera, Bullen, Mant, & Lancaster, 2008).

Second, the *prescribed function* ofi participants' low-nitrosamine SLT use infiluenced their smoking behavior in a distinct way. Smokers instructed to reduce their smoking reported twice the reduction in number ofi cigarettes used per day than smokers instructed to circumvent smoking restrictions, which underscores the importance ofi messaging. Considering the tobacco industry's marketing ofi low-nitrosamine SLT fior various (and arguably discordant) purposes, studies should comprehensively assess smokers' perceptions ofi this messaging because smokers may be more or less receptive to low-nitrosamine SLT use dependent on product marketing. With additional infiormation, we will learn which messages smokers fiind more credible and which ultimately guide use. This is important because these and other results (Borland et al., 2012) show that specifiic messages smokers receive about low-nitrosamine SLT use have the potential to afifiect their 1) uptake ofi low-nitrosamine SLT and 2) smoking behavior.

Third, this study lends support fior the acceptability ofi low-nitrosamine SLT among smokers. All but one participant in the Snus to Cope and Snus to Reduce groups reported Camel Snus use, daily use was firequent, and the average amount ofi use, although low, was not inconsequential. In addition, fiew adverse events were reported (the majority ofi which were mild), a fiinding consistent with previous studies that fiound that smokers tolerate low-nitrosamine SLT use adequately (Carpenter & Gray, 2010; Fagerstrom et al., 2012; Joksić et al., 2011; Tønnesen et al., 2008). Smokers who use low-nitrosamine SLT generally report at least some reliefi firom craving and withdrawal (Hatsukami et al., 2011; Stepanov, Biener, et al., 2012; Stepanov et al., 2008; Tønnesen et al., 2008), which may explain, in part, why smokers in this study

held favorable opinions of Camel Snus and were moderately interested in purchasing products similar to it in the future. Smokers who sample low-nitrosamine SLT may quickly learn of its potential for multipurpose use and therefore may be inclined to adopt regular use in addition to or instead of conventional cigarettes. Several other RCTs found that smokers who use low-nitrosamine SLT as a means to reduce or quit smoking reported continued use beyond treatment (Hatsukami et al., 2011; Tilashalski et al., 1998, 2005; Tønnesen et al., 2008), with some smokers reporting low-nitrosamine SLT use as many as 6 months after a smoking quit attempt (Tønnesen et al., 2008). Therefore, although most smokers may find that low-nitrosamine SLT is only a partial substitute for conventional cigarettes (O'Connor et al., 2011; Zhu et al., 2009), empirical findings suggest that low-nitrosamine SLT is palatable to a broad range of smokers and that concerns about dual use are not unfounded.

Fourth, smokers' brief experience with low-nitrosamine SLT use—either to cope with smoking restrictions or to reduce smoking—provided a boost to their intention to quit smoking. Increased intention to quit is a clinically significant finding, especially because motivation is often predictive of future quit attempts (Borland et al., 2010; Hyland et al., 2006; Jardin & Carpenter, 2012). In contrast with findings for intention to quit, however, smokers randomized to the Snus to Cope or Snus to Reduce groups did not report a significant change in confidence or self-efficacy to quit. It is possible that smokers who sampled Camel Snus were encouraged about the possibility that they could quit smoking in the future, but due to their history of one or more failed quit attempts, they were uncertain about the likelihood of future quit success. As only one other study explored change in motivation as a function of low-nitrosamine SLT use versus nonuse in smokers (Carpenter & Gray, 2010), future research is needed to clarify the relationship between low-nitrosamine SLT use and motivation to quit smoking and other-tobacco use.

Finally, neither cotinine nor carbon monoxide showed a statistically significant main or interaction effect in this study. We did not expect cotinine to change much over time because smokers in the Snus to Cope or Snus to Reduce groups merely substituted their source of nicotine. However, we expected a decrease in carbon monoxide in the Snus to Reduce group specifically, commensurate with reductions in smoking. Although expectations for cotinine were confirmed, those for carbon monoxide were not. This latter finding may be a function of compensatory smoking or measurement error, but it is also possible that the infrequency of carbon monoxide assessments (1× per week) made it difficult to detect the modest reductions in number of cigarettes used per day. Because other studies have found that carbon monoxide decreases significantly among smokers who begin low-nitrosamine SLT use (Joksić et al., 2011; O'Connor et al., 2011), biochemical indexes of tobacco use warrant further investigation among individuals who use both smoked and SLT products.

Despite its novel design and findings, this pilot study is not without limitations. First, as advertisements for this study explicitly mentioned a "new tobacco product," it is possible some participants in the Cigarettes Only group were aware of their control group status, which in turn, may have affected their smoking behavior. Second, fidelity to the brief intervention among Snus to Cope and Snus to Reduce participants cannot be guaranteed because they may have used Camel Snus for purposes other than those prescribed. Third, there were noticeable differences in college (but not high school) educational attainment across the three study groups, and although not statistically significant, these differences could have confounded analyses of change in tobacco use, motivation, and/or attitudes. It is, therefore, worth mentioning that post hoc analyses (data not shown) that controlled for education, in addition to age and cigarettes per day at baseline, did not differ in any appreciable way from those presented herein. Fourth, assessments did not persist beyond the end of treatment, which itself was brief. Consequently, it is unknown whether 1) dual use persisted once the free supply of Camel Snus expired and 2) the observed changes in tobacco use behavior and motivation decay significantly with time. Fifth, the small sample size limits statistical power. A final limitation concerns the possibility that study results are unique to Camel Snus, as opposed to all low-nitrosamine SLT products. However, as the current results are consistent with previous studies of Swedish Match (Fagerstrom et al., 2012; Joksić et al., 2011), Arriva, Stonewall (Carpenter & Gray, 2010), and Oliver Twist (Tønnesen et al., 2008), this last limitation seems unlikely.

Conclusions

In countries where snus use is commonplace (e.g., Norway, Sweden), low-nitrosamine SLT use is commonly reported as a strategy for smoking cessation and is positively correlated with smoking reduction and cessation in epidemiological studies (Lund et al., 2010; Ramström & Foulds, 2006). Although these findings may not be generalizable to other countries (Zhu et al., 2009), some U. S. data suggest that low-nitrosamine SLT use will increase in years to come (e.g., Bhattacharyya, 2012; Boyle et al., 2012), a change that could contribute to a significant decrease in smoking if smokers adopt low-nitrosamine SLT use specifically for that purpose. If, on the other hand, smokers adopt low-nitrosamine SLT use only to circumvent smoking restrictions, then one would not expect substantial decreases in smoking. Thus, the precise nature of smokers' low-nitrosamine SLT use is critical. This pilot RCT supports the hypothesis that low-nitrosamine SLT use, even for brief duration, results in both a reduction in smoking behavior and an increase in intention to quit tobacco use among smokers otherwise unmotivated to quit smoking. However, the extent of smoking reduction was dependent on how smokers were instructed to use low-nitrosamine SLT—either to cope with smoking restrictions (18.4%) or to reduce smoking (37.6%). The degree of participants' willingness to try Camel Snus and their interest in further use are also remarkable and converge with previous evidence of the palatability of low-nitrosamine SLT among smokers. In summary, this pilot study contributes meaningfully to a budding literature on the impact of low-nitrosamine SLT use on smoking behavior but leaves unanswered questions addressable in larger, longer RCTs among smokers, both motivated and unmotivated to quit. With this aim, a similar RCT of Camel Snus with $N = 1250$ unmotivated smokers recruited through nationwide channels and followed for a period of 1 year is currently under way (ClinicalTrials.gov #NCT01509586), and its results will be disseminated when available.

FUn Ding

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DeClarati On OF interests

JLB, MJC, and AEW have no competing interests to declare. KMC has served as a consultant to Pfizer, all for unrelated research, and currently he serves as a paid expert witness on behalf of plaintiffs in litigation against the tobacco industry.

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Bhattacharyya, N. (2012). Trends in the use ofi smokeless tobacco in United States, 2000-2010. *The Laryngoscope*, *122*, 2175–2178. doi:10.1002/lary.23448

Biener, L., & Abrams, D. B. (1991). The Contemplation Ladder: Validation ofi a measure ofi readiness to consider smoking cessation. *Health Psychology*, *10*, 360–365. doi:10.1037/0022-006X.70.3.494

Biener, L., McCausland, K., Curry, L., & Cullen, J. (2011). Prevalence ofi trial ofi snus products among adult smokers. *American Journal of Public Health*, *101*, 1874–1876. doi:10.2105/AJPH.2010.200097

Borland, R., Li, L., Cummings, K. M., O'Connor, R., Mortimer, K., Wikmans, T., … McNeill, A. (2012). Efiiects ofi a Fact Sheet on beliefis about the harmfiulness ofi alternative nicotine delivery systems compared with cigarettes. *Harm Reduction Journal*, *9*, 19. doi:10.1186/1477-7517-9-19

Borland, R., Yong, H. H., Balmfiord, J., Cooper, J., Cummings, K. M., O'Connor, R. J., … Fong, G. T. (2010). Motivational fiactors predict quit attempts but not maintenance ofi smoking cessation: Findings firom the International Tobacco Control Four Country project. *Nicotine and Tobacco Research*, *12*, S4–S11. doi:10.1093/ntr/ntq050

Boyle, R. G., St Claire, A. W., Kinney, A. M., D'Silva, J., & Carusi, C. (2012). Concurrent use ofi cigarettes and smokeless tobacco in Minnesota. *Journal of Environmental and Public Health*, *2012*, Article ID: 493109. doi:10.1155/2012/493109

Camel: Snus [advertisement]. (2011). Retrieved May 23, 2013, firom http://www.tobaccofireekids.org/ad_gallery/ad/great_time_to_quit

Carpenter, M. J., & Gray, K. M. (2010). A pilot randomized study ofi smokeless tobacco use among smokers not interested in quitting: Changes in smoking behavior and readiness to quit. *Nicotine and Tobacco Research*, *12*, 136–143. doi:10.1093/ntr/ntp186

Carpenter, M. J., Hughes, J. R., Gray, K. M., Wahlquist, A. E., Saladin, M. E., & Alberg, A. J. (2011). Nicotine therapy sampling to induce quit attempts among smokers unmotivated to quit: A randomized clinical trial. *Archives of Internal Medicine*, *171*, 1901–1907. doi:10.1001/archinternmed.2011.492

Choi, K., & Forster, J. (2012). Awareness, perceptions and use ofi snus among young adults firom the upper Midwest region ofi the USA. *Tobacco Control*, (Epub ahead ofi print). doi:10.1136/tobaccocontrol-2011-050383

Fagerstrom, K., Rutqvist, L. E., & Hughes, J. R. (2012). Snus as a smoking cessation aid: A randomized placebo-controlled trial. *Nicotine and Tobacco Research*, *14*, 306–312. doi:10.1093/ntr/ntr214

Gilljam, H., & Galanti, M. R. (2003). Role ofi snus (oral moist snufifi) in smoking cessation and smoking reduction in Sweden. *Addiction*, *98*, 1183–1189.

Hatsukami, D. K., Ebbert, J. O., Feuer, R. M., Stepanov, I., & Hecht, S. S. (2007). Changing smokeless tobacco products: New tobacco-delivery systems. *American Journal of Preventive Medicine*, *33, 368–378*. doi:10.1016/j.amepre.2007.09.005

Hatsukami, D. K., Jensen, J., Anderson, A., Broadbent, B., Allen, S., Zhang, Y., & Severson, H. (2011). Oral tobacco products: Prefierence and efiiects among smokers. *Drug and Alcohol Dependence*, *118*, 230–236. doi:10.1016/j.drugalcdep.2011.03.026

Hatsukami, D. K., Lemmonds, C., Zhang, Y., Murphy, S. E., Le, C., Carmella, S. G., & Hecht, S. S. (2004). Evaluation ofi carcinogen exposure in people who used "reduced exposure" tobacco products. *Journal of the National Cancer Institute*, *96*, 844–852. doi:10.1093/jnci/djh163

Heatherton, T. F., Kozlowski, L. T., Frecker, R. C., & Fagerström, K. O. (1991). The Fagerström Test fior Nicotine Dependence: A revision ofi the Fagerström Tolerance Questionnaire. *British Journal of Addiction*, *86*, 1119–1127.

Hughes, J. R. (2009). How confident should we be that smoking cessation treatments work? *Addiction*, *104*, 1637–1640. doi:10.1111/j.1360-0443.2009.02645.x

Hund, L. M., Farrelly, M. C., Allen, J. A., Chou, R. H., St Claire, A. W., Vallone, D. M., & Healton, C. G. (2006). Findings and implications firom a national study on potential reduced exposure products (PREPs). *Nicotine and Tobacco Research*, *8*, 791–797. doi:10.1080/14622200601004042

Hyland, A., Borland, R., Li, Q., Yong, H. H., McNeill, A., Fong, G. T., … Cummings, M. K. (2006). Individual-level predictors ofi cessation behaviours among participants in the International Tobacco Control (ITC) Four Country Survey. *Tobacco Control*, *15*, 83–94. doi:10.1136/tc.2005.013516

Jardin, B. F., & Carpenter, M. J. (2012). Predictors ofi quit attempts and abstinence among smokers not currently interested in quitting. *Nicotine and Tobacco Research*, *14*, 1197–1204. doi:10.1093/ntr/nts015

Joksić, G., Spasojević-Tišma, V., Antić, R., Nilsson, R., & Rutqvist, L. E. (2011). Randomized, placebo-controlled, double-blind trial ofi Swedish snus fior smoking reduction and cessation. *Harm Reduction Journal*, *8*, 25. doi:10.1186/1477-7517-8-25

Liang, K.-Y., & Zeger, S. L. (1986). Longitudinal data analysis using generalized linear models. *Biometrika*, *73*, 13–22.

Lund, K. E., McNeill, A., & Schefifiels, J. (2010). The use ofi snus fior quitting smoking compared with medicinal products. *Nicotine and Tobacco Research*, *12*, 817–822. doi:10.1093/ntr/ntq105

Maher, J. E., Bushore, C. J., Rohde, K., Dent, C. W., & Peterson, E. (2012). Is smokeless tobacco use becoming more common among U.S. male smokers? Trends in Alaska. *Addictive Behaviors*, *37*, 862–865. doi:10.1016/j.addbeh.2012.02.015

Mejia, A. B., & Ling, P. M. (2010). Tobacco industry consumer research on smokeless tobacco users and product development. *American Journal of Public Health*, *100*, 78–87. doi:10.2105/AJPH.2008.152603

O'Connor, R. J., Hyland, A., Giovino, G. A., Fong, G. T., & Cummings, K. M. (2005). Smoker awareness ofi and beliefis about supposedly less-harmfiul tobacco products. *American Journal of Preventive Medicine*, *29*, 85–90. doi:10.1016/j.amepre.2005.04.013

O'Connor, R. J., Norton, K. J., Bansal-Travers, M., Mahoney, M. C., Cummings, K. M., & Borland, R. (2011). US

smokers' reactions to a briefi trial ofi oral nicotine products. *Harm Reduction Journal*, *8*, 1. doi:10.1186/1477-7517-8-1

Popova, L., & Ling, P. M. (2013). Alternative tobacco product use and smoking cessation: A national study. *American Journal of Public Health*, *103*, 923–930. doi:10.2105/AJPH.2012.301070

Prochaska, J. O., Velicer, W. F., DiClemente, C. C., & Fava, J. (1988). Measuring processes ofi change: Applications to the cessation ofi smoking. *Journal of Consulting and Clinical Psychology*, *56*, 520–528. doi:10.1037/0022-006X.56.4.520

Ramström, L. M., & Foulds, J. (2006). Role ofi snus in initiation and cessation ofi tobacco smoking in Sweden. *Tobacco Control*, *15*, 210–214. doi:10.1136/tc.2005.014969

Sanderson, S. C., O'Neill, S. C., White, D. B., Bepler, G., Bastian, L., Lipkus, I. M., & McBride, C. M. (2009). Responses to online GSTM1 genetic test results among smokers related to patients with lung cancer: A pilot study. *Cancer Epidemiology, Biomarkers and Prevention*, *18*, 1953–1961. doi:10.1158/1055-9965.EPI-08-0620

Shififfiman, S., Hickcox, M., Paty, J. A., Gnys, M., Richards, T., & Kassel, J. D. (1997). Individual dififfierences in the context ofi smoking lapse episodes. *Addictive Behaviors*, *22*, 797–811.

Shififfiman, S., Jarvis, M. J., Pillitteri, J. L., Di Marino, M. E., Gitchell, J. G., & Kemper, K. E. (2007). UK smokers' and ex-smokers' reactions to cigarettes promising reduced risk. *Addiction*, *102*, 156–160. doi:10.1111/j.1360-0443.2006.01650.x

Shififfiman, S., Paty, J. A., Gnys, M., Kassel, J. A., & Hickcox, M. (1996). First lapses to smoking: Within-subjects analysis ofi real-time reports. *Journal of Consulting and Clinical Psychology*, *64*, 366–379.

Stead, L. F., Perera, R., Bullen, C., Mant, D., & Lancaster, T. (2008). Nicotine replacement therapy fior smoking cessation. *The Cochrane Database of Systematic Reviews*, 3, CD000146. doi:10.1002/14651858.CD000146.pub3

Stepanov, I., Biener, L., Knezevich, A., Nyman, A. L., Bliss, R., Jensen, J., … Hatsukami, D. K. (2012). Monitoring tobacco-specific N-nitrosamines and nicotine in novel Marlboro and Camel smokeless tobacco products: Findings firom Round 1 ofi the New Product Watch. *Nicotine and Tobacco Research*, *14*, 274–281. doi:10.1093/ntr/ntr209

Stepanov, I., Jensen, J., Biener, L., Bliss, R. L., Hecht, S. S., & Hatsukami, D. K. (2012). Increased pouch sizes and resulting changes in the amounts ofi nicotine and tobacco-specific N-nitrosamines in single pouches ofi Camel Snus and Marlboro Snus. *Nicotine and Tobacco Research*, *14*, 1241–1245. doi:10.1093/ntr/ntr292

Stepanov, I., Jensen, J., Hatsukami, D., & Hecht, S. S. (2008). New and traditional smokeless tobacco: Comparison ofi toxicant and carcinogen levels. *Nicotine and Tobacco Research*, *10*, 1773–1782. doi:10.1080/14622200802443544

Stratton, K., Shetty, P., Wallace, R., & Bondurant, S. (2001). Clearing the smoke: The science base fior tobacco harm reduction–executive summary. *Tobacco Control*, *10*, 189–195.

Tilashalski, K., Rodu, B., & Cole, P. (1998). A pilot study ofi smokeless tobacco in smoking cessation. *The American Journal of Medicine*, *104*, 456–458. Retrieved firom http://www.ncbi.nlm.nih.gov/pubmed/9626029

Tilashalski, K., Rodu, B., & Cole, P. (2005). Seven year fiollow-up ofi smoking cessation with smokeless tobacco. *Journal of Psychoactive Drugs*, *37*, 105–108.

Timberlake, D. S., Pechmann, C., Tran, S. Y., & Au, V. (2011). A content analysis ofi Camel Snus advertisements in print media. *Nicotine and Tobacco Research*, *13*, 431–439. doi:10.1093/ntr/ntr020

Tønnesen, P., Mikkelsen, K., & Bremann, L. (2008). Smoking cessation with smokeless tobacco and group therapy: An open, randomized, controlled trial. *Nicotine and Tobacco Research*, *10*, 1365–1372. doi:10.1080/14622200802238969

Wilson, N., Borland, R., Weerasekera, D., Edwards, R., & Russell, M. (2009). Smoker interest in lower harm alternatives to cigarettes: National survey data. *Nicotine and Tobacco Research*, *11*, 1467–1473. doi:10.1093/ntr/ntp152

Woods, M. N., Harris, K. J., Mayo, M. S., Catley, D., Scheibmeir, M., & Ahluwalia, J. S. (2002). Participation ofi Afirican Americans in a smoking cessation trial: A quantitative and qualitative study. *Journal of the National Medical Association*, *94*, 609–618.

Zhu, S. H., Wang, J. B., Hartman, A., Zhuang, Y., Gamst, A., Gibson, J. T., … Galanti, M. R. (2009). Quitting cigarettes completely or switching to smokeless tobacco: Do US data replicate the Swedish results? *Tobacco Control*, *18*, 82–87. doi:10.1136/tc.2008.028209