Original Investigation

Can the Public Be Educated About Constituents in Smokeless Tobacco? A Three-Wave Randomized Controlled Trial

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Abstract

Introduction: The U.S. Food and Drug Administration (FDA) is required by law to inform the public about levels of harmful and potentially harmful tobacco constituents in a format that is “understandable and not misleading to a lay person.” Our study addresses a critical gap in research on communicating such information for smokeless tobacco (SLT) products.

Methods: The design included random assignment to one of the experimental (online interactive) conditions differing in presentation format or a control condition (receiving no information). Experimental respondents viewed information on levels and health risks of 5 harmful constituents in up to 79 products. Outcome measures included knowledge of health risks of constituents, perception of constituent variability in SLT products, disease risk ratings, self-reported SLT use, and side-by-side product comparisons. The sample of 333 SLT users, 535 cigarette smokers, and 663 nontobacco users participated at baseline, time of intervention, and 6 weeks postintervention.

Results: Presentation formats showed few systematic differences so were combined in analyses. Experimental condition respondents increased their knowledge about constituent health effects and their perceptions of constituent variability in SLT products, from baseline to postintervention, and relative to the control condition. Changes in respondents’ ratings of disease risk and their estimates of constituent exposure from specific products were observed, but not in self-reported SLT use.

Conclusions: Interactive online graphic and numeric presentation formats can be efficient in increasing people’s knowledge of health effects and perceived variation of constituents in SLT products. Further research on longer-term behavioral assessment, and usefulness of this approach for regulatory agencies, is needed.

Implications: Research on communicating the information about harmful constituents in SLT products to lay persons is critically lacking. This study proposes novel formats for effective communication about the levels and the health effects of SLT constituents to multiple user groups. The lack of misperceptions among study participants that some tobacco products are safe suggests

that such formats can potentially be used for public display of SLT constituent data by the FDA and regulatory agencies in other countries.

Introduction

In the United States, disclosure of levels of harmful and potentially harmful constituents (HPHCs) in tobacco products by brand and subbrand is required by Section 904(d)(1) of the Federal Food, Drug, and Cosmetic Act of 2009. Yet, nearly a decade later, the public is still uninformed about the health effects of individual constituents in tobacco products, and the levels of HPHC in various product types and individual subbrands.¹ This is due, at least in part, to the lack of established and effective approaches to communicating this information to the general public in an understandable and not misleading format. The need for such approaches is evident from the existing research that shows that consumers lack rudimentary knowledge about the constituents in tobacco products and their levels and the types of risks associated with each constituent.^{2–6} Even public health experts are not always informed about the relative harms across tobacco products or which constituents contribute to disease risk.⁷ In addition, past experience with marketing “light” cigarettes showed that lower machine-generated yields of nicotine and other harmful constituents in such cigarettes were misperceived as indicators of relative safety^{8,9}; however, these cigarettes did not reduce smokers’ exposure to tobacco carcinogens and did not lower the risk of smoking-induced diseases.^{10–12}

Research on communication of tobacco constituent data to the general public is relatively limited generally, and particularly scarce for smokeless tobacco (SLT) products. This is an important gap in knowledge because SLT differs from cigarettes in design, mode of administration, number of constituents, and health effects, all of which may result in unique challenges related to consumer understanding and perceptions of harmful constituents in these products. In addition, levels of key harmful constituents such as N'-nitrosonornicotine (NNN), 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), and benzo[a]pyrene (BaP) can vary substantially across SLT product types and brands,^{13–15} and biomarker-based studies show that higher levels of these constituents lead to higher exposures in users^{15,16} and potentially higher risk for developing certain forms of cancer.^{17–19} Lastly, SLT products are used by an estimated 300 million people worldwide in over 70 countries,^{13,16} and products with extremely high levels of NNN and NNK marketed in some countries, such as Southeast Asia, are clearly associated with oral cancer and other devastating health outcomes.^{13,20} Therefore, development of effective communication strategies for SLT products can inform not only the U.S. Food and Drug Administration (FDA) but also international research community and regulatory bodies such as the World Health Organization (WHO) in their efforts to reduce the death toll associated with the use of some SLT products.

In this study, we carried out a randomized trial to investigate the effectiveness of various presentation formats communicating information on the levels of harmful constituents in SLT products, with the particular focus on how best to convey this information in an accessible form, and without misleading users and nonusers that SLT products with lower levels of harmful constituents are safe.^{7,21} The presentation formats were developed for NNN, NNK, BaP, cadmium, and nicotine. These constituents are included in the FDA list for priority reporting by the manufacturers^{14,15,22} and have been identified by WHO as targets for reduction.²³ In the development of presentation formats for this study, we used actual constituent data for

US-manufactured SLT products that were generated in our laboratory. Numerical and graphical formats have been compared in past research, with findings favoring graphical displays for conveying complex information to general audiences.²⁴ Graphic information may be more easily and quickly understood.²⁵ Numeric information, by contrast, may encourage more thoughtfulness, since numbers may be perceived as more scientific or precise. Hence, both graphic and numeric displays are included in our research.

Materials and Methods

Respondent Recruitment

Research respondents (from the United States) were recruited from Survey Sampling International (SSI)’s large opt-in internet panel to participate in a three-wave longitudinal study, including a baseline measurement (Time 1), experimental intervention or control 2 weeks later (Time 2), and postintervention measurement, 6 weeks following the intervention (Time 3). Respondents who met quota guidelines at baseline (with respect to gender, age, and current tobacco use behavior) were approximately representative of US Census-based proportions of gender and age within three usage subpopulations in the United States (SLT users, cigarette smokers, and nontobacco users), who were English-speaking, and who agreed to participate in the multiwave study, were invited to participate in all of the study’s later waves. Only those respondents who completed measures in the former time period were recruited for the next time period. SSI screened for Internet Protocol address duplicates, identified extreme responses, and terminated follow-ups when sample quotas were met. The final sample, who completed all three waves, were 1531 respondents, including 333 SLT users, 535 cigarette smokers, and 663 nonusers. Attrition rates at postintervention were higher for SLT users (53%) and cigarette smokers (44%) than for nonusers (24%), but importantly, did not vary by user assignment to intervention or control condition (attrition rates of intervention vs. control: SLT users: 53% vs. 52%; cigarette smokers: 44% vs. 43%; nonusers: 23% vs. 26%). See [Figure 1](#) and [Supplement S1](#), available at *Nicotine and Tobacco Research* online for a summary of the study design, sample characteristics, and attrition data.

Experimental Chart Formats

We employed four constituent chart formats ([Supplement S2a](#), available at *Nicotine and Tobacco Research* online), which included either color-graphs, numerical levels, both graphs and numbers, or an alternative horizontal version with both graphs and numbers. (Actual brand logos with original brand names on packages, are available upon request from the authors.) Best practices were used for developing graphic and numeric charts,¹⁹ making them comparable in overall persuasiveness and credibility. These methods, and the approach to convert the measured levels of constituents to a color-coded scale for the graphic formats, are described in [Supplements S2b and c](#), available at *Nicotine and Tobacco Research* online. For NNN, NNK, and nicotine levels, we used data for 79 moist snuff products analyzed in our laboratory by our routine methods,^{26,27} while the variation of BaP and Cd levels across these products was estimated based on our previous work and other published reports.^{14,28} The 79 products included in the presentation format development included 13 brands (eg Skoal,

Figure 1. Experimental procedures, constituent health effects, and measurements for each time period.

Grizzly, Copenhagen, Camel Snus, etc.) each being represented by several subbrands (eg such varieties as long cut, fine cut, snuff, pouches, or loose form, and flavors such as robust, mint, wintergreen, etc.).

Experimental Procedure

At the experimental intervention (Time 2), respondents were randomly assigned (by computer) to one of five conditions, including four experimental chart format conditions and one no-intervention control condition. Respondents in each of the four experimental conditions were first shown a table containing information about the health effects of the five constituents, as a way to introduce them to the reason behind the inclusion of these constituents in reporting (Supplement S3, available at *Nicotine and Tobacco Research* online). After viewing this information, respondents viewed their assigned graphic and/or numeric format in which up to five individual SLT products could be displayed (Supplement S2a, available at *Nicotine and Tobacco Research* online). A comparison to medicinal nicotine was always included. Respondents were instructed online as to how to add or remove products from the chart, using a drop-down menu that contained all 79 SLT products. When the respondent's mouse hovered over any of the individual constituents, the health effects information for that constituent appeared again, ensuring that respondents could easily access the disease risk information while reviewing constituent exposure data. A statement at the bottom of the chart read: "Warning: No tobacco product is safe. Even lower levels are not safe!" Respondents were told

to spend as much time as they needed to examine their selected products, after which they completed survey measures. Respondents in the control condition completed survey measures only; they did not view chart or constituent information (Figure 1).

Measurements

At each time period, measures included respondents' (1) knowledge of health risks associated with individual constituents, (2) perceptions that constituent exposure varies across SLT products, (3) ratings of their own disease risk, and (4) self-reported tobacco usage. Knowledge was a composite score of the 20 scale items. For each of the five constituents (BaP, Cd, NNN, NNK, and nicotine), respondents indicated whether they thought it was true (yes/no/don't know) that the constituent contributed to four established health consequences (addiction, cancer, respiratory diseases, or reproductive and/or developmental problems). Each item was coded as 1 for correct (ie a correct link between the constituent and the health effect) or 0 for not correct (ie an incorrect link or don't know response), and then summed for a total knowledge score ranging from 0 to 20. At the experimental intervention (Time 2) stage, but not baseline (Time 1) or postintervention (Time 3), respondents in the experimental, but not control, conditions had the opportunity to interact with their assigned chart in order to answer the questions about constituent health risks. That is, knowledge measures at Time 2 did not require respondents to recall the information from memory (the chart was available for them to peruse). This intervention assessment is a realistic analysis

of how people might actually use online constituent charts to learn about the different SLT products, and to learn about the health effects associated with each constituent. The postintervention assessment, by contrast, measured knowledge retention, and therefore was compared to baseline in subsequent analyses.

Perceptions of the degree to which different SLT products vary in their levels of each of the five constituents was measured on a seven-point scale ranging from “vary not at all” to “vary greatly.” These five responses were averaged to form a composite index at each time period (all α s > .93). Next, respondents were asked to rate their disease risk, that is their vulnerability to getting each health outcome (cancer, respiratory, and reproductive/developmental) sometime in their lifetime if they were to use SLT, on scales ranging from 1 (disagree) to 7 (agree). Scores were averaged across diseases (all α s > .78). The same disease risk questions were asked for cigarettes and medicinal nicotine products, again averaged across diseases.

SLT use was measured by asking all respondents whether (yes/no) they had “used any of these *smokeless tobacco products* in the past 30 days (chewing tobacco, snuff, snus, or dipping tobacco).” Brand switching was measured by asking SLT users whether (yes/no) they had “tried new brands of smokeless tobacco products since participating in this study.”

Finally, at the time of intervention (Time 2) respondents made side-by-side SLT product comparisons (illustrations in [Supplement S7a](#), available at *Nicotine and Tobacco Research* online) that listed levels of each constituent for each of two pairs of products (and levels for medicinal nicotine were also included). In the first comparison, Grizzly Fine Cut was compared to Copenhagen Long Cut, and in the second, Kodiak Moist Snuff was compared to Husky Long Cut. Each comparison was designed to include a product with somewhat *higher* levels of constituents (Grizzly or Kodiak), and one with *lower* levels (Copenhagen or Husky). Respondents were asked to estimate the level of constituent exposure resulting from the use of each product, using seven-point scales ranging from “no chemical exposure” to “a great deal of chemical exposure.”

The potential impact of constituent communication on the misperception of safety of SLT products was assessed by examining whether respondents in experimental conditions (1) decreased their disease risk ratings of SLT overall, relative to controls, at Times 2–3, (2) decreased their disease risk ratings from baseline to Times 2–3, and (3) estimated constituent exposure levels from individual products (especially, Copenhagen or Husky) as low in “chemical exposure.” Decreased rates of self-reported SLT cessation, or increased brand switching, among experimental respondents, might also signal potential misperceptions.

Statistical Analyses

Only those respondents who provided responses at all three time periods were included in statistical analyses, and ineligible responses (eg responses of never having smoked cigarettes in one survey item but reporting being a regular smoker later in the same survey; those whose time to complete Time 2 was more than 3 standard deviations above the mean) were excluded. Analyses revealed very few systematic differences between the four types of formats (graphic, numeric, graphic + numeric, horizontal graphic + numeric); therefore, comparisons reported here combine the data for the four formats, referred to as experimental conditions.

To test effects of our experimental intervention on each of three major outcome measures (knowledge, perceptions of constituent variability, and disease risk ratings), we first fitted an overall 2

(condition: experimental, control) $\times$ 3 (time period: baseline, intervention, postintervention) $\times$ 3 (user group: SLT users, cigarette smokers, nonusers) mixed model with respondents’ age, ethnicity, income, and gender being included as statistical control variables. For each outcome measure the model’s chi-square fit was significant ($ps < .05$), and thus post hoc mean comparisons using t tests were performed. Next, for each outcome measure, we performed analyses comparing user group responses as a result of the experimental intervention, including only experimental conditions. We fitted a 3 (time period: baseline, intervention, postintervention) $\times$ 3 (user group: SLT users, cigarette smokers, nonusers) mixed model, with age, ethnicity, income, and gender as control variables. Again, for each outcome measure the model’s chi-square fit was significant ($ps < .05$) and followed by post hoc mean comparisons. Analysis of side-by-side SLT product comparisons used the same models, but without the time factor (all responses to the side-by-side comparisons were at Time 2) and with F tests. Analyses were performed using STATA/SE version 14 by STATACorp LLC, with a priori level of significance set at $p < .05$, all tests two-sided, all variances set to be equal, and all covariances set at zero. Finally, two attention check measures were collected at each of Times 1 and 2. Results were not substantively changed when these checks were used as covariates in our model (complete data analysis available upon request to authors) and therefore no respondents were eliminated on this basis.

Results

Study findings are summarized in [Tables 1–3](#), with additional statistics (including analyses of all five experimental and control conditions) provided in [Supplements S4–7](#), available at *Nicotine and Tobacco Research* online.

Knowledge of Health Consequences of Constituents in SLT

Results for knowledge of constituent health consequences are summarized in [Table 1](#) and [Supplement S4](#), available at *Nicotine and Tobacco Research* online. Post hoc mean contrasts show no differences in respondents’ knowledge scores between experimental and control conditions at baseline, and no changes occurred over time in the control condition ([Table 1](#)). Respondents in experimental conditions showed greater knowledge than those in the control condition at Time 2 ($\Delta M_{\text{experimental-control}} = 4.61$, 95% confidence interval [CI: 4.06, 5.15]) and Time 3 ($\Delta M_{\text{experimental-control}} = .79$, 95% CI [0.26, 1.33]). Further, respondents in experimental conditions showed increases in their knowledge over time both at Time 2 ($\Delta M_{\text{Time2-Time1}} = 5.35$, 95% CI [5.04, 5.65]) and Time 3 ($\Delta M_{\text{Time3-Time1}} = 1.54$, 95% CI [1.25, 1.83]), relative to baseline.

Results by user group in the experimental condition revealed that, SLT users had higher knowledge scores than cigarette smokers or nonusers at baseline ($\Delta M_{\text{SLT-users-cigarette smokers}} = .84$, 95% CI [0.16, 1.53]; $\Delta M_{\text{SLT-users-nonusers}} = 1.29$, 95% CI [0.61, 1.96]), but all three user groups displayed the same level of knowledge at Time 2 ([Table 1](#)). At Time 3, SLT users again had higher knowledge scores than nonusers ($\Delta M_{\text{SLT-users-nonusers}} = 1.04$, 95% CI [0.36, 1.71]). All three user groups gained knowledge over time both at Time 2 (SLT users: $\Delta M_{\text{Time2-Time1}} = 4.54$, 95% CI [3.86, 5.22]; cigarette smokers: $\Delta M_{\text{Time2-Time1}} = 5.31$, 95% CI [4.77, 5.86]; nonusers: $\Delta M_{\text{Time2-Time1}} = 6.21$, 95% CI [5.72, 6.70]) and Time 3 (SLT users: $\Delta M_{\text{Time3-Time1}} = 1.39$, 95% CI [0.74, 2.03]; cigarette smokers:

Table 1. Scores for Knowledge of Health Consequences from SLT Constituents at the Three Time Periods^a

	Time 1	Time 2	Time 3	Time 2 vs. Time 1	Time 3 vs. Time 1
Comparisons by experimental conditions (overall model fit χ^2 (21) = 1613.99, $p < .001$)					
Experimental	4.73 (0.13) ^b	10.08 (0.13)	6.27 (0.13)	5.35 [5.04, 5.65] $p < .001$	1.54 [1.25, 1.83] $p < .001$
Control	4.94 (0.24)	5.47 (0.24)	5.47 (0.24)	0.53 [-0.04, 1.09] $p = .067$	0.53 [-0.03, 1.09] $p = .064$
Experimental vs. Control	-0.21 [-0.75, 0.32] ^c $p = .425$	4.61 [4.06, 5.15] $p < .001$	0.79 [0.26, 1.33] $p = .004$		
Comparisons by user groups ^d (overall model fit χ^2 (12) = 1258.07, $p < .001$)					
SLT	5.46 (0.28)	9.99 (0.30)	6.84 (0.28)	4.54 [3.86, 5.22] $p < .001$	1.39 [0.74, 2.03] $p < .001$
CIG	4.61 (0.21)	9.93 (0.23)	6.21 (0.21)	5.31 [4.77, 5.86] $p < .001$	1.59 [1.07, 2.11] $p < .001$
NON	4.17 (0.19)	10.38 (0.21)	5.81 (0.20)	6.21 [5.72, 6.70] $p < .001$	1.64 [1.17, 2.11] $p < .001$
SLT vs. CIG	0.84 [0.16, 1.53] $p = .016$	0.07 [-0.67, 0.80] $p = .859$	0.64 [-0.05, 1.32] $p = .069$		
SLT vs. NON	1.29 [0.61, 1.96] $p < .001$	-0.39 [-1.11, 0.34] $p = .295$	1.03 [0.36, 1.71] $p = .003$		
CIG vs. NON	0.44 [-0.12, 1.01] $p = .124$	-0.45 [-1.07, 0.16] $p = .148$	0.40 [-0.17, 0.97] $p = .170$		

^aScores for knowledge ranged from a possible 0–20 correct. The table shows mean scores, averaged across correct/incorrect responses for four health consequences and five constituents.

^bFor individual values (experimental condition or user group), means and standard errors (in parentheses) are shown.

^cFor comparisons, geometric mean and 95% confidence intervals (in brackets), as well as t test significance of post hoc mean contrasts, in bold, are shown.

^dUser group abbreviations: CIG = cigarette smokers; NON = nontobacco users; SLT = smokeless tobacco users.

Table 2. Perceptions of Constituent Variability in SLT Constituents at the Three Time Periods^a

	Time 1	Time 2	Time 3	Time 2 vs. Time 1	Time 3 vs. Time 1
Comparisons by experimental conditions (overall model fit χ^2 (21) = 610.19, $p < .001$)					
Experimental	4.51 (0.04) ^b	5.38 (0.04)	4.85 (0.04)	0.87 [0.79, 0.95] $p < .001$	0.34 [0.26, 0.42] $p < .001$
Control	4.51 (0.07)	4.55 (0.07)	4.61 (0.07)	0.04 [-0.12, 0.21] $p = .597$	0.10 [-0.06, 0.27] $p = .200$
Experimental vs. Control	0.00 [-0.16, 0.16] ^c $p = .994$	0.83 [0.67, 0.99] $p < .001$	0.23 [0.08, 0.39] $p = .004$		
Comparisons by user groups ^d (overall model fit χ^2 (12) = 510.89, $p < .001$)					
SLT	4.64 (0.08)	5.47 (0.08)	5.11 (0.08)	0.82 [0.65, 0.99] $p < .001$	0.46 [0.29, 0.63] $p < .001$
CIG	4.51 (0.06)	5.40 (0.06)	4.84 (0.06)	0.89 [0.75, 1.03] $p < .001$	0.33 [0.19, 0.47] $p < .001$
NON	4.39 (0.05)	5.29 (0.05)	4.61 (0.05)	0.90 [0.78, 1.02] $p < .001$	0.22 [0.10, 0.35] $p < .001$
SLT vs. CIG	0.13 [-0.05, 0.33] $p = .162$	0.07 [-0.12, 0.26] $p = .486$	0.27 [0.08, 0.46] $p = .006$		
SLT vs. NON	0.26 [0.07, 0.44] $p = .007$	0.18 [-0.01, 0.37] $p = .058$	0.50 [0.31, 0.68] $p < .001$		
CIG vs. NON	0.12 [-0.04, 0.28] $p = .129$	0.11 [-0.04, 0.27] $p = .161$	0.23 [0.07, 0.39] $p = .004$		

^aScores for constituent variability (averaged across five constituents, the degree to which SLT products vary along each constituent) ranged from 1 (vary not at all) to 7 (vary greatly).

^bFor individual values (experimental condition or user group), means and standard errors (in parentheses) are shown.

^cFor comparisons, geometric mean and 95% confidence intervals (in brackets), as well as t test significance of post hoc mean contrasts, in bold, are shown.

^dUser group abbreviations: CIG = cigarette smokers; NON = nontobacco users; SLT = smokeless tobacco users.

$\Delta M_{\text{Time3-Time1}} = 1.59$, 95% CI [1.07, 2.11]; nonusers: $\Delta M_{\text{Time3-Time1}} = 1.64$, 95% CI [1.17, 2.11]), compared to baseline.

Perception of Constituent Level Variability in SLT Products

Results for perceptions of constituent variability are shown in Table 2 and Supplement S5, available at *Nicotine and Tobacco Research* online. There were no differences in constituent variability perceptions between experimental and control conditions at baseline (Table 2). However, respondents in experimental conditions showed higher variability perceptions than those in the control condition at Time 2 ($\Delta M_{\text{experimental-control}} = .83$, 95% CI [0.67, 0.99]) and Time 3 ($\Delta M_{\text{experimental-control}} = .23$, 95% CI [0.08, .39]). Looking across time, relative to baseline perceptions, respondents in the control condition did not change their constituent variability perceptions either at Time 2 or Time 3, but respondents in experimental conditions increased their perception of variability at both time periods ($\Delta M_{\text{Time2-Time1}} = .87$, 95% CI [0.79, .95]; $\Delta M_{\text{Time3-Time1}} = .34$, 95% CI [0.26, .42]).

Analyses by user group in the experimental condition showed that at baseline, SLT users perceived more constituent variability than nonusers ($\Delta M_{\text{SLT_users-nonusers}} = .26$, 95% CI [0.07, .44]). At Time 2, the three user groups perceived equivalent levels of variability (Table 2). At Time 3, SLT users again perceived higher levels of constituent variability than smokers ($\Delta M_{\text{SLT_users-cigarette_smokers}} = .27$, 95% CI [0.08, .46]) or nonusers ($\Delta M_{\text{SLT_users-nonusers}} = .50$, 95% CI [0.31, .68]), and smokers perceived higher levels than nonusers ($\Delta M_{\text{cigarette_smokers-nonusers}} = .23$, 95% CI [0.07, .39]). Across time, relative to baseline, all three user groups perceived more constituent variability at both Time 2 (SLT users: $\Delta M_{\text{Time2-Time1}} = .82$, 95% CI [0.65, .99]; cigarette smokers: $\Delta M_{\text{Time2-Time1}} = .89$, 95% CI [0.75, 1.03]; nonusers: $\Delta M_{\text{Time2-Time1}} = .90$, 95% CI [0.78, 1.02]) and Time 3 (SLT users: $\Delta M_{\text{Time3-Time1}} = .46$, 95% CI [0.29, .63]; cigarette smokers: $\Delta M_{\text{Time3-Time1}} = .33$, 95% CI [0.19, .47]; nonusers: $\Delta M_{\text{Time3-Time1}} = .22$, 95% CI [0.10, .35]).

Respondent Ratings of Disease Risk (SLT, Cigarette Smoking, and Medicinal Nicotine)

Summary statistics for SLT disease risk are shown in Table 3, and those for cigarette and medicinal nicotine are provided in Supplement S6, available at *Nicotine and Tobacco Research* online. Respondents' ratings of disease risk from using SLT increased significantly at Time 2 ($\Delta M_{\text{Time2-Time1}} = .26$, 95% CI [0.19, .33]) and persisted at Time 3 ($\Delta M_{\text{Time3-Time1}} = .08$, 95% CI [0.01, .16]) in experimental (but not control) conditions. Respondents' ratings of disease risk from using cigarettes also increased in experimental (but not control) conditions at Time 2 ($\Delta M_{\text{Time2-Time1}} = .07$, 95% CI [0.02, .13]), but reverted to baseline at Time 3 ($\Delta M_{\text{Time3-Time1}} = .02$, 95% CI [-0.04, .08]). In contrast, respondents' ratings of disease risk from medicinal nicotine decreased in experimental (but not control) conditions at Time 2 ($\Delta M_{\text{Time2-Time1}} = -0.09$, 95% CI [-0.18, -0.01]) and reverted to baseline at Time 3 ($\Delta M_{\text{Time3-Time1}} = -0.01$, 95% CI [-0.10, .07]). At Time 2, respondents in experimental conditions rated medicinal nicotine as lower in disease risk than respondents in the control condition ($\Delta M_{\text{experimental-control}} = -0.22$, 95% CI [-0.42, -0.02]).

Results by user group (shown in Table 3 and S6) show that all three user groups increased their risk perceptions from baseline to Time 2 for SLT (smokeless users: $\Delta M_{\text{Time2-Time1}} = .27$, 95% CI [0.12, .42]; cigarette smokers: $\Delta M_{\text{Time2-Time1}} = .39$, 95% CI [0.28, .51]; nonusers: $\Delta M_{\text{Time2-Time1}} = .11$, 95% CI [0.01, .22]) and cigarette smokers increased their risk perceptions of cigarettes (S6: $\Delta M_{\text{Time2-Time1}} = .15$, 95% CI [0.05, .25]). At

Time 3, SLT users persisted in their higher risk ratings from using SLT ($\Delta M_{\text{Time3-Time1}} = .18$, 95% CI [0.03, .33]), while all other ratings for all user groups reverted to baseline. Disease risk ratings associated with SLT, cigarette, and medicinal nicotine usage were consistently lower for tobacco users than nonusers (Table 3 and S6).

Finally, at Time 3, in experimental conditions, disease risk ratings were highest for cigarettes ($M_{\text{cigarette}} = 5.95$), followed by SLT ($M_{\text{SLT}} = 5.12$) and medicinal nicotine products ($M_{\text{nicotine}} = 4.34$).

Self-Reported SLT Brand Switching and Cessation Rates

Among SLT users, rates of self-reported switching to a different SLT brand, from baseline to Time 3, were nonsignificantly different in experimental (23.9%) and control (20.0%) conditions ($\chi^2(1) = .44$, $p = .51$). Nor did cessation rates of SLT users, comparing baseline to Time 3, differ significantly for experimental (20.5%) and control (15.4%) respondents; ($\chi^2(2) = 1.18$, $p = .56$).

Side-by-Side SLT Product Comparisons

Table 4 summarizes results of side-by-side comparisons, by experimental-control conditions and by user groups (see also Supplemental S7b, available at *Nicotine and Tobacco Research* online). For products with higher levels of constituents (Grizzly and Kodiak), respondents in experimental conditions estimated higher levels of exposure than the control condition (who viewed only the package icon) if one were to use that product: (Grizzly: $\Delta M_{\text{experimental-control}} = .43$, 95% CI [0.29, .57]; Kodiak: $\Delta M_{\text{experimental-control}} = .42$, 95% CI [0.29, .57]). For products with lower levels of constituents (Copenhagen and Husky), only Husky was estimated as producing less constituent exposure by respondents in experimental conditions than the control condition (Husky: $\Delta M_{\text{experimental-control}} = -0.51$, 95% CI [-0.67, -0.34]).

By user group, SLT users estimated lower levels of exposure than cigarette smokers for Copenhagen ($\Delta M_{\text{SLT_users-cigarette_smokers}} = -0.28$, 95% CI [-0.47, -0.10]) and Husky ($\Delta M_{\text{SLT_users-cigarette_smokers}} = -0.30$, 95% CI [-0.51, -0.08]) and lower levels than nonusers for three products (Copenhagen: $\Delta M_{\text{SLT_users-nonusers}} = -0.35$, 95% CI [-0.53, -0.17]; Grizzly: $\Delta M_{\text{SLT_users-nonusers}} = -0.23$, 95% CI [-0.40, -0.06]; Husky: $\Delta M_{\text{SLT_users-nonusers}} = -0.50$, 95% CI [-0.71, -0.28]). Cigarette smokers estimated lower levels than nonusers for Grizzly ($\Delta M_{\text{cigarette_smokers-nonusers}} = -0.15$, 95% CI [-0.29, -0.02]) and Husky ($\Delta M_{\text{cigarette_smokers-nonusers}} = -0.20$, 95% CI [-0.37, -0.02]).

Discussion

By law, the FDA is required to inform the public about levels of HPHCs in a format that is "understandable and not misleading to a lay person." Our study demonstrates that US users and nonusers of SLT products can gain accurate information about the health effects and the levels of harmful constituents in tobacco products. Respondents were able to (1) gain relevant information from the charts to accurately report the health risks associated with tobacco constituents; (2) understand that smokeless products vary significantly in constituent levels; and (3) form judgments about overall exposure from particular products.

Past research has identified constituents of which consumers are aware,^{3,29} evaluated consumer perceptions of disease risk of SLT products,³⁰ and provided initial evaluations of interventions designed to increase knowledge of constituents.^{2,7,31-33} Our study is a novel contribution to the literature in this field as it employs a comprehensive approach by providing to respondents the information

Table 3. Ratings of Own Disease Risk from Using SLT Products at the Three Time Periods^a

	Time 1	Time 2	Time 3	Time 2 vs. Time 1	Time 3 vs. Time 1
Comparisons by experimental conditions (overall model fit χ^2 (21) = 273.63, $p < .001$)					
Experimental	5.03 (0.04) ^b	5.29 (0.04)	5.12 (0.04)	0.26 [0.19, 0.33] $p < .001$	0.08 [0.01, 0.16] $p = .022$
Control	5.12 (0.08)	5.18 (0.08)	5.13 (0.08)	0.06 [-0.08, 0.19] $p = .442$	0.01 [-0.13, 0.15] $p = .844$
Experimental vs. Control	-0.09 [-0.26, 0.08] ^c $p = .318$	0.11 [-0.05, 0.29] $p = .170$	-0.01 [-0.19, 0.15] $p = .848$		
Comparisons by user groups ^d (Overall model fit χ^2 (12) = 235.62, $p < .001$)					
SLT	4.68 (0.08)	4.95 (0.08)	4.86 (0.08)	0.27 [0.12, 0.42] $p < .001$	0.18 [0.03, 0.33] $p = .018$
CIG	4.87 (0.06)	5.26 (0.06)	4.92 (0.06)	0.39 [0.28, 0.51] $p < .001$	0.05 [-0.06, 0.18] $p = .352$
NON	5.58 (0.06)	5.69 (0.06)	5.59 (0.06)	0.11 [0.01, 0.22] $p = .036$	0.01 [-0.09, 0.12] $p = .779$
SLT vs. CIG	-0.19 [-0.40, 0.02] $p = .076$	-0.31 [-0.52, -0.10] $p = .003$	-0.06 [-0.27, 0.14] $p = .534$		
SLT vs. NON	-0.90 [-1.10, 0.69] $p < .001$	-0.74 [-0.95, -0.54] $p < .001$	-0.73 [-0.94, -0.53] $p < .001$		
CIG vs. NON	-0.71 [-0.88, -0.54] $p < .001$	-0.43 [-0.60, -0.26] $p < .001$	-0.67 [-0.84, -0.50] $p < .001$		

^aRatings of disease risk (averaged across four diseases, vulnerability to getting each health outcome sometime in their lifetime if they were to use smokeless tobacco), ranged from 1 (disagree) to 7 (agree).

^bFor individual values (experimental condition or user group), means and standard errors (in parentheses) are shown.

^cFor comparisons, geometric mean and 95% confidence intervals (in brackets), as well as t test significance of post hoc mean contrasts, in bold, are shown.

^dUser group abbreviations: CIG = cigarette smokers; NON, nontobacco users; SLT = smokeless tobacco users.

Table 4. Respondents' Estimates of Amount of Chemical Exposure During Side-by-Side SLT Product Comparisons^a

	Comparison 1 ^b		Comparison 2 ^b	
	Copenhagen	Grizzly	Husky	Kodiak
Comparisons by experimental conditions				
Experimental	5.71 (0.03) ^c	6.13 (.03)	5.24 (0.04)	6.14 (0.03)
Control	5.77 (0.06)	5.70 (.06)	5.75 (0.07)	5.72 (0.06)
Overall Test of Experimental vs. Control	$p = .492$	$p < .001$	$p < .001$	$p < .001$
Experimental vs. Control	95% CI [-0.19, 0.09] ^d $p = .492$	95% CI [0.29, 0.57] $p < .001$	95% CI [-0.67, -0.34] $p < .001$	95% CI [0.29, 0.57] $p < .001$
Comparisons by user groups ^e				
SLT	5.47 (0.07)	6.00 (0.07)	4.92 (0.09)	6.02 (0.07)
CIG	5.75 (0.06)	6.08 (0.05)	5.22 (0.07)	6.17 (0.05)
NON	5.82 (0.05)	6.23 (0.05)	5.42 (0.06)	6.19 (0.05)
Overall Test of User Group	$p < .001$	$p = .014$	$p < .001$	$p = .141$
SLT vs. CIG	95% CI [-0.47, -0.10] $p = .002$	95% CI [-0.24, 0.10] $p = .388$	95% CI [-0.51, -0.08] $p = .006$	95% CI [-0.32, 0.03] $p = .097$
SLT vs. NON	95% CI [-0.53, -0.17] $p < .001$	95% CI [-0.40, -0.06] $p = .008$	95% CI [-0.71, -0.28] $p < .001$	95% CI [-0.34, 0.00] $p = .056$
CIG vs. NON	95% CI [-0.22, 0.08] $p = .371$	95% CI [-0.29, -0.02] $p = .028$	95% CI [-0.37, -0.02] $p = .027$	95% CI [-0.16, 0.12] $p = .760$

^aRespondents' estimated level of constituent exposure resulting from the use of each product ranged from a possible 1 (no chemical exposure) to 7 (a great deal of chemical exposure).

^bGrizzly appeared in the charts to have higher levels than Copenhagen, in comparison #1, and Kodiak appeared to have higher levels than Husky in comparison #2.

^cFor individual values (experimental condition or user group), means and standard errors (in parentheses) are shown.

^dFor comparisons, geometric mean and 95% confidence intervals (in brackets), as well as t test significance of post hoc mean contrasts, in bold, are shown.

^eUser group abbreviations: CIG = cigarette smokers; NON = nontobacco users; SLT = smokeless tobacco users.

about levels of several representative harmful constituents and enabling comparisons of a large number of SLT products found in the current marketplace. Our focus was on how the information on SLT constituent yields should be presented and if the information that is presented is understood; therefore, we did not include all SLT priority HPHCs. The constituents we chose represent different HPHC sources in SLT (those present in tobacco plant and those formed or deposited during tobacco processing) and a range of health effects (addiction, cancer, and toxicity). Furthermore, levels of these constituents vary across SLT products; for example, levels of unprotonated nicotine (biologically available form) and NNN varied approximately 50-fold and 24-fold, respectively, across products included in this study. Previous research, including our studies, shows that such variations result in differences in consumers' exposures¹⁵ and affect health outcomes such as addiction³⁴ and cancer risk.¹⁴ Lastly, since nicotine, NNN, and NNK are specific to tobacco, while BaP and metals are ubiquitous contaminants, there could be potential differences in recognition of these constituents and in perceptions of the associated risks. The remaining three constituents from the abbreviated HPHC list—formaldehyde, acetaldehyde, and crotonaldehyde—are present at relatively low levels in SLT products and were not included. Particular strengths of our research design are that we included randomized assignment to experimental and control conditions, tested multiple user groups with large sample sizes, and assessed longitudinal change over time. In addition, the chart formats developed have pragmatic advantages of being easily accessible (online) and promoting active engagement by the respondent in choosing which individual products to compare. Also important, using a website tool such as the one developed by professional graphic designers for this research is more engaging than embedding information within a point-of-purchase retail setting, where there are distractions and less time and access to the full information array.

Just as consumers and policy makers in developed and developing countries rely on food labels to indicate levels of unhealthy ingredients, such as saturated fat, sugar, and salt content, and accurate learning of such ingredients increases over time, our results suggest that formats for providing constituent levels in tobacco products have potential to better inform the public and increase knowledge. When faced with choice options in a tobacco or convenience store, for example, retention of knowledge of constituents may influence the choices a SLT user makes. Since *multiple* exposures to health messages sustained over time are most likely to produce long-term change,^{35,36} future research might test whether multiple and varied exposures with tobacco constituent charts further increase knowledge and ward off memory decay over time.³⁷ In addition, while ratings of disease risk from SLT use continued to be moderately high to high, self-reported SLT use was not affected. Future research might examine the conditions under which knowledge gains affect longer-term changes in frequency and amount of tobacco consumed and reduce the gap between disease risk perceptions and tobacco use behavior. Future research might also be directed toward understanding whether certain individuals or subgroups of the population are more prone to understanding and using constituent information appropriately or whether certain subgroups (eg adolescents, not included in the present study) are prone to misperceptions and consequent increased use of certain tobacco products.

Importantly, tobacco users in our study did not form certain types of misperceptions about SLT products. For example, consistent with warning information provided in our intervention ([Supplement 2a](#),

available at *Nicotine and Tobacco Research* online) that no tobacco product is safe, even at lower levels, smokeless users' estimated constituent exposure levels from individual SLT products were moderately high to high (well above the midpoint), even for products that appeared to have lower exposure levels. Further, at intervention, smokeless users increased their ratings of disease risk from SLT, and this increase persisted 6-week postintervention. These results indicate that learning about constituent levels did not lead tobacco users to believe that smokeless products in general, or that individual SLT products, in particular, were safe to use. Nevertheless, the belief that all SLT tobacco products are unsafe is only one type of evidence needed to guard against misperceptions. For example, our study did not directly assess whether the understanding of constituent level variations across products affected the perceived relative levels of safety of different SLT product brands. However, after a single exposure, we found no significant difference in product switching rates between the experimental and control conditions. This suggests that there was no apparent shift among SLT users toward products that may be misperceived as safer than other brands due to their low HPHC levels. Tobacco use status is another potentially important factor. For example, tobacco users in our study reported, relative to nonusers, lower estimates of exposure to harmful constituents from specific SLT brands and lower disease risk from tobacco.

There are several limitations to this study, such as an incomplete HPHC list and the relatively narrow range of health effects that were tested. Another potential limitation is that not all respondents viewed all 79 SLT products or for the same length of time, as the setting allowed them to use the charts as they wish. Creating a uniform amount of time and number of product comparisons would produce elements of artificiality to the design, a different type of limitation. In addition, since we did not focus on youth and other vulnerable populations and had higher attrition rates for tobacco users than nonusers, applicability of our findings to the general population is limited. Lastly, our study was based on US-based respondents and products. Nevertheless, our findings should be helpful in informing approaches to tobacco constituent communication in other countries, such as India and some other Southeast Asian countries where SLT products are highly diverse in their formulations and chemical composition,²⁰ and communication of this information to consumers is virtually nonexistent.

In summary, this study addresses an important gap in research literature on the methods and outcomes of SLT constituent communication to lay persons. Additional behavioral research on SLT use in response to constituent level reporting might determine whether and how informing the public is beneficial. Regardless, informing the public about the association between constituent levels and harm to users, is urgently needed, for tobacco products marketed in the United States and other countries.

Supplementary Material

Supplementary data are available at *Nicotine and Tobacco Research* online.

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Declaration of Interests

None declared.

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References

- Margolis KA, Bernat JK, Keely O'Brien E, Delahanty JC. Online information about harmful tobacco constituents: a content analysis. *Nicotine Tob Res.* 2017;19(10):1209–1215.
- Borgida E, Loken B, Williams AL, Vitriol J, Stepanov I, Hatsukami D. Assessing constituent levels in smokeless tobacco products: a new approach to engaging and educating the public. *Nicotine Tob Res.* 2015;17(11):1354–1361.
- Hall MG, Ribisl KM, Brewer NT. Smokers' and nonsmokers' beliefs about harmful tobacco constituents: implications for FDA communication efforts. *Nicotine Tob Res.* 2014;16(3):343–350.
- O'Connor RJ, Hyland A, Giovino GA, Fong GT, Cummings KM. Smoker awareness of and beliefs about supposedly less-harmful tobacco products. *Am J Prev Med.* 2005;29(2):85–90.
- O'Connor RJ, McNeill A, Borland R, et al. Smokers' beliefs about the relative safety of other tobacco products: findings from the ITC collaboration. *Nicotine Tob Res.* 2007;9(10):1033–1042.
- Øverland S, Herland J, Aarø LE. Relative harm of snus and cigarettes: what do Norwegian adolescents say? *Tob Control.* 2008;17(6):422–425.
- Biener L, Nyman AL, Stepanov I, Hatsukami D. Public education about the relative harm of tobacco products: an intervention for tobacco control professionals. *Tob Control.* 2014;23(5):385–388.
- Borland R, Cooper J, McNeill A, O'Connor R, Cummings KM. Trends in beliefs about the harmfulness and use of stop-smoking medications and smokeless tobacco products among cigarettes smokers: findings from the ITC four-country survey. *Harm Reduct J.* 2011;8:21.
- Shiffman S, Pillitteri JL, Burton SL, Rohay JM, Gitchell JG. Smokers' beliefs about "Light" and "Ultra Light" cigarettes. *Tob Control.* 2001;10(suppl 1):i17–i23.
- Hecht SS, Murphy SE, Carmella SG, et al. Similar uptake of lung carcinogens by smokers of regular, light, and ultralight cigarettes. *Cancer Epidemiol Biomarkers Prev.* 2005;14(3):693–698.
- Harris JE, Thun MJ, Mondul AM, Calle EE. Cigarette tar yields in relation to mortality from lung cancer in the cancer prevention study II prospective cohort, 1982–8. *BMJ.* 2004;328(7431):72.
- Benowitz NL. Compensatory smoking of low-yield cigarettes. In: Burns DM, Shopland DR, Benowitz N, eds. *Tobacco Control Monograph Series No. 13: Risks Associated with Smoking Cigarettes with Low Tar Machine-Measured Yields of Tar and Nicotine*. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute; 2001:39–63.
- National Cancer Institute, Centers for Disease Control and Prevention. *Smokeless Tobacco and Public Health: A Global Perspective*. Bethesda, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institutes of Health, National Cancer Institute; 2014.
- Stepanov I, Hatsukami D. Call to establish constituent standards for smokeless tobacco products. *Tob Reg Sci.* 2016;2(1):9–30.
- Hatsukami DK, Stepanov I, Severson H, et al. Evidence supporting product standards for carcinogens in smokeless tobacco products. *Cancer Prev Res (Phila).* 2015;8(1):20–26.
- World Health Organization. WHO Study Group on Tobacco Product Regulation: Report on the Scientific Basis of Tobacco Product Regulations: Fifth Report of a WHO Study Group. Geneva: World Health Organization; 2015.
- Boffetta P, Hecht S, Gray N, Gupta P, Straif K. Smokeless tobacco and cancer. *Lancet Oncol.* 2008;9(7):667–675.
- Stepanov I, Sebero E, Wang R, Gao YT, Hecht SS, Yuan JM. Tobacco-specific N-nitrosamine exposures and cancer risk in the Shanghai Cohort Study: remarkable coherence with rat tumor sites. *Int J Cancer.* 2014;134(10):2278–2283.
- Yuan JM, Gao YT, Murphy SE, et al. Urinary levels of cigarette smoke constituent metabolites are prospectively associated with lung cancer development in smokers. *Cancer Res.* 2011;71(21):6749–6757.
- Stepanov I, Gupta PC, Parascandola M, et al. Constituent variations in smokeless tobacco purchased in Mumbai, India. *Tob Reg Sci.* 2017;3(3):305–314.
- Kozłowski LT, Edwards BQ. "Not safe" is not enough: smokers have a right to know more than there is no safe tobacco product. *Tob Control.* 2005;14(suppl II):ii3–ii7.
- Food and Drug Administration Center for Tobacco Products (CTP). Reporting Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke Under Section 904(a)(3) of the Federal Food, Drug, and Cosmetic Act. Draft Guidance. Silver Spring, MD: U.S. Department of Health and Human Services, Food and Drug Administration Center for Tobacco Products (CTP); 2012.
- World Health Organization. WHO Study Group on Tobacco Product Regulation: Report on the Scientific Basis of Tobacco Product Regulation: Third Report of a Who Study Group. Geneva: World Health Organization; 2010.
- Lipkus IM. Numeric, verbal, and visual formats of conveying health risks: suggested best practices and future recommendations. *Med Decis Making.* 2007;27(5):696–713.
- Hildon Z, Allwood D, Black N. Impact of format and content of visual display of data on comprehension, choice and preference: a systematic review. *Int J Qual Health Care.* 2012;24(1):55–64.
- Stepanov I, Abrams J, Jain V, Walter K, Kittner DL. Variations of toxic and carcinogenic constituents in nasvai: call for systematic research and regulation. *Tob Control.* 2017;26(3):355–356.
- Stepanov I, Biener L, Yershova K, et al. Monitoring tobacco-specific N-nitrosamines and nicotine in novel smokeless tobacco products: findings from round II of the new product watch. *Nicotine Tob Res.* 2014;16(8):1070–1078.
- Stepanov I, Villalta PW, Knezevich A, Jensen J, Hatsukami D, Hecht SS. Analysis of 23 polycyclic aromatic hydrocarbons in smokeless tobacco by gas chromatography-mass spectrometry. *Chem Res Toxicol.* 2010;23(1):66–73.
- Morgan JC, Byron MJ, Baig SA, Stepanov I, Brewer NT. How people think about the chemicals in cigarette smoke: a systematic review. *J Behav Med.* 2017;40(4):553–564.
- Lund I, Scheffels J. Perceptions of the relative harmfulness of snus among Norwegian general practitioners and their effect on the tendency to recommend snus in smoking cessation. *Nicotine Tob Res.* 2012;14(2):169–175.
- Baig SA, Byron MJ, Boynton MH, Brewer NT, Ribisl KM. Communicating about cigarette smoke constituents: an experimental comparison of two messaging strategies. *J Behav Med.* 2017;40(2):352–359.
- Thrasher JF, Murukutla N, Pérez-Hernández R, et al. Linking mass media campaigns to pictorial warning labels on cigarette packages: a cross-sectional study to evaluate effects among Mexican smokers. *Tob Control.* 2013;22(e1):e57–e65.
- Brewer NT, Jeong M, Mendel JR, et al. Cigarette pack messages about toxic chemicals: a randomised clinical trial. *Tob Control.* 2019;28(1):74–80.

-
34. Henningfield JE, Fant RV, Buchhalter AR, Stitzer ML. Pharmacotherapy for nicotine dependence. *CA Cancer J Clin.* 2005;55(5):281–299; quiz 322.
 35. Donnelly GE, Zatz LY, Svirsky D, John LK. The effect of graphic warnings on sugary-drink purchasing. *Psychol Sci.* 2018;29(8):1321–1333.
 36. Wakefield MA, Loken B, Hornik RC. Use of mass media campaigns to change health behaviour. *Lancet.* 2010;376(9748):1261–1271.
 37. Brewer NT, Hall MG, Noar SM, et al. Effect of pictorial cigarette pack warnings on changes in smoking behavior: a randomized clinical trial. *JAMA Intern Med.* 2016;176(7):905–912.