Nicotine & Tobacco Research Advance Access published August 7, 2015

Associations of proposed relative-risk warning labels for snus with perceptions and behavioral intentions among tobacco users and non-users

Brad Rodu, DDS[a,b,c], Nantaporn Plurphanswat, PhD[b], John R. Hughes, MD[d] , Karl Fagerström, PhD[e]

[a] Department of Medicine, School of Medicine, University of Louisville, Louisville, KY USA

[b] James Graham Brown Cancer Center, University of Louisville

[d] Center for Behavior and Health, Department of Psychiatry, University of Vermont, Burlington, VT USA

[e] Fagerström Consulting, Vaxholm, Sweden

[c]Corresponding Author: 505 South Hancock Street, University of Louisville, Louisville, KY 40202, Phone: 502-852-7793; Fax: 502-852-7979; Email: brad.rodu@louisville.edu

Word Count (manuscript body only): 3,986

ABSTRACT (250 Words)

Introduction. The U.S. FDA can require changes in warning statements for modified risk tobacco products (MRTP). We report an independent analysis of a consumer perception survey sponsored by Swedish Match as part of an Modified Risk Tobacco Product application to change warning labels for Swedish snus products.

Methods. The survey exposed each of 4,324 daily exclusive cigarette smokers, 1,033 daily smokeless tobacco users, 1,205 daily other tobacco users, 726 former users and 5,915 triers/never users to one of four current warnings and two proposed relative-risk labels (No tobacco product is safe, but this product presents lower risks to health than cigarettes, or No tobacco product is safe, but this product presents substantially lower risks to health than cigarettes) for snus. Descriptive and logistic regression analyses examined four outcomes: believability, harmfulness, motivation to use and intention to buy snus.

Results. Compared with the current not-safe-alternative warning, adult tobacco users who viewed the proposed labels perceived them as less believable, perceived snus as less harmful and were more likely to use and buy snus. The proposed labels had no impact on former smokers' likelihood to use and buy snus; triers/never users viewing the substantially lower risk label were more likely to buy snus.

Conclusions. Tobacco users viewing the proposed labels perceived snus as less harmful than cigarettes and may be more likely to use and buy snus. If labeling changes lead to increased snus use and cigarette reduction or abstinence, public health may benefit. If the opposite occurs, public health could suffer.

Key words: Snus, health warnings, risk perception, modified risk tobacco product, tobacco regulation

INTRODUCTION

In most countries health warnings have been mandated on tobacco products, particularly cigarettes, since the 1960s. They increase knowledge about the adverse health effects of smoking (1), promote intention to quit, increase the number of quit attempts, reduce smoking intensity (2) and decrease relapse (3), but the effects are not typically long-lasting (4,5).

Much less evaluation and research have been directed at smokeless tobacco (ST) product warning labels, three of which were mandated in 1986 when the U.S. Congress passed the Comprehensive Smokeless Tobacco Health Education Act: This product can cause mouth cancer; This product can cause gum disease and tooth loss; This product is not a safe alternative to cigarettes. In 2009 Congress added a fourth warning (Smokeless tobacco is addictive) when it passed the Family Smoking Prevention and Tobacco Control Act (TCA) (6).

According to the TCA, a tobacco manufacturer cannot market a product with either explicit or implicit claims that it is associated with less health risk than other tobacco products (e.g. conventional cigarettes) unless such claims are substantiated in a formal modified risk tobacco product (MRTP) application by the manufacturer (6). The application should include scientific data that marketing of the product is likely to "benefit public health," taking into account both current users and non-users of tobacco products. The Food and Drug Administration (FDA) can issue orders about the labeling of an MRTP, including the wording of warning statements. The process reflects concern for the potential, unintended consequences of the marketing, such as making current tobacco users less likely to quit tobacco, encouraging former tobacco users to take up tobacco again, and increasing uptake of tobacco among never users. To address such potential for unintended consequences, the possible effects of proposed marketing changes must be formally tested in a premarket setting (7).

Swedish snus is a non-fermented ST product that has been traditionally used in Scandinavia since the early 1800s. The health risks of snus use have been estimated at 10% or less compared to smoking (8-

10). Although many agree that the availability of snus has benefited public health in Sweden and Norway through decreased primary uptake of cigarettes and smokers switching to snus (11), the potential impact of snus use in other countries is unclear because snus is not popular outside Scandinavia.

In June, 2014, Swedish Match, the major manufacturer of snus in Scandinavia, submitted an MRTP application to the FDA Center for Tobacco Products (CTP) to replace three of the existing, mandated warning labels on its products (mouth cancer, gum disease/tooth loss, not-safe-alternative) with labels the company maintains more accurately reflect the available science about Swedish snus (No tobacco product is safe, but this product presents lower risks to health than cigarettes, or No tobacco product is safe, but this product presents substantially lower risks to health than cigarettes). These labels would be the first to directly compare the relative risks of one tobacco product with another product. In the application, the company requested that the current warning about addiction remains unchanged (12).

To provide information about the potential population impact of the proposed labels, in November-December 2013 Swedish Match funded a premarket study measuring perceptions of the current and proposed labels among 13,200 participants in the U.S. using a quantitative, randomized, online survey. The main findings were included in the Company's MRTP application, which was made public by the CTP in August 2014. Before fielding the study the protocol was discussed with CTP staff. The protocol, questionnaire, raw data and report from the study are available on the FDA website (12).

METHODS

Survey design

Swedish Match contracted with a private marketing research **firm** (InsightExpress, Stamford, Connecticut) to design the survey and conduct it using an online questionnaire. Upon our request, Swedish Match provided the original survey dataset. The current analysis employed different definitions and methods than those used by Swedish Match in its report to the FDA (13).

Sample

Almost all of the participants were recruited from existing consumer-based panels (n=12,553, 95%), consisting of members who had opted to participate in marketing research studies and had provided personal identification details; they did not know that Swedish Match was the sponsor. Invitations were distributed via email and included a hyperlink to the survey questionnaire. The remaining participants (n=650) were recruited through online advertisements (e.g. banner and pop-up ads) on various websites. Individuals who chose to participate received an incentive whose amount was considered proprietary. The minimum age for participation in the survey was the minimum age for tobacco purchase. This is 18 years for all states except Alabama, Alaska, New Jersey, New York, and Utah, where the minimum age is 19 years.

Survey Procedures

Participants were enrolled as current users (those who used any type of tobacco product daily) and non-users, which included former users, triers (used only once or twice) and never users of any type of tobacco product (Supplemental Table 1). Thus, there were no exclusive occasional users of tobacco products. **Approximately 1,100 current users and 1,100 non-users were assigned into 6 cells, one for each label, based on the distribution of smokers in the 2005-2010 National Health Interview Survey with respect to age, sex, ethnicity, income and geography (14).** Participants were shown three high-resolution color images of the warning label on cans of General Nordic Mint, General Classic Blend, or General Wintergreen snus (Supplemental Figure 1). There was no time limit for viewing the labels, and there was a link on every subsequent webpage to allow participants to view the label again. The warning labels covered at least 30% of the surface area of the can as mandated by Section 204 of the Tobacco Control Act.

Measures

Tobacco Status

We constructed mutually exclusive categories of tobacco use, using the following hierarchy (Supplemental Table 2): daily exclusive cigarette smokers (hereafter "smokers," n=4,324); daily smokeless tobacco users (hereafter "ST users," n=1,033); daily users of other tobacco products (hereafter "other tobacco users," n=1,205; former tobacco users (n=726) and triers/never users (n=5,915). Subgroups of smokers consisted of those who intended to quit or to reduce in the next month (Supplemental Table 2).

Outcomes

We constructed outcome variables for warning label believability, perceived harm from snus, motivation to buy snus and likelihood to use snus using the questions and responses in Supplemental Table 2.

Demographic characteristics

Demographic characteristics we included were sex, age group (18-24, 25-44, and 45+ years), race/ethnicity (white, black, and other, i.e. Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and Hispanic), household income (<$45,000 and ≥ $45,000), geography (Northeast, Midwest, South, and West), marital status (married and not married), and education (< college and ≥ college).

Logistic regression analyses

We used multiple logistic regression analysis to examine the associations of all six warning labels and believability, harm from snus, motivation to buy and likelihood to use snus across all labels. Then we specifically compared the current not-safe-alternative warning label and the proposed lower risk and substantially lower risk labels. We analyzed separate models for smokers (and the subsets who intended

to quit or reduce smoking), ST users, other tobacco users, former users, and triers/never users. All models were adjusted for recruitment criteria: age, sex, region, race and ethnicity, and income, education and marital status.

Ethical considerations

To ensure that the proposed labels would not be construed by participants as a product endorsement, at the end of the survey they were required to watch a video documenting that "none of the claims made as part of this study have been validated or approved by any regulators of smokeless tobacco products, including snus," and emphasizing "that the information you have just examined has not been substantiated by the FDA." In addition, the video specified that "all smokeless tobacco products referenced in this study must carry one of the following warnings," after which the current warnings were read.

Although the study involved anonymous surveys, the protocol was reviewed by the Chesapeake Institutional Review Board (IRB), which determined that the project was exempt from IRB oversight. The University of Louisville IRB reviewed the plan for our secondary analysis and decided that it did not meet the "Common Rule" definition.

RESULTS

Descriptive statistics

Since participants were randomly assigned to view labels according to sex, age, race/ethnicity, income and geographic location, we found no differences in tobacco status across the labels (Supplemental Table 3).

Figures 1 and 2 present the percentage of subjects reporting that the warning labels were believable, that snus is harmful, the likelihood to use snus and the motivation to buy snus after viewing the warning

labels by tobacco status. **Simple correlation coefficients between believability and the other outcome variables were generally low and often not statistically significant.**

For smokers, more than 80% of respondents who viewed one of the current warnings, (mouth cancer, gum and tooth, addictive and not-safe-alternative) reported that these warnings were believable while approximately 60% reported that the proposed relative-risk labels were believable. Regardless of the label viewed, about 90% of smokers perceived that using snus is harmful. The proportions of smokers who saw either of the proposed labels reported that they were more likely to use snus and buy snus than those who viewed the four current warnings.

With smokers as the referent group: (1) lower proportions of ST users believed the current warnings (the differences were significant except for the not-safe-alternative warning), and significantly higher percentages believed the proposed labels; (2) across all labels significantly smaller proportions of ST users perceived snus as harmful and significantly higher proportions reported that they were likely to use snus and motivated to buy snus.

Other tobacco users were similar to smokers with respect to the proportions of users who believed the current warnings and who perceived snus as harmful. The proportions of other tobacco users who reported that they were likely to use snus and likely to buy snus were intermediate between the proportions of smokers and ST users. Again, those who viewed either proposed label reported being significantly more motivated to buy or likely to use snus.

Among former users, about 80-97% of respondents who viewed the current warnings reported that the labels were believable, while 67% and 62% viewed the lower risk and substantially lower risk labels as believable. Similar to smokers and other tobacco users, most former users perceived that using snus was harmful. Only small proportions of former users stated that they were likely to use snus (4-11%) and likely to buy snus (3-7%).

Similarly, triers/never users were more likely to believe the current warnings than the proposed labels (73-85% versus 48-49%). Over 90% of triers/never users perceived that using snus is harmful, and very few were likely to use snus (10-14%) or motivated to buy snus (6-11%) after viewing any of the labels.

Logistic Regression analysis comparing the proposed labels to the current not-safe-alternative warning

Table 1 illustrates the comparison of the current not-safe-alternative warning with the two proposed labels with respect to the outcomes (believability, harm from snus, likely to use snus and motivation to buy snus) for each category of tobacco users (models 1 to 5). The odd ratios were adjusted for sex, age, race/ethnicity, income, region, education and marital status.

Compared to the current not-safe-alternative warning, smokers viewing the two proposed labels had lower odds for believability (OR ~= 0.32 for both) and for snus as harmful (OR = 0.51 for lower risk and OR = 0.45 for substantially lower risk). The odd ratios were greater for likelihood to use snus (OR = 1.80 and 2.07) and for motivation to buy snus (OR = 3.50 and 4.04) for the proposed labels compared with the current warning. We also conducted an analysis of a subgroup of smokers reporting that they were likely to attempt to quit within the next month and a subgroup reporting that they were likely to attempt to reduce cigarette use in the next month. The results were very similar to those reported for all smokers.

ST users viewing the proposed labels also had lower odds for believability (OR = 0.59) and for snus as harmful (OR = 0.39 and 0.53). They were also more likely to use (OR = 2.04 for substantially lower) and more motivated to buy snus (OR = 1.92 and 2.15) compared to viewers of the current warning.

Among other tobacco users believability was significantly lower for both proposed labels compared to the current warning (OR =0.39 and 0.56), but harm from snus did not differ across labels. The proposed labels also had significantly higher ORs for likelihood to use (OR = 2.29) and motivation to buy snus (OR = 1.93) only for the substantially lower risk label.

Among former tobacco users, we found no significant differences in all outcomes, except for lower believability of the proposed labels (OR = 0.49 and 0.40). Among triers/never users, both proposed labels had lower believability (OR ~= 0.35 for both), but the substantially lower risk label had lower odds for snus is harmful (OR = 0.53) and higher odds for motivation to buy snus (OR = 1.88) but not for likelihood to use snus.

There were no significant differences in the ORs for lower risk versus substantially lower risk labels among tobacco users and former smokers. Among triers/never users the ORs were significantly different for snus harm and for motivation to buy snus between lower and substantially lower labels.

DISCUSSION

This study revealed that most participants, regardless of tobacco status, found that all of the current warnings were believable. In contrast, compared with the current not-safe-alternative warning, the two proposed relative-risk labels had lower odds of believability among all groups. The vast majority of all respondents, with minimal variation according to labels, also perceived that using snus is harmful. The odds of harm were mostly lower with the proposed labels, but these differences were not always statistically significant.

Among smokers, ST users and other tobacco users, likelihood to use and motivation to buy snus was almost always significantly greater for the proposed relative-risk labels compared with the not-safe-alternative warning. Among former tobacco users, no increases in likelihood to use or motivation to buy were seen with the proposed labels. In triers/never users an increase in motivation to buy snus was noted for the substantially lower risk label; neither proposed label had higher odds for likelihood to use snus. **While these findings suggest that the proposed warnings would not lead to tobacco recidivism among former users or initiation among never users, conclusive evidence will only be provided by appropriate post-market surveillance.**

The findings regarding believability are not surprising. American health authorities have ignored a substantial body of evidence documenting that ST use is less harmful than smoking (8-11, 15-20) and have continued to promote the message that ST is not a safe alternative to cigarettes. As a result, most American adults (21) and smokers (22-25) – even the highly educated, including health professionals (26) – assume that the risks of ST use are similar to those of smoking.

While tobacco users viewing the proposed labels were more likely than those viewing the not-safe-alternative warning to use or buy snus, the overall effect is modest. For example, the likelihood to use snus was 21-23% among smokers viewing the proposed labels versus 12% among those viewing the current warning; the corresponding percentages for motivation to buy were 19-21% versus 6%.

Compared with the current not-safe-alternative warning, smokers viewing the proposed labels had significantly higher odds of using or buying snus, and the same was true for ST users and other tobacco users viewing the substantially lower risk label. This indicates that the proposed labels might foster a transition from cigarettes to snus. A transition from other combustible products and other ST products to snus is also possible.

These results in current tobacco users are consistent with a previous study of 18-30 year old Canadian smokers completing an online survey (27). Participants were shown packages of four ST products (including two snus products) that were digitally altered with combinations of text and graphic health warning labels and/or a relative risk message ("Using smokeless tobacco is less harmful than smoking cigarettes"). Viewing the relative risk message had no effect on the appeal of the products, but it did increase the odds of correctly reporting that ST products are less harmful than cigarettes, of reporting future use, and of being willing to try smokeless tobacco as a smoking cessation aid.

The benefit of a transition from cigarettes to snus has been widely debated. In 2006, a panel of tobacco research and policy experts estimated that the introduction of a low nitrosamine ST product such as snus under strict regulation, including a warning label specifying that "this product is substantially less

harmful than cigarettes," would result in a two percentage point reduction in smoking prevalence in the U.S., or an additional 4 million former smokers (28). An earlier survey of young adults entering the U.S. Air Force in 1999-2000 suggested that smokers who believed that switching to ST would reduce health risks were more likely to quit during a one-year follow-up period (OR = 1.10, p= 0.009) (25).

In contrast to the results among smokers and ST users, the proposed labels showed nonsignificantly lower odds for using or buying snus among former tobacco users, which suggests that they are unlikely to be enticed to take up snus, an auspicious finding that needs confirmation. Triers/never users who viewed the substantially lower risk label were more motivated to buy, but not more likely to use snus; however, the lower risk label had no effect. In a previous study a reduced-risk advertising message did not increase non-smokers intent to use ST (29). Nevertheless, our findings suggest that any increased motivation to buy snus among never tobacco users should be monitored closely by post-marketing surveillance, because population health outcomes will be based on the balance between snus uptake among users of higher risk tobacco products and among non-users who would otherwise have remained abstinent.

Another study showed that the provision of relative risk information to smokers can result in modest correction of misperceptions about the relative health risks of ST use and smoking (30). Investigators recruited convenience samples of smokers from four countries (Australia, Sweden, the United Kingdom and the United States), who were shown a fact sheet summarizing current scientific knowledge (in ~2011) of the relative risks of nicotine and ST use compared with smoking. In all four countries, viewing the fact sheet resulted in a significant increase in the percentage of smokers correctly perceiving that ST use was less harmful than smoking, and it also resulted in significantly increased interest in trying ST except in Sweden, where the post-fact sheet question was not asked due to prevalent snus use.

The main limitation of our study was that it was based on a cross-sectional survey in which each participant viewed only one label; thus, direct within-person comparisons between existing and proposed labels were not possible. Cross sectional associations suggest but do not prove causality. In addition, the

questions about buying and using snus did not address partial or complete transition from cigarettes to snus. Another limitation is that the questions did not allow participants to indicate how much the label changed their beliefs, but rather simply had participants indicate their current beliefs and intentions after viewing the label. Prior to viewing the labels, survey participants did not receive information that the current warnings were sourced and endorsed by the federal government and that the others were proposed by Swedish Match, which may be relevant to the perceptions they generated. Capella et al. tested the effect of manufacturer-sourced reduced-risk messages for ST products ("Using this product is [90% less dangerous or 90% safer] than cigarettes") in the presence or absence of the four government-mandated warnings (29). They found that the reduced-risk messages had limited impact in altering smokers' perceptions of ST risks in the presence of conflicting government warnings. When smokers viewed the reduced-risk messages in the absence of the government warning, there was an improvement in smokers' perceptions of ST lower risks. The authors suggested that effective harm reduction communication for ST products would require not just an additional message but a change in the government warnings.

Other limitations were that participants were obtained from online consumer panels, **which under-represent subjects with lower education and literacy. In addition,** recruitment was designed to enroll equal numbers of tobacco users and non-users; thus, the results may not be generalizable. Tobacco status was based on self-report, but unvalidated self-report in non-treatment settings is thought to be reliable (31). Each participant viewed only one label, so the results from the proposed labels may be different if participants see them in the context of other warnings rotated over time. Finally, individuals may habituate to the messages, and the labels may become less effective over time.

Strengths of our study include the large sample sizes of the five tobacco-use subgroups that were demographically similar. The survey was specifically designed and executed to examine the perception of existing and proposed snus warnings among users of tobacco and non-users, according to recommendations included in a guidance document for modified risk applications published by the CTP

(7). Perhaps the most important strength was that our results were reasonably consistent across the three tobacco user groups and across the two non-user groups, suggesting convergent validity.

Are the effects of the proposed labels seen in this study large enough to change tobacco use behavior in a meaningful public health context? That is an open question. It is possible that the introduction and repeated viewing of a new label under FDA supervision could have larger effects than were measured by this study. Post-market surveillance, which is prescribed in the TCA, will provide valuable information on whether negative or positive public health outcomes occur.

In summary, although one cannot impute causality from association, our analysis of this pre-marketing survey suggests that tobacco users viewing the proposed relative-risk labels are more likely to perceive snus as less harmful than cigarettes and may be more likely to use and buy snus. Although snus use is not completely risk-free, the risks pale in comparison to those of smoking. If increased snus use results in cigarette reduction or abstinence, this is likely to outweigh any harm from snus use per se. The substantially lower risk label increased motivation to buy snus among non-users, which could be a public health risk if it led to increased smoking. But if mostly non-users who would have started smoking are diverted to snus, this could a public health benefit. Clearly, well-designed post- marketing studies will be necessary to understand the impact of the proposed new labeling.

FUNDING

None

DECLARATION OF INTERESTS

Swedish Match formed an advisory board for consultation during the submission to the CTP. After Swedish Match's FDA submission, the board independently decided to undertake its own analysis of the premarket survey. BR and NP are supported by unrestricted grants from tobacco manufacturers, including Swedish Match, to the University of Louisville, and by the Kentucky Research

Challenge Trust Fund. Neither has any financial or other personal relationship with regard to the sponsors. JRH has received consulting and speaking fees from several companies that develop or market pharmacological and behavioral treatments for smoking cessation or harm reduction, and from several non-profit organizations that promote tobacco control. He serves on the Swedish Match advisory board with no compensation. JRH's time was supported by grant P50 DA036114 from the US National Institute on Drug Abuse. KF has received consulting and speaking fees from several companies that develop or market treatments for smoking cessation or harm reduction. He serves on the Swedish Match advisory board with no compensation.

ACKNOWLEDGMENTS

The authors express their appreciation to Dr. Lars Erik Rutqvist and Mr. Vijay Rajan of Swedish Match for providing many technical and logistic details about the survey design and implementation. The authors are grateful for comments and suggestions provided by Dan Casciano, Mark Frankel and Nancy Ostrove, who also serve on the advisory board for the MRTP application.

REFERENCES

1. Borland R., Hill D. Initial impact of the new Australian tobacco health warnings on knowledge and beliefs. *Tob Control*. 1997;6:317-25. doi.org/10.1136/tc.6.4.317

2. Borland R. Tobacco health warnings and smoking related cognitions and behaviours. *Addiction.* 1997;92:1427-1435. doi.org/10.1111/j.1360-0443.1997.tb02864.x

3. Partos TR, Borland R, Yong HH, Trasher J, Hammond D. Cigarette packet warning labels can prevent relapse; findings from the International Tobacco Control 4-country policy evaluation cohort study. *Tob Control.* 2013;22:226-233. doi.org/10.1136/tobaccocontrol-2011-050254

4. Hammond D, Fong GT, Borland R, Cummings KM, McNeill A, Driezen P. Text and graphic warnings on cigarette packages: findings from the international tobacco control four country study. *Am J Prev Med.* 2007;32:202-209. doi.org/10.1016/j.amepre.2006.11.011

5. Hitchman SC, Driezen P, Logel C, Hammond D, Fong GT. Changes in effectiveness of cigarette health warnings over time in Canada and the United States, 2002-2011. *Nicotine Tob Res.* 2014;16:536-43. doi.org/10.1093/ntr/ntt196

6. U.S. Department of Health and Human Services, Food and Drug Administration. Public Law 111-31, June 22, 2009. Family Smoking and Prevention and Tobacco Control and Federal Retirement Reform. Available at: http://www.gpo.gov/fdsys/pkg/PLAW-111publ31/pdf/PLAW-111publ31.pdf (Accessed March 24, 2015).

7. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Tobacco Products. Guidance for Industry. Modified Risk Tobacco Product Applications DRAFT GUIDANCE. March 2012. Available at:

http://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM297751.pdf (Accessed March 24, 2015).

8. Levy DT, Mumford EA, Cummings KM, Gilpin EA, Giovino G, Hyland A, et al. The relative risks of a low-nitrosamine smokeless tobacco product compared with smoking cigarettes: estimates of a panel of experts. *Cancer Epidemiol Biom Prev.* 2004;13:2035-2042. doi not found.

9. Nutt DJ, Phillips LD, Balfour D, Curran HV, Dockrell M. Estimating the harms of nicotine-containing products using the MCDA approach. *Eur Addict Res.* 2014;20:218-252. doi.org/10.1159/000360220

10. Lee PN. Epidemiological evidence relating snus to health – an updated review based on recent publications. *Harm Red J.* 2013;10**:**10-36. doi:10.1186/1477-7517-10-36

11. Rodu B. The scientific foundation for tobacco harm reduction, 2006-2011. *Harm Red J.* 2011;8**:**19. doi:10.1186/1477-7517-8-19

12. U.S. Department of Health and Human Services, Food and Drug Administration. Swedish Match North America MRTP Applications. Regulations.gov Docket FDA-2014-N-1051. Available at: http://www.accessdata.fda.gov/Static/widgets/tobacco/SMNA_MRTPA_FDA-2014-N-1051.html (Accessed March 24, 2015).

13. U.S. Department of Health and Human Services, Food and Drug Administration. Swedish Match Premarket Consumer Research Report. Available at: http://www.accessdata.fda.gov/Static/widgets/tobacco/MRTP/23%20appendix-6f-sm-premrkt-cnsmer-percept/premarket-consumer-research-report_Redacted.pdf (Accessed March 24, 2015).

14. Centers for Disease Control and Prevention. Vital signs: current cigarette smoking among adults aged ≥ 18 years – United States, 2005-2010. *Morbid Mortal Weekly Rep*. 2011;35:1207-1212. Available at:

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6035a5.htm?s_cid=mm6035a5_w (Accessed March 24, 2015).

15. Lee PN. Circulatory disease and smokeless tobacco in Western populations: a review of the evidence. *Int J Epidemiol.* 2007;36:789–804. doi.org/10.1093/ije/dym039

16. Lee PN, Hamling JS. Systematic review of the relation between smokeless tobacco and cancer in Europe and North America. *BMC Medicine*. 2009;7:36. doi:10.1186/1741-7015-7-36.

17. Royal College of Physicians of London. Protecting smokers, saving lives: the case for a tobacco and nicotine authority. London,England, 2002. Available at: https://www.rcplondon.ac.uk/publications/protecting-smokers-saving-lives (Accessed March 24, 2015).

18. Rodu B. An alternative approach to smoking control. *Am J Med Sci*. 1994;308:32-34. dx.doi.org/10.1097/00000441-199407000-00007

19. Vigneswaran N, Tilashalski K, Rodu B, Cole P. Tobacco use and cancer: a reappraisal. *Oral Surg Oral Med Oral Pathol*. 1995;80:178-182. dx.doi.org/10.1016/S1079-2104(05)80199-4

20. Rodu B, Cole P. Nicotine maintenance for inveterate smokers. *Technol*. 1999;6:17-21. Doi not available.

21. Regan AK, Dube SR, Arrazola R. Smokeless and flavored tobacco products in the U.S.: 2009 Styles survey results. *Am J Prev Med.* 2012;42:29-36. doi.org/10.1016/j.amepre.2011.08.019

22. O'Connor RJ, Hyland A, Giovino G, Fong GT, Cummings KM. Smoker awareness of and beliefs about supposedly less-harmful tobacco products. *Am J Prev Med.* 2005;29:85-90. doi.org/10.1016/j.amepre.2005.04.013

23. Cummings KM. Informing consumers about the relative health risks of different nicotine delivery products", paper presented at the National Conference on Tobacco and Health, New Orleans, LA, November, 2001.

24. 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;9:1033-1042. doi.org/10.1080/14622200701591583

25. Haddock CK, Lando H, Klesges RC, Peterson AL, Scarinci IC. Modified tobacco use and lifestyle change in risk-reducing beliefs about smoking. *Am J Prev Med.* 2004;27:35-41. doi.org/10.1016/j.amepre.2004.03.010

26. Peiper N, Stone R, Van Zyl R, Rodu B. University faculty perceptions of the health risks related to cigarettes and smokeless tobacco. *Drug Alcohol Rev*. 2010;29:121-130. doi.org/10.1111/j.1465-3362.2009.00143.x

27. Callery WE, Hammond D, O'Connor RJ, Fong GT. The appeal of smokeless tobacco products among young Canadian smokers: the impact of pictorial health warnings and relative risk messages. *Nicotine Tob Res*. 2011;13:373-383. doi.org/10.1093/ntr/ntr013

28. Levy DT, Mumford EA, Cummings KM, et al. The potential impact of a low-nitrosamine smokeless tobacco product on cigarette smoking in the United States: estimates of a panel of experts. *Addict Behav*. 2006;31:1190-1200. doi.org/10.1016/j.addbeh.2005.09.010

29. Capella ML, Taylor CR, Kees J. Tobacco harm reduction advertising in the presence of a government-mandated warning. *J Consumer Aff*. 2012;46:235-259. doi.org/10.1111/j.1745-6606.2012.01229.x

30. Borland R, Li L, Cummings MK, et al. Effects of a fact sheet on beliefs about the harmfulness of alternative nicotine delivery systems compared with cigarettes. *Harm Red J*. 2012;9:19 doi:10.1186/1477-7517-9-19.

31. Caraballo RS, Giovino GA, Pechacek TF, Mowery PD. Factors associated with discrepancies between self-reports on cigarette smoking and measured serum cotinine levels among persons aged 17 years or older. *Am J Epidemiol*. 2001;153:807–814. doi.org/10.1093/aje/153.8.807

FIGURE LEGENDS

Supplemental Figure 1. Images of the four current warnings and the two proposed labels shown to survey participants. Reproduced with permission from Swedish Match.

Figure 1. **The percentage of subjects, according to tobacco status, who reported that the warning was believable, that using snus daily was harmful*, that they were likely to use snus and motivated to buy snus, for mouth cancer, gum and tooth, and addictive warnings.**

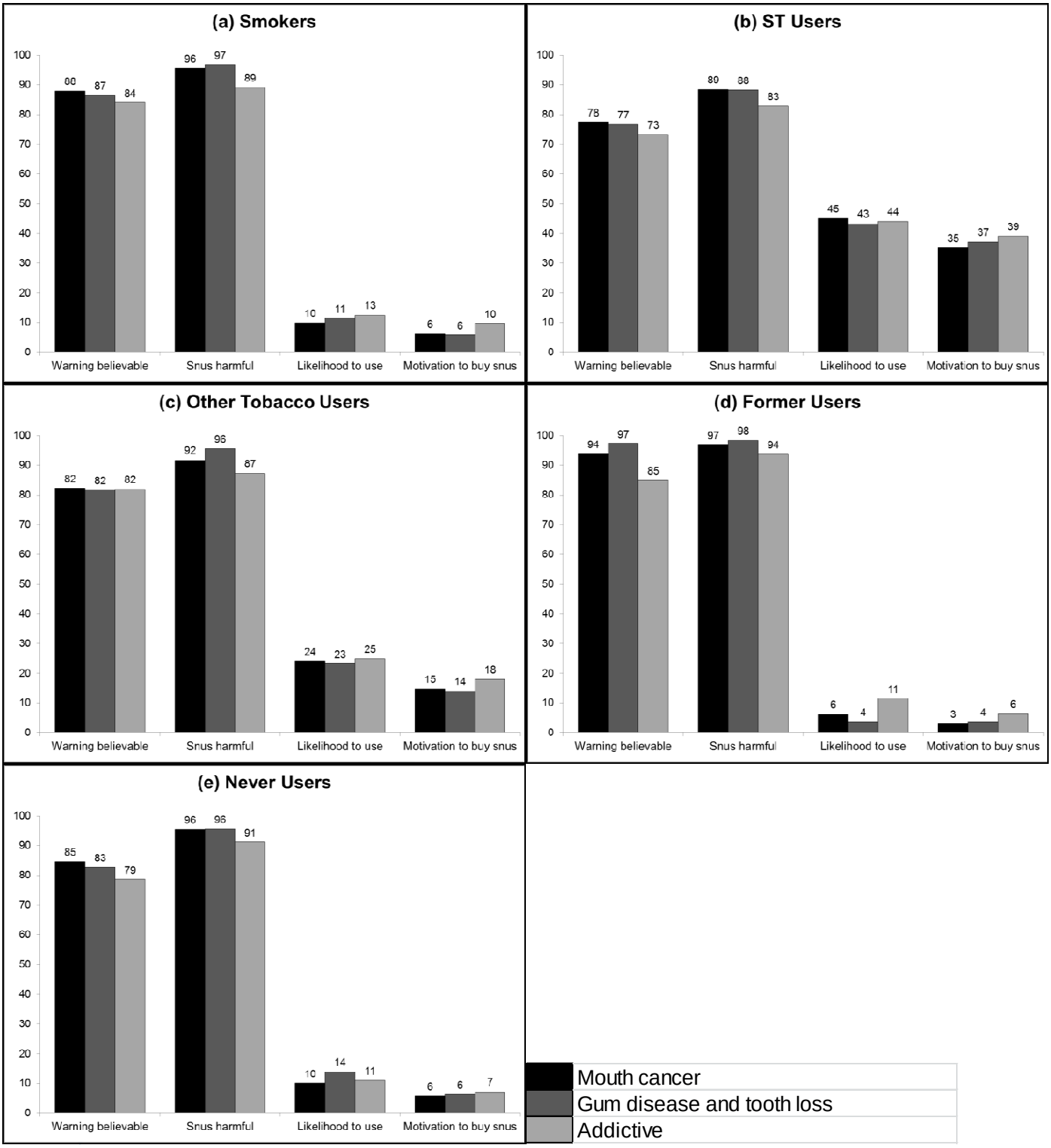
Figure 2. The percentage of subjects, according to tobacco status, who reported that the label was believable, that using snus daily was harmful*, that they were likely to use snus and motivated to buy snus, for the not-safe-alternative, lower-risk, and substantially-lower-risk labels.

Table 1. Adjusted* odds ratios with 95% CI for outcomes for proposed warning labels compared with the current not-safe-alternative label, according to tobacco status

	Believable	Daily Snus Harmful	Likelihood to Use Snus	Motivation to Buy Snus
Model 1: Smokers				
Warning label: ref. Not-safe-alternative				
Lower risk	**0.32 [0.25,0.40]**	**0.51 [0.33,0.80]**	**1.80 [1.35,2.43]**	**3.50 [2.43,5.04]**
Substantially lower risk	**0.33 [0.26,0.42]**	**0.45 [0.29,0.69]**	**2.07 [1.55,2.77]**	**4.0 [2.82,5.79]**
Observation	2170	2009	2170	2170
Model 2: ST users				
Warning label: ref. Not-safe-alternative				
Lower risk	**0.59 [0.35,0.97]**	**0.39 [0.21,0.72]**	1.45 [0.93,2.27]	**1.92 [1.21,3.05]**
Substantially lower risk	**0.59 [0.35,0.98]**	0.53 [0.28,1.00]	**2.04 [1.29,3.24]**	**2.15 [1.35,3.41]**
Observation	510	502	510	510
Model 3: Other tobacco users				
Warning label: ref. Not-safe-alternative				
Lower risk	**0.39 [0.25,0.62]**	0.89 [0.47,1.71]	1.51 [0.94,2.42]	1.47 [0.91,2.38]
Substantially lower risk	**0.56 [0.36,0.88]**	0.71 [0.38,1.30]	**2.29 [1.45,3.64]**	**1.93 [1.21,3.08]**
Observation	590	564	590	590
Model 4: Former tobacco users				
Warning label: ref. Not-safe-alternative				
Lower risk	**0.49 [0.27,0.92]**	1.02 [0.21,4.99]	0.72 [0.28,1.83]	0.40 [0.09,1.74]
Substantially lower risk	**0.40 [0.22,0.73]**	0.80 [0.19,3.24]	0.56 [0.21,1.44]	0.97 [0.30,3.13]
Observation	347	307	347	347
Model 5: Triers/never users				
Warning label: ref. Not-safe-alternative				
Lower risk	**0.36 [0.30,0.43]**	0.86 [0.58,1.27]	1.02 [0.77,1.35]	1.31 [0.93,1.84]
Substantially lower risk	**0.35 [0.29,0.42]**	**0.53 [0.37,0.76]**	1.24 [0.95,1.63]	**1.88 [1.35,2.60]**
Observation	2972	2801	2972	2972

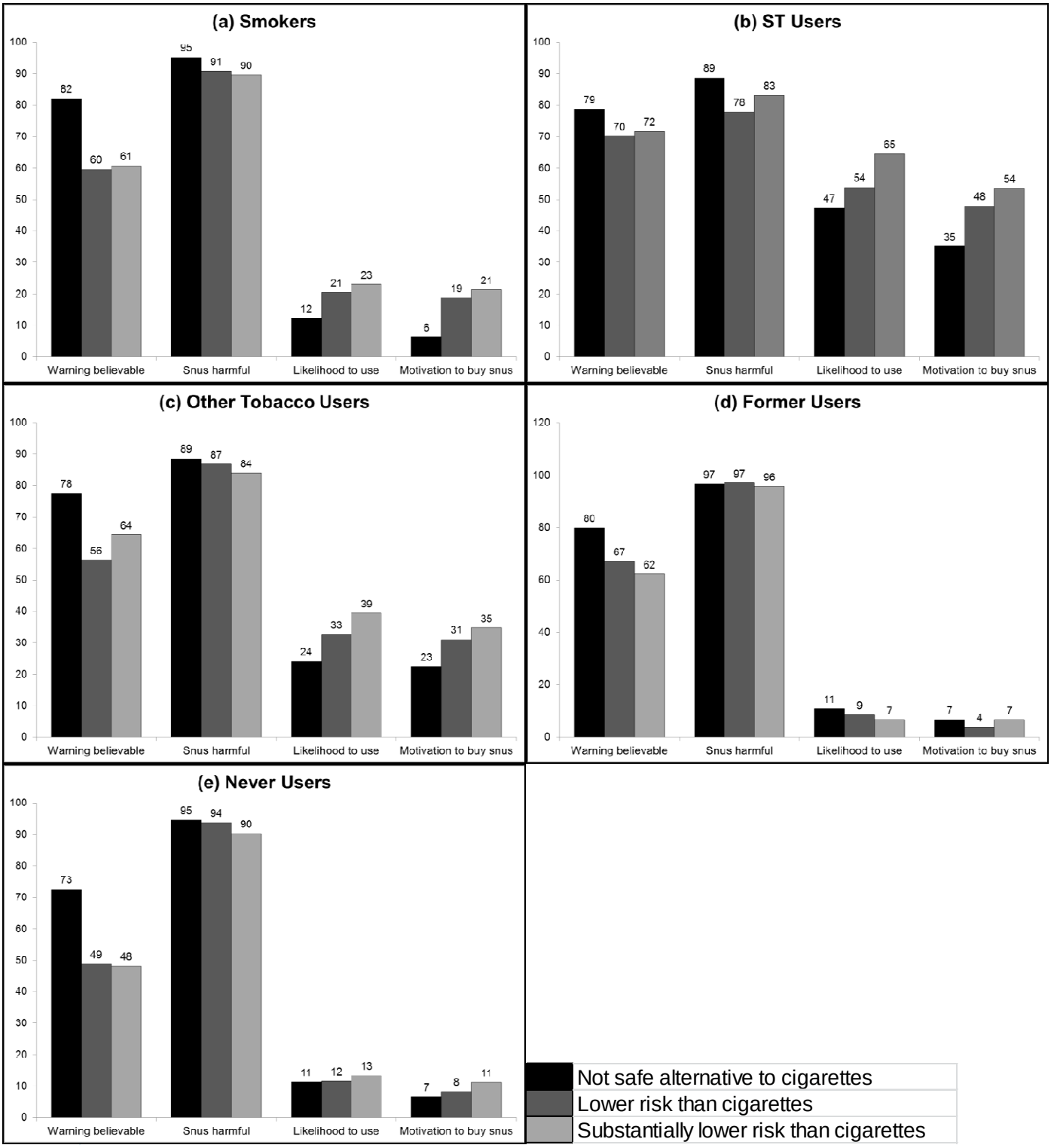
* All models adjusted for sex, age, race/ethnicity, income, region, education and marital status.
Bold numbers indicate statistically significant at 95% confident level.

Figure 1.



* The final samples for perceived harm of using snus daily are 12,571 (4,057 smokers, 1,022 ST users, 1,157 other tobacco users, 694 former users and 5,641 triers/never users).

Figure 2.



* The final samples for perceived harm of using snus daily are 12,571 (4,057 smokers, 1,022 ST users, 1,157 other tobacco users, 694 former users and 5,641 triers/never users).