

7.5.2-2: UPDATE: USER BEHAVIOR LITERATURE SUMMARY

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LIST OF ABBREVIATIONS

ACE	adverse childhood experience
AHS	Agricultural Health Study
ALDH2	aldehyde dehydrogenase 2 family
ANP	alternative nicotine product
AOR	adjusted odds ratio
APC	annual percentage change
aRRR	adjusted relative risk ratio
ATP	alternative tobacco product
AUDADIS	Alcohol Use Disorder and Associated Disabilities Interview Schedule
BRFSS	Behavioral Risk Factor Surveillance System
CI	confidence interval
C-OS	cigarette-only smokers
CTN	Clinical Trials Network
CU	concurrent use
DECOY	Documenting Experiences with Cigarettes and Other Tobacco in Young Adults
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders
EC	electronic cigarette
EEG	electroencephalography
ETP	emerging tobacco product
FDA	Food and Drug Administration
FOR	fecundability odds ratio
FTND-ST	Fagerstrom Test for Nicotine Dependence – smokeless tobacco
HED	heavy episodic drinking
HIV	human immunodeficiency virus
LCC	little cigar/cigarillo
LCMS	liquid chromatography mass spectrometry
LGBT	lesbian, gay, bisexual, and transgendered
MATCH	Mexican American Tobacco Use in Children
mCES	modified version of the Cigarette Evaluation Scale (also referred to as the Cigarette Evaluation Questionnaire)
mFTND	modified version of the Fagerstrom Test for Nicotine Dependence
MNWS-R	Minnesota Nicotine Withdrawal Scales-Revised
mQSU-brief	modified version of the Questionnaire on Smoking Urges
MRTPA	Modified Risk Tobacco Product Application
MSC	moist snuff consumers
NATS	National Adult Tobacco Survey
NCTP	noncigarette tobacco products
NCYTS	North Carolina Youth Tobacco Survey
ND	nicotine dependence
NESARC	National Epidemiologic Survey on Alcohol and Related Conditions
NHIS	National Health Interview Survey
NIDA	National Institute on Drug Abuse
NMR	nicotine metabolite ratio
NNN	N-nitrosornicotine
NNAL	nitrosamine, 4-(methylnitrosamino-1-(3-pyridyl)-1-butanol
NRT	nicotine replacement therapy
NSDUH	National Survey on Drug Use and Health
NTC	non-tobacco consumers
NYC YRBS	New York City Youth Risk Behavior Survey
NYTS	National Youth Tobacco Surveys
OR	odds ratio
OTP	other tobacco product

PATH	Population Assessment of Tobacco and Health
PBMC	peripheral blood mononuclear cell
PLWH	persons living with human immunodeficiency virus
PROMIS	Patient Reported Outcomes Measurement Information System
PTU	polytobacco use
qPCR	quantitative polymerase chain reaction
RR	relative risk
SD	standard deviation
SERGEF	Secretion Regulating Guanine Nucleotide Exchange Factor
SES	socioeconomic status
SLC6A4	Solute Carrier Family 6 Member 4
SMK	consumers of cigarettes
ST	smokeless tobacco
TDS	Tobacco Dependence Screener
TNCP	tobacco and nicotine containing product
TRH-DE	thyrotropin-releasing hormone-degrading ectoenzyme
TTP	time-to-pregnancy
TUS-CPS	Tobacco Use Supplement to the Current Population Survey
U.S.	United States
USAF	United States Air Force
YRBS	Youth Risk Behavior Survey

7.5.2-2. TOBACCO USER BEHAVIOR LITERATURE SUMMARY

The Food and Drug Administration's 2012 Modified Risk Tobacco Product Applications (MRTPAs) draft guidance Section VI (A) (2) recommends that applicants address:

- the likelihood that current tobacco product users will start using the candidate product;
- the likelihood that consumers will use the candidate product in conjunction with other tobacco products;
- the likelihood that users who may have otherwise quit using tobacco products will instead use the candidate product;
- the expected rates of use of the tobacco product by current tobacco users;
- the effect the tobacco product and its marketing may have on tobacco use behavior among current tobacco users; and
- nonclinical and/or human studies to assess the abuse liability and the potential for misuse of the candidate product as compared to other tobacco products on the market.

To update the assessments in Section 7.5.2-1 describing how the candidate modified risk tobacco products may affect user behavior as outlined in Section VI(A)(2) of the MRTPA 2012 Draft Guidance, this section summarizes the more recently published scientific literature on smokeless tobacco (ST) use behaviors and abuse liability of ST products typically marketed in the United States (U.S.).

7.5.2-2.1.Literature Search and Review Process

A comprehensive literature review was conducted through December 2014 that reviewed the health and behavioral effects of ST (Section 7.5.1), and literature summaries were drafted in areas that are important in the assessment of a modified risk tobacco product candidate. A second literature review was conducted for the period of December 08, 2014, to February 06, 2017, to update the original search. During the new search, 1,029 citations were identified, and, after applying predetermined inclusion and exclusion criteria, 165 articles were deemed to be in-scope. In general, the in-scope articles were peer-reviewed and included ST products commercially available in the U.S.

A keyword assignment exercise was performed to determine how many of these articles provide information informing the likelihoods and potential effects described in the Draft Guidance document (switching to ST, use of ST in conjunction with other tobacco products, intercepting quitters, patterns of use, and abuse liability of ST). There were 14, 47, 3, 62, and 7 articles for each of the topics, respectively. However, five of these articles had been included in the first review even though they were published after the review's cut-off date. To avoid presenting the same article in both the original and updated literature reviews, we excluded from the update two articles addressing the use of ST in conjunction with other

tobacco products, one article addressing patterns of ST use, and two articles addressing the abuse liability of ST from the updated review.

This section is intended to supplement the previous literature review (Section 7.5.2-1) to provide a current, updated literature review of the aforementioned topics.

7.5.2-2.2. The Likelihood that Current Tobacco Users Will Start Using the Product

Noteworthy articles found in this literature review update that inform the likelihood that current tobacco users will switch to the candidate product are highlighted below, and all 14 articles are summarized in [Table 7.5.2-2-1](#).

7.5.2-2.2.1. Clinical Trials

Carpenter et al. ([Carpenter et al., 2016](#)) and Burris et al. ([Burris et al., 2016](#)) presented data from a study in current cigarette smokers who had not used smokeless tobacco or other reduced exposure products in the prior 6 months and who were not interested in quitting smoking. Both of these reports are discussed also in Section 7.5.2-2.4.1. Subjects were randomized to receive samples of snus or not for a 6-week sampling period. After the sampling period, the groups were monitored for 1 year for tobacco use. Carpenter et al. reported the quit attempts for cigarettes during the period and found that smokers in the snus group (n = 626) were less likely to make quit attempts than smokers in the control group (n = 610) but that there were no group difference in any measure of abstinence between the snus group and the no intervention group. Burris et al. focused on the 626 subjects in the snus group and noted that the study closely mimicked “the tobacco industry's direct-to-consumer approach.” At the end of the sampling period, 47.1% of the group were current users of snus, and 17.6% of the group were frequent user of snus. At Week 58 6.5% were current users of snus, and 1.9% were frequent users of snus. Adoption of snus, which the authors defined as purchase of snus, occurred in 11.0% of the snus group, and 40.6% of the subjects who purchased snus once purchased it at least one more time.

Hatsukami et al. ([2016](#)) reported on a clinical trial in which cigarette users interested in switching to snus or nicotine gum were randomized to receive either snus or nicotine gum for 12 weeks. The smokers were instructed to completely switch from cigarettes to the provided product. At Week 6, of the group assigned to snus (n = 149), 37.6% were only using snus, 55.0% were using snus and cigarettes, 3.4% were only using cigarettes, and 4.0% were not using either snus or cigarettes. At Week 12, among the group assigned to snus (n = 138), 26.8% were only using snus, 52.9% were using snus and cigarettes, 11.6% were only using cigarettes, and 8.7% were not using either snus or cigarettes. There was no statistical difference in the tobacco product use between those assigned to snus and nicotine gum. Meier et al. ([2016](#)) reported on the flavor selection for this study and stated that majority of the consumers selected the snus with a mint flavor.

Rousu et al. ([Rousu, O'Connor, Bansal-Travers, Pitcavage, & Thrasher, 2015](#)) investigated consumer demand for alternative nicotine products by using an experimental auction. Current cigarette smokers were randomized to receive an offering of a free trial of one of three novel ST products (snus, dissolvable tobacco, or medicinal nicotine) or to join the control group

(no trial offered). After the free trials were completed, all participants were requested to bid for the products to investigate the demand. Free trials of the novel ST products were not strongly associated with product demand as determined by willingness to pay for them.

7.5.2-2.2.2. Surveys

Rodu et al. (Rodu, Plurphanswat, Hughes, & Fagerstrom, 2016) surveyed exclusive cigarette smokers, daily ST users, daily users of other tobacco products, former users, and never-users about their response to proposed relative-risk labels for snus. Tobacco users viewing the proposed label perceived snus as less harmful than cigarettes and were more likely to intend to use and buy snus. Schauer et al. (2016) analyzed the 2010-2011 Tobacco Use Supplement to the Current Population Survey (TUS-CPS) for the impact of use of other forms of tobacco on smoking cessation. Dual tobacco use was not associated with decreased attempts to quit smoking cigarettes.

7.5.2-2.2.3. Longitudinal Data

Tam et al. (Tam, Day, Rostron, & Apelberg, 2015) conducted a systematic review of literature published from 2000 to 2014 on transitions between ST and cigarette use and identified six studies containing longitudinal data on some or all of the transitions that users can undergo between ST and cigarette use. While there were considerable differences between the six studies, the authors noted that “the existing data indicate that switching behaviors from exclusive smoking to exclusive [ST] use are limited (adults: 0%-1.4%, adolescents: 0.8%-3.8%) but may be more common from exclusive [ST] use to exclusive smoking (adults: 0.9%-26.6%, adolescents: 16.6%-25.5%).”

7.5.2-2.2.4. Adolescents

Kaufman et al. (Kaufman, Land, Parascandola, Augustson, & Backinger, 2015) evaluated transitions between cigarette and ST use from four waves of the National Longitudinal Study of Adolescent Health between 1995 (adolescence) and 2008 to 2009 (young adulthood). Results indicated that adolescents who use multiple tobacco products are likely to continue such use as they move into young adulthood. Subjects who had reported exclusive cigarette use and who were female, black, and younger were less likely to report subsequent ST use than exclusive cigarette smokers who were male, white, and older.

The risk for transitioning between cigarettes and ST was higher for males and those who were older.

Persoskie et al. (Persoskie, Donaldson, & King, 2016) investigated curiosity about tobacco products and if it leads to ever-use of these products. Data from the 2012 and 2014 National Youth Tobacco Surveys (NYTS), in which never-users of specific tobacco products were asked about their curiosity about the product, were analyzed. Between the two surveys, ever-use of and curiosity about ST did not change significantly. In 2014, the proportion of young people who had never used ST and were “definitely” or “probably” curious about ST was 4.4%.

7.5.2-2.2.5. Updated Findings

Information in the updated literature review on the likelihood that current tobacco users will start using the candidate product is consistent with that seen in the initial literature review. The conclusions from the initial literature review (Section [7.5.2-1.1.4](#)) have not changed based on the updated literature review.

A tabular summary of the literature informing the likelihood of current tobacco users switching to ST is presented in [Table 7.5.2-2-1](#).

Table 7.5.2-2-1: Literature Summary for Switching to Smokeless Tobacco Products

Author	Title	Study Methods	Primary Study Measurement and Endpoints	Author's Findings Related to Switching to Smokeless Tobacco Products	Comments ^a
(Carpenter et al., 2016)	Snus undermines quit attempts but not abstinence: a randomized clinical trial among US smokers	Adult smokers (N = 1,236) throughout U.S. who denied intention to quit in the next 30 days were randomized to receive (n = 626; mean age: 48.7 years; 70% female; 89% Caucasian) or to not receive (n = 610; mean age: 48.7 years; 65% female; 87% Caucasian) free snus during a 6-week sampling period. Subjects were then advised to quit all tobacco use and were followed for 1 year. Objective: To examine the impact of snus use within a naturalistic, noncessation context.	Primary outcomes: Self-reported quit attempts, floating abstinence, and 7-day point-prevalence abstinence at 6 months and 1 year. Secondary outcomes: Changes in smoking, motivation and confidence to quit, and adverse events.	<p>Within snus group, 82% used at least once, and 16% used regularly at the end of the sampling period.</p> <p>Compared with control subjects, smokers in the snus group were less likely to make any quit attempt (RR = 0.83; 95% CI: 0.70 to 1.00) and any 24-hour quit attempt (RR = 0.77; 95% CI: 0.63 to 0.95). There were no statistically significant differences between the groups on any measure of abstinence.</p> <p>Subjects in both groups reduced the number of cigarettes smoked per day (by 23%) and increased both their motivation and confidence to quit smoking. There were no statistically significant differences between the snus and control groups, and motivation to quit smoking remained low at the end of the sampling period and at the final follow-up.</p>	Limitations: (1) Only one product was used; (2) study sample consisted primarily of Caucasian women; (3) participants were smokers who did not want to quit, which may create the impression that it was methodologically biased against snus; and (4) there is a lack of biochemical verification of abstinence.

Author	Title	Study Methods	Primary Study Measurement and Endpoints	Author's Findings Related to Switching to Smokeless Tobacco Products	Comments ^a
(Courtemanche, Palmer, & Pesko, 2017)	Influence of the flavored cigarette ban on adolescent tobacco use	Data from the 1999-2013 NYTS (N = 197,834 middle school and high school students; age: 11-19 years) were evaluated for tobacco use before and after the FDA's 2009 ban on flavored cigarettes Objective: To estimate the association between U.S. FDA's 2009 ban on flavored cigarettes and adolescents' tobacco use.	Outcomes were past 30-day cigarette use; cigarettes smoked in the past 30 days among smokers; rate of menthol cigarette use among smokers; and past 30-day use of cigars, ST, pipes, any tobacco products besides cigarettes, and any tobacco products including cigarettes. The analysis controlled for a quadratic time trend, demographic variables, prices of tobacco products, and teenage unemployment rate.	Banning flavored cigarettes was associated with reduction in the probability of being a cigarette smoker (17%, $p < 0.001$) and cigarettes smoked by smokers (58%, $p = 0.005$). However, the ban was positively associated with the use by smokers of menthol cigarettes (45%, $p < 0.001$), cigars (34%, $p < 0.001$), and pipes (55%, $p < 0.001$), implying substitution toward the remaining legal, flavored tobacco products. Overall there was a 6% ($p < 0.001$) reduction in the probability of using any tobacco. The change in ST use in the past 30 days was small and insignificant, being 0.042% before the ban and 0.041% after the ban. ST had a low rate of use throughout the sample period.	Limitations: (1) Estimating the causal effect of any national law is difficult because only time-series variation is available for identification; (2) NYTS data do not allow for the analysis of several relevant outcomes; (3) although the analysis controlled for a quadratic time trend, it did not allow for separate trends before and after the ban; and (4) NYTS consists of repeated cross-sections, preventing the observation of changes among the same individuals from before to after the ban.

Author	Title	Study Methods	Primary Study Measurement and Endpoints	Author's Findings Related to Switching to Smokeless Tobacco Products	Comments ^a
(Popova, So, Sangalang, Neilands, & Ling, 2017)	Do emotions spark interest in alternative tobacco products?	In 2013, 1,226 (48% male; 38.6% white) U.S. adult nonsmokers (n = 403) and current smokers (n = 823) viewed advertisements for moist snuff, snus, and ECs with various warning labels and then indicated their emotional responses in terms of anger, anxiety, sadness, guilt, disgust, discouragement, hope, and contentment. Objective: To evaluate the association of discrete positive and negative emotions with interest in alternative tobacco products.	Outcomes were openness to using moist snuff, snus, and ECs in the future and interest in a free sample of each product.	Hope was positively associated with openness and interest across all alternative tobacco products as well as contentment for moist snuff and snus. "Anger was negatively associated with openness to moist snuff and [ECs], disgust was associated negatively to moist snuff and snus, and anxiety was associated negatively to [ECs]. Being a current smoker, ever trying a corresponding product, being male, and being younger in age were associated with greater openness to and interest in moist snuff and snus. For [ECs], being a current smoker, ever trying [ECs], and being female were associated with greater openness, and being a current smoker was associated with greater odds of selecting a free sample."	Limitations: (1) The use of convenience sample led to findings that may not be generalizable to the overall U.S. population; and (2) a single forced exposure to advertisements and a lack of behavioral outcome limit ecological validity.

Author	Title	Study Methods	Primary Study Measurement and Endpoints	Author's Findings Related to Switching to Smokeless Tobacco Products	Comments ^a
(Banerjee, Greene, Li, & Ostroff, 2016)	The effect of comparatively-framed versus similarity-framed e-cigarette and snus print ads on young adults' ad and product perceptions	A total of 1,051 young adults (18-24 years of age; 76% women; 50% smokers) from existing consumer panels were recruited in a within-subjects quasi-experiment to view four online advertisements, varied by tobacco product type (e-cigarette or snus) and ad framing (comparative versus similarity framing). Objective: To compare the effects of comparative framing versus similarity framing in e-cigarette and snus ads on young adult smokers' and nonsmokers' ad- and product-related perceptions.	The dependent measures for this study were ad perceptions, ad credibility, absolute and comparative risk perceptions, product appeal, and product use intentions.	Former and current smokers (but not never-smokers) rated comparative framing ads as more persuasive than similarity framing ads; and rated EC ads with more favorable ad perceptions, low absolute and comparative perceptions, high product appeal, and high product use intentions as compared with snus ads. The study indicated that that EC and snus print ads, particularly the ones that exhibit comparisons with conventional cigarettes or ST, provide compelling risk reduction beliefs and reduce the strong likelihood of product use among young adult current and former smokers.	Limitations: (1) The use of online convenience sampling limited the generalizability of the findings to all young adults; (2) the study used a quasi-experimental study design that limited the control over stimuli; (3) the study did not control for brand or current e-cigarette– and snus-use status of subjects; and (4) the study relied on self-reported data and did not measure actual behavior.

Author	Title	Study Methods	Primary Study Measurement and Endpoints	Author's Findings Related to Switching to Smokeless Tobacco Products	Comments ^a
(Burris et al., 2016)	A longitudinal, naturalistic study of U.S. smokers' trial and adoption of snus	Adult smokers (N = 1,236) throughout U.S. who denied intention to quit in the next 30 days were randomized to receive (n = 626; mean age: 48.7 years; 70% female; 89% Caucasian) or not receive (n = 610; mean age: 48.7 years; 65% female; 87% Caucasian) free snus during a 6-week sampling period. Subjects were then advised to quit all tobacco use and were followed for 1 year. Objective: To advance the current literature via a detailed description of snus uptake during a longitudinal study with adult U.S. smokers who denied intention to stop smoking in the near future.	Tobacco use outcomes were collected at each follow-up assessment (Week 0 to 58). Subjects in the snus group, if they decided to use snus, were asked about the reason they decided to use snus.	84% of subjects reported trial of snus. 11% reported purchase (i.e., adoption). Current use declined from 47.1% at the end of the sampling period to 6.5% at the end of follow-up. Frequency and quantity of snus use among current users were low. Among snus users, 79.3% said it functioned as an alternative to smoking, and 58.4% said it provided a means of coping with smoking restrictions. Smokers showed willingness to try snus, but product interest waned over time. Snus as currently marketed is unlikely to play a prominent role in U.S. tobacco control efforts.	Strength: It was a longitudinal study. Limitations: (1) Only a single snus product was offered; (2) study population consisted of smokers who reported little-to-no interest in smoking cessation; (3) white, non-Hispanics and females are both overrepresented in this U.S. sample.

Author	Title	Study Methods	Primary Study Measurement and Endpoints	Author's Findings Related to Switching to Smokeless Tobacco Products	Comments ^a
(Hatsukami et al., 2016)	Randomized clinical trial of snus versus medicinal nicotine among smokers interested in product switching	Cigarette smokers (n = 391; mean age: 43.9 years; 47.1% female; 81.8% non-Hispanic, white) recruited in Minnesota and Oregon were randomized to either snus or 4 mg nicotine gum for 12 weeks and asked to stop smoking. Objective: To compare snus versus nicotine gum on the extent to which smokers can completely switch to these products, the pattern of the product use, and effects on biomarkers of exposure; and to compare the effects of both products on withdrawal symptom relief, product evaluation and adverse events.	Product use and any cigarette smoked on daily basis collected by IVR system. At follow-up, recall of tobacco products were assessed by time line follow-back.	At Week 6, for the group assigned to snus, 37.6% was only using snus, and 55.0% was using snus and cigarettes. At Week 12, this group had 26.8% only using snus, and 52.9% was using snus and cigarettes. There was no statistical difference in the tobacco product use between those assigned to snus and those assigned to nicotine gum. Dual use of cigarettes and these products was observed in 52.9% and 58.2% of those assigned to snus and nicotine gum, respectively, at Week 12.	Limitations: (1) Potential lack of generalizability to a general population of smokers because the study examined smokers interested in trying an alternative product in a clinical setting; (2) only one snus product tested; (3) encouragement to use a specified number of pieces of each of the products; (4) implementation of a tapering period, which might have constrained substitution behavior; and (5) not examining the data by sex since women might respond more positively to snus.

Author	Title	Study Methods	Primary Study Measurement and Endpoints	Author's Findings Related to Switching to Smokeless Tobacco Products	Comments ^a
(Macy, Li, Xun, Presson, & Chassin, 2016)	Dual trajectories of cigarette smoking and smokeless tobacco use from adolescence to midlife among males in a Midwestern US community sample	This study included all male subjects in a longitudinal study who reported cigarette smoking or ST use in 1987, 1993, 1999, 2005, or 2011 (N = 2,230; mean age: 20.1 years in 1987; 93% white). Objective: To identify tobacco-use trajectories from adolescence to midlife and to test correlates of trajectory group membership.	Group-based trajectory analyses were conducted with zero-inflated Poisson models and analysis of covariance was used to test adolescent health beliefs associated with trajectory group membership.	Five smoking trajectory groups (consistent abstinence from cigarettes; late onset intermittent, then cessation; early onset regular, then cessation; delayed onset regular, then cessation; and consistent regular) and four ST trajectory groups (early onset, then cessation; consistent abstinence from ST; late onset, escalating; and consistent regular) were identified. "The prevalence of dual use of cigarettes and ST was low, and there was little evidence to suggest switching between tobacco products occurred." "The two groups that indicated switching from cigarettes to ST were (1) early onset regular, then cessation for smoking and late onset, escalating for smokeless (0.6%) and (2) delayed onset regular, then cessation for smoking and late onset, escalating for smokeless (0.8%) for a total of 1.4%."	Strength: The study shows longitudinal data. Limitations: (1) Subjects were predominantly white, non-Hispanic, and located in the Midwestern U.S.; (2) Any short-term changes in tobacco use behaviors (less than 6 years) were unable to be detected; (3) the missing data from 1987 on health beliefs should be taken into account because subjects in the regular use trajectory groups for both cigarettes and ST were more likely to be missing these data than subjects in the other groups; (4) dual use was defined using seven subcategories of smoking, but there were only three subcategories of ST use; and (5) the health beliefs tested were measured during adolescence, predicting future use, and beliefs may change over time.

Author	Title	Study Methods	Primary Study Measurement and Endpoints	Author's Findings Related to Switching to Smokeless Tobacco Products	Comments ^a
(Meier et al., 2016)	Preference for flavored noncombustible nicotine products among smokers motivated to switch from cigarettes	Subjects (mean age: 43.9 years; 52.9% males; 81.8% non-Hispanic, white), who were smokers and interested in completely switching from cigarettes to an alternative product, were recruited from Minneapolis/St. Paul, Minnesota and Eugene, Oregon. They were randomized to either medicinal nicotine (n = 195) or snus (n = 196) for 12 weeks. They were free to choose any flavor of their assigned products. Objective: To test whether smokers willing to switch to an alternative product would prefer flavored versus nonflavored products.	Subject demographic variables and smoking history were recorded, as well as switching between flavored and nonflavored tobacco.	<p>Among subjects assigned to nicotine gum, only 0.5% chose original flavor, 40% chose mint, 35.4% chose fruit, and 24.1% chose cinnamon. Of these subjects, 12.8% switched from one flavored product to another, and none switched from flavored to a nonflavored gum.</p> <p>For subjects assigned to snus, 71.4% chose Winterchill, 7.7% chose Frost, 4.6% chose Mellow (no flavor), and 16.3% chose Robust (no flavor). Of these subjects, 13.3% switched from one flavored product to another, 2.6% switched from flavored to non-flavored, 5.2% switched from nonflavored to flavored, and 6.1% made multiple switches during the treatment period. No significant differences were observed between those who chose flavored products and those who chose nonflavored products for smoking history, cigarettes per day, number of quit attempts, dependence as measured by the Fagerstrom Test for Nicotine Dependence, and demographic variables.</p> <p>The study showed that more flavored oral tobacco and medicinal nicotine products are chosen among smokers who are switching to a noncombusted product.</p>	Limitations: (1) Subjects were predominantly non-Hispanic white; and (2) there were not any other ST products besides snus offered.

Author	Title	Study Methods	Primary Study Measurement and Endpoints	Author's Findings Related to Switching to Smokeless Tobacco Products	Comments ^a
(Persoskie et al., 2016)	Ever-use and curiosity about cigarettes, cigars, smokeless tobacco, and electronic cigarettes among US middle and high school students, 2012-2014	Data came from the 2012 (n = 24,658; age: 9+ years; 51.1% male; 53.9% non-Hispanic, white) and 2014 (n = 22,007; 50.2% male; 53.2% non-Hispanic, white) NYTS (U.S. students in Grades 6-12). For cigarettes, cigars, ST, and ECs (2014 only), students were classified as ever-users or never-users of each product. Objective: To examine whether curiosity about, as well as ever-use of, tobacco products among U.S. middle school and high school students changed from 2012 to 2014.	Among never-users, curiosity about using each product was assessed by asking subjects if they had “definitely,” “probably,” “probably not,” or “definitely not” been curious about using the product.	From 2012 to 2014, there were declines in ever-use of cigarettes and cigars overall and among students who were Hispanic or black. The proportion of never-users reporting they were “definitely not” curious increased for cigarettes and cigars. Ever-use and curiosity about ST tobacco did not change significantly from 2012 to 2014. In 2014, the proportion of subjects who were “definitely” or “probably” curious never-users of each product was as follows: cigarettes, 11.4%; ECs, 10.8%; cigars, 10.3%; and ST, 4.4%.	Strengths: (1) Large sample size that allowed for robust estimates of ever-use and curiosity within subgroups of adolescents varying by sex, age, and race/ethnicity; and (2) the study used measure of curiosity that longitudinally predicts cigarette smoking and is associated in theoretically expected ways with exposure to advertising for other tobacco products. Limitations: (1) The self-reported curiosity measure was subject to social-desirability and recall bias; (2) the study did not include other types of tobacco products such as hookah; and (3) diverse products (cigars, cigarillos, and little cigars) were grouped into single categories.

Author	Title	Study Methods	Primary Study Measurement and Endpoints	Author's Findings Related to Switching to Smokeless Tobacco Products	Comments ^a
(Rodu et al., 2016)	Associations of proposed relative-risk warning labels for snus with perceptions and behavioral intentions among tobacco users and nonusers	The survey exposed 4,324 daily exclusive cigarette smokers, 1,033 daily ST 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 for snus. The minimum age to participate in the survey was the minimum age for tobacco purchase (i.e., either 18 or 19 years, depending on the state). Objective: To analyze a consumer perception survey sponsored by Swedish Match as part of a Modified Risk Tobacco Product application to change warning labels for Swedish snus products.	The data were examined for four outcomes: believability, harmfulness, motivation to use, and intention to buy snus.	“Compared with those who viewed 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, whereas triers or never-users viewing the substantially lower risk label were more likely to buy snus.	Strengths: (1) Large sample sizes of the five tobacco-use subgroups that were demographically similar; (2) the survey was designed to examine the perception of existing and proposed snus warnings among users of tobacco and nonusers of tobacco, according to recommendations included in a guidance document for modified risk applications published by the Center for Tobacco Products. Limitations: (1) The study was based on a cross-sectional survey in which each subject viewed only one label; (2) the questions about buying and using snus did not address partial or complete transition from cigarettes to snus; (3) the questions did not allow subjects to indicate how much the label changed their beliefs, but rather simply had subjects indicate their current beliefs and intention after viewing the label; (4) subjects were obtained from online consumer panels, which under-represent subjects with lower education and literacy; (5) recruitment was designed to enroll equal numbers of tobacco users and nonusers; thus, the results may not be generalizable; (6) tobacco status was based on self-report; and (7) subjects may habituate to the messages, and the labels may become less effective over time.

Author	Title	Study Methods	Primary Study Measurement and Endpoints	Author's Findings Related to Switching to Smokeless Tobacco Products	Comments ^a
(Schauer et al., 2016)	Past year quit attempts and use of cessation resources among cigarette-only smokers and cigarette smokers who use other tobacco products	Data were analyzed from 24,448 current cigarette-only (age: 18+ years; 51.08% male; 73.54% non-Hispanic, white), 1,064 cigarette- and cigar-only (age: 18+ years; 78.58% male; 69.97% non-Hispanic, white), and 508 cigarette and ST users (age: 18+ years; 94.69% male; 89.21% non-Hispanic, white) who responded to 2010-2011 Tobacco Use Supplement to the Current Population Survey. Objective: To assess differences in past-year cigarette-smoking-quit attempts and use of counseling and medication among current cigarette-only users, cigarette and cigar users, and cigarette and ST users.	Demographic differences among tobacco use groups; differences in a variety of cessation measures; and the association between tobacco use group and making a past-year cigarette-smoking-quit attempt or using evidence-based cessation resources.	Dual users are just as likely as cigarette-only users to intend to quit smoking cigarettes in the next 30 days and to report having tried to quit smoking at least once in the past year. Dual users were also just as likely as cigarette-only users to report use of counseling or medication when trying to quit smoking cigarettes. In unadjusted analyses, cigarette and ST dual users had higher odds of trying to quit cigarettes in the past year than cigarette-only users (OR = 1.31, 95% CI: 1.05, 1.64); no differences were found for cigarette and cigar dual users. However, when adjusting for demographic and cigarette-smoking variables, both groups of dual users had similar odds as cigarette-only users for having made a past-year cigarette-smoking-quit attempt.	Strength: The study was able to assess and compare cigarette smoking-cessation behaviors among the two most common dual-use groups (cigarettes and cigars users; and cigarettes and ST users). Limitations: (1) The data are cross-sectional and cannot be used to assess causality or temporality; (2) sample size limitations precluded the assessment of users of other combinations of tobacco products; (3) heterogeneity may exist within the dual-use groups assessed because both cigars and ST include multiple products, each with potentially different use profiles; (4) cessation behaviors were assessed only among current smokers; (5) findings from cigarette and ST group apply primarily to males; and (6) although dual users appear to attempt to quit at rates similar to those of cigarette-only users, the study was unable to assess quit rates due to insufficient sample sizes.

Author	Title	Study Methods	Primary Study Measurement and Endpoints	Author's Findings Related to Switching to Smokeless Tobacco Products	Comments ^a
(Kaufman et al., 2015)	Tobacco use transitions in the United States: the National Longitudinal Study of Adolescent Health	A sample of 20,774 adolescents (49.4% male) in Grades 7-12 in 1995 were selected to participate in the survey, conducted in four waves, and followed into young adulthood (2008-2009). Objective: To evaluate and describe transitions in cigarette and ST use, including dual use, prospectively from adolescence into young adulthood.	The data were analyzed for prevalence of cigarette smoking, ST use and dual use; patterns of tobacco use over time, including transitions between ST and cigarette use; and how the transitions differ across demographic groups.	<p>Among the study population, 48.7% reported using cigarettes, 12.8% reported using ST, and 7.2% reported dual use (cigarettes and ST in the same wave) in at least one wave. Subjects who had reported exclusive cigarette use and who were female, black, and younger were less likely to report subsequent ST use than exclusive cigarette smokers who were male, white, and older. Dual users exhibited a high probability (81%) of continuing dual use over time.</p> <p>The authors estimated transition probabilities between the four states of "current use" for white males: neither, cigarettes only, ST only, dual use. The probability for a dual user to become an exclusive ST user was <1%.</p>	Strength: The study analyzed prospective data on cigarette and ST product use in a nationally representative cohort followed from adolescence into young adulthood. Limitations: (1) The study relied on self-reports of tobacco-product use without biochemical validation; (2) the results were not weighted to provide nationally representative estimates; (3) the data were drawn from 1995 to 2009, since which, changes have occurred in both tobacco-control efforts and tobacco marketing and product availability; and (4) the survey did not collect data on some other forms of tobacco use.

Author	Title	Study Methods	Primary Study Measurement and Endpoints	Author's Findings Related to Switching to Smokeless Tobacco Products	Comments ^a
(Rousu et al., 2015)	The impact of free trial acceptance on demand for alternative nicotine products: evidence from experimental auctions	An experimental auction (n = 258 adult smokers; 44% female; 65% white) wherein subjects were randomly assigned to one of four experimental conditions (given the opportunity to try, but did not have to accept, one of three relatively novel ST products, or were placed in a control group). All the subjects then bid on all three of these products, as well as on cigarettes. Objective: To explore the relationship between product trials and consumer demand for ANPs.	The assessment of interest in using ANPs based on both trial of the product and bids placed for the products in the experimental auction.	"Fewer smokers were willing to try snus (44%) than dissolvable tobacco (64%) or medicine nicotine (68%). For snus, modest evidence suggests that willingness to try is associated with greater demand for the product. For dissolvable tobacco or medicinal nicotine, there is no evidence that those who accept the product trial have higher demand for the product."	Limitations: (1) Because subjects were not required to try the products, self-selection bias could not be ruled out; (2) insufficient sample size to randomize the presentation order, and there appears to be an impact based on ordering; (3) subjects were assigned to try only one of three products offered and thus cannot directly compare the impact of trials on demand within subjects across products; and (4) experimental auctions in a controlled setting may not adequately represent what happens in the real world.

Author	Title	Study Methods	Primary Study Measurement and Endpoints	Author's Findings Related to Switching to Smokeless Tobacco Products	Comments ^a
(Tam et al., 2015)	A systematic review of transitions between cigarette and smokeless tobacco product use in the United States	A systematic review of published literature on transitions between ST and cigarette use was performed. Search was performed through PubMed, Web of Science and EbscoHost databases from January 2000 to March 2014. Information were extracted on the proportion of the sample population transitioning from baseline to follow-up. Objective: To identify systematic information on transitions between ST and cigarette use in the U.S.	Information on the study characteristics including study population, follow-up, definitions for each tobacco use categories, and how transitions were calculated were extracted.	Six articles met all selection criteria. The following are findings from the selected articles: Switching to ST: <u>Adults:</u> After 1 year, 4.9% of male dual users and 0% of female dual users were exclusive ST users; after 4 years, 17.4% of male dual users were exclusive ST users. After 1 year, 0.3% of male exclusive smokers and 0% of female exclusive smokers were exclusive ST users; after 4 years, 1.4% of male exclusive smokers were exclusive ST users. <u>Adolescents:</u> After 1-2 years, 1.6% of exclusive smokers and 8.5% of dual users were exclusive ST users. After 2 years, 3.8% of male exclusive smokers were exclusive ST users. After 4 years, 0.8% of male exclusive smokers and 34.2% of male dual users were exclusive ST users.	Limitations: (1) Estimates from some studies are not generalizable to the U.S. population; (2) there was variability in tobacco use definitions and follow-up time; (3) there is a potential bias in estimates from some studies due to tobacco use prevention or ban; (4) there are an absence of confidence intervals; and (5) estimates for females are missing, with the exception of one article.

^a Comments are largely author-defined, methodological strengths and limitations.

7.5.2-2.3. The Likelihood that Consumers Will Use the Product in Conjunction with Other Tobacco Products

Noteworthy articles found in this literature review update that inform the behavioral and health risks associated with dual use or polytobacco use (PTU) that includes ST products are highlighted below, and all 45 articles are summarized in [Table 7.5.2-2-2](#).

7.5.2-2.3.1. Prevalence of Dual Use

Concurrent cigarette and ST use was the most common dual use of tobacco products reported among ST users in the current literature search ([Table 7.5.2-2-2](#)) but information on other combinations, such as concurrent electronic cigarette (EC) and ST use, cigar/little cigar/cigarillos and ST use, and hookah and ST use, were also reported among ST users. Besides dual use, concurrent PTU (concurrent use of more than two tobacco products) was also reported.

Depending on the population studied, the prevalence of dual tobacco use increased, remained unchanged, or decreased over time. Dual cigarette and ST use among smokers increased overall among adolescents who are cigarette smokers in New York City from 2001 to 2013 ($p < 0.001$) ([Elfassy, Yi, & Kansagra, 2015](#)). Creamer et al. ([Creamer, Perry, Harrell, & Diamond, 2015](#)) reported no significant change in dual cigarette and ST or dual cigar and ST use among high school students between 1999 and 2013. For adults (≥ 18 years old), Nguyen et al. ([2015](#)) examined changes over time in dual cigarette and ST use by state in the U.S. They reported a slight increase in the prevalence, which ranged from 2% to 12.5% in 2011 and from 3.1% to 13.5% in 2013. However, a study by Choi et al. ([Choi, Bestrashniy, & Forster, 2017](#)) of Midwestern young adults (mean age of 24.0 [1.7] years during the 2010-2011 survey) showed a decrease over time in dual cigarette and snus use: 6.3% (2010-2011), 5.1% (2011-2012), and 4.6% (2012-2013).

Most articles presented in [Table 7.5.2-2-2](#) reported the prevalence of dual use or PTU by sociodemographic factors and reinforced the observation that dual users of cigarette and ST are predominantly males. In addition, a study by Sung et al. ([Sung, Wang, Yao, Max, & Lightwood, 2016](#)) showed that among current chewing tobacco and snuff users who participated in the Cancer Control Supplements of the National Health Interview Surveys (NHISs), polytobacco users were significantly less prevalent among adults aged greater than 25 years, and college graduates. Another study performed among U.S. Air Force trainees found that dual users of cigarettes and ST were significantly more likely to be younger than 21 years old than single-product users ($p < 0.05$) ([Little et al., 2016](#)).

Neff et al. ([Neff et al., 2015](#)) reported that concurrent use of two or more types of tobacco products was common among middle school and high school students that participated in the 2014 NYTS. For the group that reported tobacco product use on 1 to 5 days during the preceding 30 days, 63.4% were ST users. Approximately 85% and 80% of ST users used multiple tobacco products on 6 to 19 days, and 20 to 30 days, of the previous 30 days, respectively. When comparing dual use of cigarette and ST (excluding snus) in adults (age: ≥ 18 years) and adolescents (age: 12 to 17 years), Kasza et al. ([Kasza et al., 2017](#)) reported the prevalence was the same (4%) among polytobacco users in both age groups in the U.S.

based on Wave 1 of the Population Assessment of Tobacco and Health (PATH) study. Additionally, the same study showed that 3% of adolescents were concurrent cigarette, EC, and ST users.

Creamer et al. (Creamer et al., 2015) reported that, among high school students, there was no change in the prevalence of dual cigarette and ST use among boys, but there was a significant increase among girls between 1999 and 2013, from 1.3% to 4.4% ($p = 0.02$). Another study (Chang, Meza, & Levy, 2016) found that, in adult males and females, dual cigarette/ST use declined significantly by 5.3% and 8.4% per year ($p < 0.05$), respectively, between 1992 and 2011.

Schauer et al. (2014) reported that the prevalence of dual cigarette and ST use was significantly different among daily (5.1%) and nondaily (7.6%) smokers ($p < 0.05$). A study performed by Dunbar et al. (Dunbar, Shadel, Tucker, & Edelen, 2016) demonstrated that current use of snus was reported in 2.96% and 1.68% of nondaily and daily smokers, respectively, whereas current use of snuff or chewing tobacco was reported in 2.96% and 1.37% of nondaily and daily smokers, respectively; these authors also concluded that there were no significant difference in ST use between nondaily and daily smokers. Another study (Kish et al., 2015) showed that concurrent cigarette and snus users smoked an average of 12.6 cigarettes per day, whereas concurrent cigarette and chewing tobacco users smoked an average of 16 cigarettes per day.

Dual use of ST and EC, the latter an emerging class of tobacco products, appeared to be approximately as prevalent as dual use of ST and cigarettes among studies in the literature review. A study among high school students showed an increase in the prevalence of dual EC and ST use from Grade 9 to Grade 12: 4.4%, 3.6%, 4.6%, and 6.5% in Grades 9 through 12, respectively (Anand et al., 2015). In addition, Owusu et al. (Owusu et al., 2017) reported that 2.8% of subjects who were adolescents in predominantly rural area in Central Appalachia concurrently used EC and ST.

7.5.2-2.3.2. Environmental Factors Associated with Dual Use

Kish et al. (Kish et al., 2015) conducted a study among adult cigarette smokers from a homeless shelter in Dallas, Texas. The study showed that polytobacco users were generally younger, had more homelessness episodes, had higher expired breath carbon monoxide levels, and had higher stress (all p -values < 0.05). Other studies demonstrated that binge drinking was associated with dual cigarette and ST use (Graber et al., 2016; Kalkhoran, Padilla, Neilands, & Ling, 2016; Sung et al., 2016).

Boredom relief (Wong, Haardorfer, Windle, & Berg, 2016), living with someone who used ST (Linde et al., 2016), having received free tobacco products at a bar or social event, and having peers who used tobacco (Lee, Hebert, Nonnemaker, & Kim, 2015; Little et al., 2016) are each associated with dual cigarette and ST use. Additionally, cigarette-smoking restrictions in some areas and availability of alternative tobacco products was also associated with dual cigarette and ST use (Dunbar et al., 2016).

7.5.2-2.3.3. Patterns of Transition into or out of Dual Use

Some articles presented in [Table 7.5.2-2-2](#) reported patterns of transition into or out of dual use. For example, a study was conducted among males who reported any cigarette smoking or ST use ([Macy et al., 2016](#)). For the study, subjects participated in the Indiana University Smoking Surveys in 1987, 1993, 1999, 2005, or 2011. Among dual users, 2.6%, 2.9%, 1.1%, and 2.2%, respectively, belonged to an author-defined trajectory group: consistent regular cigarette and ST; consistent regular for smoking and late onset escalating for ST; late onset intermittent, then cessation for smoking and late onset escalating for ST; and late onset intermittent, then cessation for smoking and consistent regular for ST. Another study ([Wei, Blount, Xia, & Wang, 2016](#)) reported that among subjects who were nondaily smokers at baseline, 69.7% remained nondaily smokers, 18.4% became daily smokers, and 11.9% quit smoking, when followed up a year later.

A study that utilized four waves of the National Longitudinal Study of Adolescent Health followed transitions in cigarette and ST use, including dual use, from adolescence into young adulthood (1995-2009) ([Kaufman et al., 2015](#)). Among subjects, 7.2 percent reported dual use in at least one wave. Among white male subjects reporting dual use, the transition probability to neither product 1 year later was 15 percent. Continuance of both products 1 year later was 80 percent. Among subjects reporting dual use of cigarettes and ST, the 1-year transition probability to use of neither product was 13%, to cigarette use only was 5.5%, to ST use only was less than 1%, and continuance of dual use was 81%.

Based on the data from the 2012-2013 National Adult Tobacco Survey (NATS), concurrent cigarette and ST use was not associated with stopping ST use at least once in the past 30 days ([Agaku, Rolle, Singh, & Ayo-Yusuf, 2016](#)). However, another study showed that, among U.S. adult subjects, dual users of cigarettes and ST were more likely than exclusive cigarette smokers to have made a quit-smoking attempt in the last year ([Brown-Johnson & Popova, 2016](#)). Schauer et al. (2016) reported that a higher percentage of dual cigarette and ST users tried to quit smoking cigarettes for a day or more in the past year (45.7 percent) than exclusive cigarette smokers (36.6 percent). However, after the authors adjusted for other sociodemographic and smoking characteristics, dual use was no longer a significant correlate with attempting to quit in the past year or with using counseling or medication during a quit attempt.

7.5.2-2.3.4. Health Effects Associated with Dual Use

Cigarette smoking is well known to cause cancers, but few articles were identified that reported cancer risks of dual cigarette and ST use. Andreotti et al. ([Andreotti et al., 2016](#)) reported that dual cigarette and ST users generally had cancer risks (including risks for smoking-related, lung, gastrointestinal, urinary tract, and head and neck cancers) similar to those of exclusive cigarette smokers regardless of cigarette-smoking status, duration, or frequency.

Levels of a carcinogen biomarker of tobacco use, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), was assessed among subjects who were exclusive cigarette smokers, concurrently used cigarette and other combustible tobacco products, or were dual cigarette and ST users ([Berg, Schauer, Ahluwalia, & Benowitz, 2012](#)). Dual use of ST with cigarettes

was significantly associated with increased NNAL levels ($p < 0.001$) in nondaily smokers, but there was no significant association among daily smokers ($p = 0.71$).

Urinary NNAL was also measured among subjects who are smokers and randomized to receive either nicotine gum or snus for 12 weeks (Hatsukami et al., 2016). When comparing between baseline and Week 4, the mean of total NNAL of dual cigarette and nicotine gum users was decreased from 1.58 pmol/mg creatinine to 1.11 pmol/mg creatinine, whereas a slight increase was observed among dual cigarette and snus users (from 1.47 pmol/mg creatinine to 1.55 pmol/mg creatinine). Therefore, total NNAL was significantly higher among dual cigarette and snus users than among dual cigarette and nicotine gum users at Week 4 ($p < 0.005$). Additionally, when comparing between baseline and Week 4, the mean of total N-nitrosornicotine (NNN), a carcinogen, was also decreased from 0.09 pmol/mg creatinine to 0.05 pmol/mg creatinine among dual cigarette and nicotine gum users, whereas a slight decrease was observed among dual cigarette and snus users (from 0.13 pmol/mg creatinine to 0.11 pmol/mg creatinine). However, there were no significant differences in the total NNN between dual cigarette and nicotine gum users and dual cigarette and snus users at Week 4.

Lee et al. (Lee et al., 2015) reported that PTU (cigarette and at least two other tobacco products) among U.S. middle school and high school students was significantly associated with nicotine dependence. In this study, nicotine dependence was measured by the time it takes to first tobacco product use within 30 minutes of waking. Moreover, another study (Harrell, Plunk, Naqvi, Ji, & Martins, 2016) performed on adolescents and young adults showed that polytobacco users were more likely to report nicotine dependence than exclusive cigarette smokers. However, Baggett et al. (Baggett, Campbell, Chang, & Rigotti, 2016) found that concurrent use of cigarettes and ST among homeless cigarette smokers was not significantly correlated with nicotine dependence.

7.5.2-2.3.5. Updated Findings

Information in the updated literature review on the likelihood that tobacco users will use the candidate product in conjunction with other tobacco products is consistent with that seen in the initial literature review. Although the conclusions from the initial literature review (Section 7.5.2-1.3.5) have not changed, there was additional information gathered from the updated literature review. Dual cigarette and ST use was positively associated with drug and alcohol use, nicotine dependence, influence from friends or other people living with subjects, boredom relief, self-enhancement, smoking restrictions, and availability of alternative tobacco products. Dual cigarette and ST users generally had the same risks for cancers, regardless of cigarette-smoking status, duration, or frequency, as exclusive cigarette smokers. Also, dual cigarette and ST use was associated with increased urinary NNAL levels as compared with those for dual cigarette and EC use.

A tabular summary of the literature informing the behavioral and health risks associated with dual use or PTU that includes ST products is presented in Table 7.5.2-2-2.

Table 7.5.2-2-2: Literature Summary for Dual Use or Polytobacco Use of Smokeless Tobacco Products

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Dual Use	Comments ^a
(Carpenter et al., 2016)	Snus undermines quit attempts but not abstinence: a randomised clinical trial among US smokers	A total of 1,236 smokers who did not want to quit throughout the U.S. (snus group: n = 626, mean age: 48.7 years, 70% female, 89% Caucasian; control group: n = 610, mean age: 48.7 years, 65% female, 87% Caucasian) were randomized to receive a 6-week supply of snus or not, after which, everyone was advised to quit all tobacco products and was then followed for 12 months. Objective: To better understand the real-world impact of snus on smoking behavior, a large-scale, long-term clinical trial of naturalistic snus use among smokers.	Primary outcomes: Self-reported quit attempts, floating abstinence, and 7-day point-prevalence abstinence at 6 months and 1 year. Secondary outcomes: Changes in smoking, motivation, and confidence to quit.	Within snus group, 82% used at least once, 26% used irregularly, and 16% used regularly at the end of sampling period. Smokers in the snus group were less likely to make any quit attempt (RR = 0.83; 95% CI: 0.70, 1.00), and any 24 h quit attempt (RR = 0.77; 95% CI: 0.63, 0.95) compared with control participants. There were no group differences on any measure of abstinence.	Limitations: (1) Only one product was used; (2) study sample consisted primarily of Caucasian women; (3) participants were smokers who did not want to quit, which may create the impression that it was methodologically biased against snus; and (4) there is a lack of biochemical verification of abstinence.
(Choi et al., 2017)	Trends in awareness, use of, and beliefs about electronic cigarette and snus among a longitudinal cohort of US Midwest young adults	Data collected in three annual cycles (2010-2013) were used in the study (subjects aged 21-29 years; n = 2,622). The subjects had an average age of 24.0 years in the first collection year. The percentage of females remained nearly constant for all three years (52.4%-53.2%), as did the percentage of non-Hispanic whites (89.3%-90.0%). Participants were asked if they had heard of and ever used EC and snus, and the number of	Beliefs about whether these products are less harmful than cigarettes, less addictive than cigarettes, and could help people quit smoking were assessed.	The prevalence of past-30-day snus users among current smokers decreased over time: 6.3% (2010-2011), 5.1% (2011-2012), and 4.6% (2012-2013). “...among current smokers, number of days using snus in the past 30 days was not associated with number of days smoked in the past 30 days (p = .51).”	Strength: The study's longitudinal design, which allowed the authors to assess within-person changes over time, provided additional statistical power to test interactions compared with serial cross-sectional studies. Limitations: (1) Attrition may introduce bias to the findings; and (2) the U.S. Midwest sample in the study limits the ability to generalize the findings to young adults in other U.S.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Dual Use	Comments ^a
		days they used these products in the past 30 days. Objective: To assess the trends in awareness and use of, as well as beliefs about, EC and snus, among a cohort of young adults (age: 21-29 years) from the U.S. Midwest based on data collected annually during 2010-2013.			regions.
(Dunbar et al., 2017)	Frequency of e-cigarette use, health status, and risk and protective health behaviors in adolescents	Adolescent participants (n = 2,488), with a mean age of 17.31 years were 46% male and 47% Hispanic, completed a survey on EC and cigarette use, protective health behaviors, and alcohol and other drug use. Objective: To examine the correlation between EC use and health status and protective health behaviors.	Logistic regression compared EC-only users to dual EC/cigarette users, cigarette-only users, and nonusers.	The prevalence rate of past-year ST use increased among EC-only users (4.92%), cigarette-only users (8.05%), and EC/cigarette dual users (12.56%).	Limitations: Data were self-reported, and ST use was dichotomized between past-year use and no past-year use.
(Kasza et al., 2017)	Tobacco-product use by adults and youths in the United States in 2013 and 2014	Prevalence for 12 types of tobacco products were analyzed using data from U.S. adult (n = 32,320; aged 18-65+ years; 48.1% male; 66.0% non-Hispanic white) and youth (n = 13,651; aged 12-17 years; 51.3% male; 54.6% non-Hispanic white) participants from Wave 1 of the PATH study (2013-2014). Objective: To examine the prevalence of tobacco use among adults and youths according to type of tobacco product and category of	Estimates of the prevalence of use for each product were determined according to use category (e.g., current use or use in the previous 30 days) and demographic subgroup, and the prevalence of multiple-product use was explored.	Of adult multiple-product users (n = 6,238), 4% were cigarette/ST users and 1% were cigar/ST users, where snus pouches were not included in the definition of ST. Of youth multiple-product users (n = 467), 4% were cigarette/ST (excluding snus pouches) users and 3% were cigarette/EC/ST (excluding snus pouches) users.	Strengths: The data were derived from a nationally representative survey. Limitation: The data came from only the first wave of the PATH study, and, therefore, questions about transitions among multiple-product use, single-product use, nonuse of tobacco, and former tobacco use could not be determined.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Dual Use	Comments ^a
		tobacco use.			
(Owusu et al., 2017)	The use of e-cigarettes among school-going adolescents in a predominantly rural environment of Central Appalachia	Data from 894 participants (88.8% <18 years old, 42.2% male) were collected in a school-based survey conducted in 2016 in northeast Tennessee. Objective: To estimate the prevalence of EC use with two tobacco products among school-going adolescents.	Data were analyzed to estimate the prevalence and delineate the associations between EC use and OTPs.	"Responses show 5.6% of participants currently used [ECs] and cigarettes and 2.8% of participants were current users of [ECs] and [ST]."	Strengths: relatively large sample size. Limitations: (1) Institutional constraints limited the study's ability to generate a truly representative sample; (2) the study is susceptible to recall and social-desirability biases because the data were collected by self-report; (3) the results need to be interpreted in the context that the majority of participants were under the age of 18 years; and (4) there were no adjustments for school differences.
(Wei et al., 2016)	Factors associated with short-term transitions of non-daily smokers: socio-demographic characteristics and other tobacco product use	Data were obtained from the 2003, 2006/07 and 2010/11 TUS-CPS (n = 13,673; age: 18+ years; 54.8% male; 61.5% non-Hispanic white) of U.S. adults who have smoked for more than 5 years and were nondaily smokers 12 months before the interview. Objective: To examine the transitions in smoking status among nondaily smokers who transitioned to daily or former smokers or remained as nondaily smokers during a 12-month period.	Data were analyzed for the correlates of nondaily to daily, stable nondaily and nondaily to former smoking transitions among nondaily smokers at baseline. The study was controlled for sociodemographic factors and the use of cigars and ST.	Among participants, 2.6% were nondaily smokers at baseline. Among these, 69.7% remained nondaily smokers, 18.4% became daily smokers, and 11.9% quit smoking after 12 months. The nondaily to daily versus stable nondaily smoking transition was less likely among those who were aged 65+ (p = 0.018), male (p < 0.001), Hispanic (p < 0.001), with an income of \$25000-49999 or ≥\$75000 and current users of ST (p = 0.003).	Strength: The data were derived from a large national U.S. survey. Limitations: (1) The study examined retrospectively the change in cigarette smoking behaviors over a 12-month period for each smoker, but all covariates were measured only at the interview; (2) the TUS-CPS did not ask the frequency of life-time use for each OTP; (3) the study did not differentiate former smokers who had just quit cigarette smoking in the past 30 days from nondaily

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					smokers who had smoked for a few days in 30 days; (4) the TUS-CPS did not ask about the use of emerging tobacco products; (5) tobacco use and smoking status were self-reported and may be subject to recall bias and social-desirability bias; (6) a small proportion of participants had missing values for cigar use or ST use and was excluded from the regression analysis; and (7) the study focused on smokers who had established a pattern of nondaily smoking.
(Agaku et al., 2016)	Exposure and response to current text-only smokeless tobacco health warnings among smokeless tobacco users aged ≥ 18 years, United States, 2012-2013	Data were from the 2012-2013 NATS. Past-30-day exposure to ST health warnings among past-30-day ST users (n = 1,626; aged 18-65+ years; 93.7% male; 72.3% non-Hispanic, white) was a self-report of seeing warnings on ST packages: "Very often," "Often," or "Sometimes." Objective: To assess U.S. adult ST users' exposure and response to ST health warnings, which were in text-only format, covering 30% of the two primary surfaces of ST containers and 20% advertisements.	Data from U.S. adult ST users were analyzed for association between ST health warning exposure and perception of ST harmfulness and addictiveness.	Prevalence of exposure to ST health warning labels among past-30-day ST users was 77.5%. "Prevalence was significantly higher among past-30-day [ST] users who did not smoke cigarettes (84.6%) compared with those who also smoked cigarettes (67.7%) (p < 0.001)." "Concurrent users of [ST] and cigarettes were less likely to report thinking about the health risks of [ST] use when compared to [ST] users who did not smoke cigarettes (AOR = 0.65; 95% CI: 0.42-0.98)." CU of ST with cigarettes was not associated with stopping ST use at least once in the past 30 days because of ST health warnings (AOR = 1.07; 95% CI: 0.62-1.85).	Strength: The use of recent, nationally representative data to assess exposure and response to existing ST health warnings among past-30-day ST users. Limitations: (1) The retrospective self-reports may have been subject to habituation, recall bias, or misclassification of exposure from alternative sources or alternative time-windows; (2) the temporal sequence between exposure and some outcomes could not be established because of the cross-sectional design, and as such, only associations can be inferred;

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					and (3) the relatively low survey response rate of 44.9% might have resulted in nonresponse bias, even after adjustment for nonresponse.
(Andreotti et al., 2016)	Tobacco use and cancer risk in the Agricultural Health Study	Cancer incidence in relation to exclusive use of six tobacco products and ST in the AHS was analyzed. Among the 84,015 subjects (age groups from <30 to ≥70 years at enrollment), 63.2% were male. Current cigarette and ever ST dual users made up 2.6% of the total population (3.3% of males and 0.4% of females). Objective: To examine the risks of cancer associated with exclusive use of cigarettes, pipes, cigars, cigarillos, chewing tobacco, and snuff, as well as the use of cigarettes and at least one additional tobacco product.	Cancer risks associated with the use of cigarettes and OTPs were evaluated.	When adjusted for age, sex, race, state of residence, education, and alcohol frequency, current cigarette users smoked an average of 14.6 cigarettes per day for an average of 21.0 years (mean cigarette pack-years = 16.7). After the same adjustments, current cigarette and ever ST dual users smoked an average of 11.9 cigarettes per day for an average of 14.8 years (mean cigarette pack-years = 9.3). “Dual cigarette-[ST] users generally had cancer risks similar to exclusive cigarette smokers regardless of cigarette smoking status, cigarette smoking duration, or frequency.”	Limitation: Analysis of NCTPs was limited to ever versus never use for both exclusive and dual use.
(Baggett et al., 2016)	Other tobacco product and electronic cigarette use among homeless cigarette smokers	Time-location sampling was used to conduct a cross-sectional, in-person survey of currently homeless adult cigarette smokers (n = 306; 74.8% male; 35.5% non-Hispanic, white; 8% ST use in the past month) in April-July 2014 from 5 clinical sites at Boston Health Care for Homeless Program. Objective: To determine the prevalence and correlates of	Past-month use of tobacco products was analyzed. Reasons for using ECs were assessed among EC users. Participants characteristics associated with the use of each product were also assessed.	“Past-month [ST] users and non-users did not significantly [differ] in their past-month average daily cigarette consumption in unadjusted (13.5 vs. 11.7 cigarettes/day, p = 0.21) or adjusted (β 1.8, p = 0.21) analyses.” CU of ST in this sample of homeless cigarette smokers was closely correlated with drug use severity (AOR = 1.45; 95% CI: 1.16, 1.82), but not significantly correlated with subsistence difficulty, alcohol severity score, psychiatric	Limitations: (1) Clinical sample of homeless smokers limited the generalization of the findings; (2) the study relied on self-report to determine current smoking status; (3) other tobacco type products use was never assessed; (4) use of tobacco products by homeless individuals who are current nonsmokers; (5) frequency of tobacco products use in

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		OTP and EC use in a clinic-based sample of homeless cigarette smokers.		severity score, ND score, readiness to quite score, or past-year quit attempts.	the past month was never assessed to identify regular versus experimental users; (6) reasons for OTPs use were never asked; and (7) the small number of participants who used certain products limited the power to detect potentially meaningful correlates of using these products.
(Bonhomme et al., 2016)	Flavoured non-cigarette tobacco product use among US adults: 2013-2014	Data from 2013-2014 NATS (n = 75,233) of U.S. adults aged ≥18 years were assessed. Objectives: (1) To describe the proportion of current NCTP users reporting past-30-day flavored product use, by product type, demographics, and tobacco-use characteristics; (2) to identify flavor types most commonly used by U.S. adults for each NCTP type, both overall and by age; and (3) to characterize associations between flavors used and other demographic characteristics, frequency of product-use and cigarette-smoking status.	Past-30-day NCTP use, flavored NCTP use and flavor types were assessed using bivariate analysis.	Among past-30-day ST users (n = 1,984), 607 were also current smokers. Among past-30-day flavored ST users (n = 919), 330 were also current smokers.	Strength: Data were derived from a nationally representative survey. Limitations: (1) A small number of current users of hookah and pipes were excluded from the analyses for each product; (2) self-reported flavor type assessment could be subject to recall bias; and (3) the low response rate may have biased results.
(Brown-Johnson & Popova, 2016)	Exploring Smoking Stigma, Alternative Tobacco Product Use, and Quit Attempts	Participants (U.S. adults, n = 1,812; aged 18+ years; 52.6% male; 41.7% white), including nonsmokers, ST users exclusive smokers, and ST and cigarette "dual users," responded to an online survey. Objective: To expand	Subject tobacco-use status was assessed, and participants answered questions about smoking stigma. Smokers were asked if they had made a quit	Dual users (n = 500) were 60.2% male, 43.8% aged 18-29 years, 41.4% black or African American, and 76.6% non-Hispanic. "Dual users perceived the highest smoking stigma."	Limitations: (1) The study is a cross-sectional data set, not a longitudinal data set; and (2) measures of stigma were limited.

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		quantitative exploration of smoking stigma by assessing the association between smoking stigma and quit smoking attempts and how smoking stigma differs by tobacco product.	attempt in the past year and if they intended to quit smoking in the future.	<p>“Dual users reported the highest levels of secrecy and guilt, and second highest level of discrimination. “</p> <p>Dual users were more likely than exclusive smokers to have made a quit smoking attempt in the last year (OR = 1.64; 95% CI: 1.20, 2.23).</p>	
(Burris et al., 2016)	A longitudinal, naturalistic study of U.S. smokers' trial and adoption of snus	<p>Adult smokers (N = 1,236) throughout U.S. who denied intention to quit in the next 30 days were randomized to receive (n = 626; mean age: 48.7 years; 70% female; 89% Caucasian) or not receive (n = 610; mean age: 48.7 years; 65% female; 87% Caucasian) free snus during a 6-week sampling period. Subjects were then advised to quit all tobacco use and were followed for 1 year.</p> <p>Objective: To advance current literature via a detailed description of snus uptake during a longitudinal study with adult U.S. smokers who denied intention to stop smoking in the near future.</p>	Frequency and quantity of use in the past week were measured separately for cigarettes and snus. Outcome data were collected via phone.	<p>Among participants, 84% reported trial and 11% purchase of snus. Current use declined from 47.1% at the end of sampling period to 6.5% at the end of follow-up. Frequency and quantity of snus use among current users appeared stable over time. About 79.3% of snus users said snus functions as an alternative to smoking and 58.4% as a method of coping with smoking restrictions. In most cases, participants' snus use was concurrent with continued smoking. Dual use (4.2%-47.5% across time) or smoking in isolation (51.7%-87.3% across time) was more common than exclusive snus use (<1%), with dual use decreasing over time.</p>	<p>Strengths: Longitudinal study design in a large group of U.S. smokers.</p> <p>Limitations: (1) Only a single snus product was offered; (2) the study population consisted of smokers who reported little to no interest in smoking cessation; and (3) white non-Hispanics and females are both overrepresented in this study.</p>
(Chang et al., 2016)	Trends and Factors Related to Smokeless Tobacco Use in the United States	<p>ST consumption by adults (age: 18+) from 1985 to 2011 was obtained from Federal Trade Commission Smokeless Tobacco Report.</p> <p>Objective: To assess the sensitivity of ST use trend estimates to the use definition; to update analysis of trends in</p>	The study used TUS-CPS to examine trends and factors related to ST use using joinpoint and logistic regression models. Sensitivity analyses were conducted for	<p>Smoking prevalence decreased with APC of -2.7% (1998-2011) and -2.5% (1992-2011) by adult males and females, respectively (p < 0.05). Total ST use significantly decreased at an APC of -4.5% (1992-2003; p < 0.05).</p> <p>Dual use of ST and smoking significantly declined 5.3% and 8.4% per year (p <</p>	<p>Strengths: (1) This study used the TUS-CPS data that allowed quantitative joinpoint analysis of ST use trends for the past two decades in relevant demographic groups; and (2) it examined ST-use trends and ST consumption,</p>

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		ST use under different definitions from the 1980s to 2000, with three additional waves from the TUS-CPS from 2003 to 2011; and to examine the factors associated with ST prevalence in the U.S.	assessing the impact of varying frequency definitions of ST use.	0.05) by adult males and females, respectively, from 1992-2011. However, when analysis is restricted to males aged 18-24 y, different trends are observed from 1992-2003 (APC = -8.6%; $p < 0.05$) and from 2003-2010 (APC = 2.3%; $p > 0.05$).	allowing for comparisons between self-reported data and market sales. Limitations: (1) All information was self-reported; (2) the survey data were cross-sectional; (3) the changes across survey years of ST use definitions may have introduced bias, in particular going from questions about regular use to questions about ever-use; and (4) tobacco companies have continued to introduce new ST products on the market, making the interpretation of trends difficult, given the variability in available products each year.
(Dunbar et al., 2016)	Use of and reasons for using multiple other tobacco products in daily and nondaily smokers: Associations with cigarette consumption and nicotine dependence	Data were combined from the two studies conducted through the RAND Corporation's PROMIS Smoking Initiative. Daily smokers (n = 656) and nondaily smokers (n = 203) aged at least 18 years provided information on their use of different OTPs, reasons for using OTPs, and cigarette consumption and ND. Objective: To examine the ways in which cigarette consumption and nicotine dependence among current daily and nondaily smokers are associated with likelihood of	The association of smoking status with OTP use and reasons for use were assessed. Additionally, within each smoking group, the associations of OTP use and reasons for use with cigarette consumption and ND were analyzed.	Current use of snus is reported in 2.96% and 1.68% of nondaily and daily smokers, respectively. Current use of snuff/chew is reported in 2.96% and 1.37% of nondaily and daily smokers, respectively. After controlling for demographics, there was not a significant difference in the prevalence of current snus use (OR = 1.35; 95% CI: 0.46, 3.97) or current snuff/chew use (OR = 1.49; 95% CI: 0.47, 4.72) in nondaily versus daily smokers. A majority of daily smokers responded that "Just wanted to try it" was a reason	Limitations: (1) Biochemical measures of nicotine intake to validate self-reported data on tobacco consumption were not collected; (2) there was no information on heaviness of cigarette consumption on smoking days for nondaily smokers, nor were there data on the frequency of OTP use among daily or nondaily smokers.

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		OTP use, number of different types of tobacco products used, and reasons for OTP use.		for their snus (55.56%) or snuff/chew use (59.80%). Less common reasons for use of snus and snuff/chew among daily smokers were "Cigarette smoking not allowed" (25.40% and 19.61%, respectively) and "Trying to cut down on smoking" (12.70% and 15.69%, respectively). There were no significant differences between nondaily and daily smokers in the reasons for snus or snuff/chew use.	
(Evans-Polce, Lanza, & Maggs, 2016)	Heterogeneity of alcohol, tobacco, and other substance use behaviors in U.S. college students: A latent class analysis	The study assessed subgroups of individuals in their fourth year of college (n = 608; mean age: 21.5 years) based on their patterns of seven substance use behaviors. Objective: To identify subgroups of college student with distinct profiles of traditional and alternative types of tobacco, alcohol, and other substance use and to examine how demographic characteristics and academic and social activities are associated with subgroup membership.	Seven substance use behaviors were considered: Extreme HED, cigarette use, cigar/cigarillo/little cigar use, ST use, hookah use, marijuana use, and non-medical prescription drug use. Demographic characteristics and academic and social activities were then incorporated as predictors of these subgroups.	Five classes were established for the considered population. Three of the classes contained tobacco users. Of ST users, 29.8% of non-hookah tobacco users, 0.1% of hookah and marijuana users, 69.4% of polysubstance users were ST users.	Limitations: (1) A more in-depth measure of substance use frequency or intensity would permit more fine-grained analysis; (2) newer tobacco products such as ECs were not assessed; (3) marijuana use, hookah use, and nonmedical prescription drug use were assessed in the past 12 months, while extreme HED, cigarette use, cigar use, and ST use were assessed in the past 30 days; and (4) the study focused on undergraduate students at a single institution in 2010.
(Graber et al., 2016)	Cigarettes, smokeless tobacco, and poly-tobacco among workers in three dusty industries	Data from the 2006 through 2012 NSDUH were considered for males in three blue-collar industries with a potential for significant occupational dust exposure compared with all other industries (agriculture, n = 2,031; construction, n = 12,708; extraction/mining, n = 990; other work,	Bivariate and multivariate analyses were used to compare tobacco use prevalence among male blue-collar workers in "dusty" industries to all other employed men.	Dual cigarette and ST use was increased in construction (OR = 1.5; 95% CI: 1.3, 1.8) and extraction (OR = 2.6; 95% CI: 1.8, 3.6) workers compared with other workers, but dual use was decreased in agriculture workers compared with other workers (OR = 1.8; 95% CI: 1.3, 2.5). "[T]he odds of dual use declined monotonically with increasing age among	Limitations: (1) The study was a cross-sectional study design, which precludes the ability to make inferences about the directionality of observed associations; (2) the data used were based on self-report; (3) there is a paucity of information on the reliability and validity of

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		n = 72,853). Participants were 18 to 64 years old. Objective: To assess and compare tobacco-use prevalence and risk factors among workers in three dusty industries: agriculture, construction, and extraction; and to explore trends over time and the frequency of product use among single and dual tobacco product users.		construction workers, while among agricultural and extraction industry workers was elevated among those age 18 to 35.” “For all industry groups, the odds of smoking and dual use were increased among men who smoked cigars or participated in binge drinking.”	survey questions for other types of tobacco use, including ST; and (4) estimates of tobacco use vary between national surveys and between studies.
(Guydish et al., 2016)	Use of multiple tobacco products in a national sample of persons enrolled in addiction treatment	A random sample of treatment programs was drawn from the NIDA CTN. Participants (n = 1,113) in each program completed surveys about use of tobacco products. Objective: To explore use of tobacco products in relationship to marketing exposure among persons in addiction treatment.	Exposure to tobacco marketing and counter-marketing, advertising receptivity, and perceived health risks of smoking were tested for their association with PTU.	Among weekly ST users (n = 58), 79.3% were also smokers.	Limitations: (1) Generalizability is limited due to challenges in recruiting randomly selected programs, including those that were no longer active in the CTN or who declined participation; (2) the study did not represent private and for-profit addiction treatment programs that serve employed and insured patients, who would likely have lower rates of smoking and tobacco use; and (3) the study overrepresented residential patients, in whom smoking rates tend to be higher than those for outpatients.
(Harrell et al., 2016)	Patterns of youth tobacco and polytobacco usage: the shift to alternative tobacco products	Data analysis was conducted to examine the 6,841 tobacco users (12.2% aged 9-13 years, 85.6% aged 14-18 years, and 2.2% aged 19+ years; 59.9% male; 47.7% white, non-	The study analyzed participants' past-month use of tobacco products and their sociodemographic	Nine classes of users emerged. The third largest class (12.3% of the sample) was characterized by a high probability of ST use (96%) and moderate probabilities for cigar (19%), cigarette (27%), and snus (22%) use.	Strength: Large sample size. Limitations: (1) Causal effects of the classes could not be determined due to the cross-sectional study conducted; and (2) it is

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		Hispanic) in the NYTS (2012 and 2013). Snus use was assessed separately from other ST products. Objectives: To identify patterns of youth tobacco use and to examine associations with sociodemographic characteristics and tobacco dependence.	characteristics and tobacco dependence.	<p>The fifth largest class (10.7% of the population) was characterized by high probabilities of cigarette (87%), cigar (89%), ST (75%), and pipe (69%) use. Snus use had an 18% probability).</p> <p>The seventh largest class (3.3% of the sample) was characterized by high probabilities for cigarette (83%), ST (100%), cigar (59%), and snus (55%) use, as well as moderate probabilities for EC (48%), hookah (28%), and pipe (20%) usage.</p> <p>The smallest class (1.7% of the sample) was characterized by high probabilities for use of all considered tobacco products, including ST (86%) and snus (97%).</p> <p>Polytobacco users were more likely than cigarette smokers to report dependence, defined as having a first tobacco craving within 5 min after waking (AOR = 2.77, 95% CI: 1.49-5.18).</p>	unclear if the proxy measure of ND used is appropriately modified.
(Hatsukami et al., 2016)	Randomised clinical trial of snus versus medicinal nicotine among smokers interested in product switching	Cigarette smokers (n = 391; mean age: 43.9 years; 52.9% male; 81.8% non-Hispanic, white) recruited in Minnesota and Oregon were randomized to either snus or 4 mg nicotine gum for 12 weeks and were asked to stop smoking. Objective: To compare snus versus nicotine gum on the extent to which smokers can completely switch to these	Urine samples were collected and analyzed for carcinogenic tobacco-specific nitrosamine metabolites and nicotine metabolites levels.	Dual use of cigarettes and these products was observed in 52.9% and 58.2% of those assigned to snus and nicotine gum, respectively, at Week 12.	Limitations: (1) Potential lack of generalizability to a general population of smokers because the study examined smokers interested in trying an alternative product in a clinical setting; (2) only one snus product tested; (3) encouragement to use a specified number of pieces of each of the products; (4)

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		products, the pattern of the product use, and effects on biomarkers of exposure; and to compare the effects of both products on withdrawal symptom relief, product evaluation, and adverse events.			implementation of a tapering period, which might have constrained substitution behavior; and (5) not examining the data by sex since women might respond more positively to snus.
(Jitnarin et al., 2016)	Prevalence and correlates of late initiation of smokeless tobacco in US firefighters	Data derived from two firefighter health studies with 1,447 male firefighters, of whom, 207 have ST data available (n = 174 used ST before joining their company, mean age: 36.4 years, 89% white; n = 33 used ST after joining, mean age: 36.8, 87.5% white). Objective: To examine characteristics associated with late ST initiation in a sample comprising male career firefighters from two large cohort studies.	Participants were analyzed for correlates of late ST initiation.	The percentage of firefighters that smoked cigarettes and used ST before joining their company was 17.6%, whereas it was 25.0% in those that initiated ST use after joining. The percentage of firefighters that smoked cigars and used ST before joining was 20.2%, whereas it was 16.0% in those that initiated ST use after joining.	Strengths: (1) Large sample size; (2) the use of standardized and validated health measures. Limitations: (1) The study was based on cross-sectional data, limiting its ability to explore the longitudinal relationship between ST use and demographic and health characteristics; because the two studies were designed for other purposes, this study could only examine variables that were measured similarly in both studies.
(Kalkhoran et al., 2016)	Multiple tobacco product use among young adult bar patrons in New Mexico	Cross-sectional surveys were collected from young adults (n = 2,291; age: 18+ years) in bars in Albuquerque, New Mexico, using time-location sampling between 2011 and 2013. Surveys were conducted 2 and 3 years into an intervention to reduce cigarette use, and analyzed in 2014-2015. Objective: To identify use of OTPs among young adult bar patrons in the context of a bar-based intervention to decrease cigarette smoking.	Participants reported current use of cigarettes, snus, dip, cigarillos, hookah, and EC, demographics, and tobacco-related attitudes.	There was no significant difference in PTU (cigarettes + at least one OTP) between daily and nondaily smokers. Over 60% of current cigarette smokers also used another tobacco product: EC (46%), hookah (44%), cigarillos (24%), dip (15%), and snus (14%) in 2012-2013. Among polytobacco users, 30% used dip and 25.6% used snus. Odds of PTU were greater among males (AOR = 1.89; 95% CI: 1.37, 2.60; p < 0.001) and those reporting past-30-day binge drinking (AOR = 1.97; 95% CI:	Limitations: (1) Data collection used cross-sectional surveys; (2) the data are from one U.S. city; (3) the data were collected as a part of an evaluation of an intervention to reduce cigarette use, which may have affected cigarette and OTP use rates; (4) current use of tobacco products included any past-30-day use and therefore included a range of use patterns; (5) the exclusion of highly

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				1.35, 2.90; $p < 0.01$), and lower in those who believed secondhand smoke exposure is harmful (AOR = 0.60; 95% CI: 0.40, 0.89; $p < 0.05$).	intoxicated individuals from the study may have resulted in lower reported rates of tobacco use; (6) trends observed could be due in part to population growth or shifting in demographics; and (7) the results were subject to reporting bias due to self-reported data.
(Linde et al., 2016)	Smokeless tobacco use among United States Air Force trainees	Data collected from a cross-sectional survey of USAF technical training school personnel at Joint Base San Antonio-Lackland and Fort Sam Houston (n = 14,810 total; n = 11,024 males; n = 6,816 age < 20 years; n = 12,546 not Hispanic). Objective: To assess the prevalence of ST use and the sociodemographic correlates of ST use among individuals entering the USAF.	Data were analyzed for the associations between demographic variables, tobacco use, and social factors for both regular and infrequent ST users.	The percent of participants that smoke at least one cigarette per month was 10% among infrequent ST users (<1 use per month) and 26% among regular ST users (≥ 1 use per month). Infrequent (AOR = 5.00; 95% CI: 4.20, 5.96) and regular (AOR = 5.42; 95% CI: 4.81, 6.09) ST use were associated with monthly cigarette use.	Strengths: Large sample size. Limitations: (1) Generalizability to other USAF service members because individuals assessed were early in their military career; (2) ST use in the USAF is not representative of ST use across the service branches, since rates for the USAF are consistently lower than those for the rest of the military; and (3) self-reported and cross-sectional data were used in this study.
(Little et al., 2016)	Types of dual and poly-tobacco users in the US Military	A cross-sectional survey of tobacco product use among 13,873 Air Force trainees (demographic data not presented) from 2013 to 2014 were assessed for prevalence of the use of 10 different tobacco products. Objective: To explore the prevalence of dual use and PTU and the type of use, specifically, the likelihood of	Demographic and environmental factors, such as risk perceptions of tobacco use, peer use, and tobacco-company influences were determined for polytobacco users. Types of polytobacco users were also determined.	Among participants, 27.1% were tobacco-product users, and 50% used >1 products. One class of polytobacco user identified was cigarette and ST dual users: 55% cigarette use and 99% ST use. The cigarette-ST use class, compared with single-product users, was significantly more likely to be male (OR = 7.89; 95% CI: 4.35, 14.30; $p < 0.0001$), age < 21 years (OR = 1.32; 95% CI: 1.01, 1.72; $p < 0.05$), and have received	Strengths: (1) Large sample population; and (2) the population under study (non-college-bound young adults aged 18-24 years). Limitations: (1) Generalizability to other Air Force service members because individuals assessed were early in their military career; (2) ST use in the USAF was not

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		combinations of products among USAF trainees, and to examine potential correlates of these groups to identify whether they differed from monousers in terms of demographic and psychosocial characteristics.		tobacco products for free at a bar or social event (OR = 1.71; 95% CI: 1.37, 2.14; p < 0.0001). They were less likely to perceive harm from tobacco products (OR = 0.83; 95% CI: 0.75, 0.92; p < 0.05) and have tobacco use among their peers (OR = 0.80; 95% CI: 0.72, 0.89; p < 0.0001).	representative of ST use across the service branches, since rates for the USAF were consistently lower than those for the rest of the military; (3) the study did not include airmen reenlisting in the USAF; (4) participants were asked about their tobacco use before Basic Military Training; and (5) this was a cross-sectional survey.
(Macy et al., 2016)	Dual trajectories of cigarette smoking and smokeless tobacco use from adolescence to midlife among males in a Midwestern US community sample	This study included all male participants in a longitudinal study who reported cigarette smoking or ST use in 1987, 1993, 1999, 2005, or 2011 (in 1987: n = 2,230; mean age: 20.1 years). Objective: To identify trajectories of ST use and cigarette smoking from adolescence to midlife.	Group-based trajectory analyses were conducted with zero-inflated Poisson models and analysis of covariance was used to test adolescent health beliefs associated with trajectory group membership.	Regarding dual use of cigarettes and ST, "2.6% of the sample belonged to trajectory groups representing consistent regular use of both cigarettes and smokeless tobacco. An additional 2.9% were consistent regular for smoking and late onset, escalating for smokeless; 1.1% were late onset intermittent, then cessation for smoking and late onset, escalating for smokeless; and 2.2% were late onset intermittent, then cessation for smoking and consistent regular for smokeless. Thus, a total of 8.7% were members of trajectory groups that represented any dual use over the 35-year time period."	Strength: The study uses longitudinal data. Limitations: (1) Participants were predominantly white, non-Hispanic and located in Midwestern U.S.; (2) any short-term changes in tobacco-use behaviors (less than 6 years) could not be detected; and (3) dual use was defined using seven subcategories of smoking, but there were only three subcategories of ST use.
(Pacek, Sweitzer, McClernon, & Pacek, 2016)	Non-cigarette tobacco and poly-tobacco use among persons living with HIV drawn from a nationally representative sample	Data were derived from 472 HIV-positive adults (age: ≥12 years from 2005-2013 NSDUH, of which 276 were past-year tobacco users (95.8% cigarettes, 19.3% cigars, and 3.1% ST). Objective: To characterize the prevalence of cigarette and	Data were analyzed for tobacco use, sociodemographics, substance use, mental health, and risk variables.	The prevalence of PTU was overall 8.7%, and 16.6% among past-year tobacco users. Of polytobacco users, 100% used cigarettes, 98.1% used cigars, and 12.3% used ST. The most common combination was cigarettes + cigars (87.7%), followed by cigarettes + cigars + ST (10.3%) and by cigarettes + ST (1.9%)	Strengths: Utilized a nationally representative sample to examine PTU in PLWH. Limitations: (1) NSDUH is a cross-sectional survey; (2) all answers were obtained via self-report; (3) ND in NSDUH is cigarette based,

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		noncigarette tobacco use, PTU, and correlates of tobacco use status among a nationally representative sample of PLWH.		Compared with those aged 18 to 25 years, participants who were aged 26-34 years (aRRR = 0.13, 95% CI: 0.03, 0.65) and 35+ (aRRR = 0.24, 95% CI: 0.09, 0.63), and with lifetime anxiety disorder(s) (aRRR = 0.18, 95% CI: 0.006, 0.57) were less likely to be polytobacco users than single product users. Participants who liked to do risky things were more likely to be polytobacco users than single product users (aRRR = 2.95, 95% CI: 1.27, 6.84).	which limits the opportunity to test how nicotine dependence factors into PTU; (4) NSDUH did not capture information on certain types of tobacco products; and (5) the study did not explore frequency of tobacco-product use.
(Sapra, Sundaram, Buck, Barr, & Maisog, 2016)	Time-to-pregnancy associated with couples' use of tobacco products	Couples (n = 501; males aged 18+ years, females aged 18-40 years) in 16 counties in Michigan and Texas, who discontinued contraception to become pregnant, were followed until positive pregnancy test or 12 months of trying. Objective: To assess the relationship between paternal preconception tobacco use (ST and combustible) and prospectively TTP; and to evaluate blood heavy metal and serum cotinine concentrations among various tobacco-product users and nonusers to determine if specific chemicals may contribute to changes in TTP.	Participants were interviewed on lifetime and current cigarette, cigar, and ST (chew/snuff) use and provided blood samples for quantification of heavy metals and cotinine. FORs were estimated and adjusted for demographics and lifestyle (FOR < 1 indicates a longer TPP).	FOR of male partners who used snuff and/or chew only was 1.09 (95% CI: 0.67, 1.79) when compared with never-use of tobacco products, whereas FOR of male partners who were exclusive cigarette smokers was 0.35 (95% CI: 0.21, 0.56). FOR of male partners who used cigarettes and snuff/chew was 0.73 (95% CI: 0.32, 1.67) when compared with never-user.	Strengths: (1) The relationships between several types of tobacco products at different times and TTP were assessed; (2) recall bias associated with reporting exposure after the outcome was known was minimized; (3) preconception recruitment of couples allowed the authors to prospectively observe trying time for pregnancy without relying upon retrospective report of trying time; and (4) the possible biological mechanisms underlying the observed associations were able to be investigated by measurements of cotinine and heavy metal concentrations from biological samples. Limitations: (1) Small numbers of ST users; (2) EC

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					data were not available; and (3) because men and women lost to follow-up were more likely to be current smokers than couples completing the study, the findings might underestimate the association between cigarette use and TTP.
(Schauer et al., 2016)	Past year quit attempts and use of cessation resources among cigarette-only smokers and cigarette smokers who use other tobacco products	Data came from 24,448 current cigarette-only users (age: 18+ years; 51.08% male), 1,064 cigarette and cigar-only users (age: 18+ years; 78.58% male), and 508 cigarette and ST users (age: 18+ years; 94.69% male) who responded to 2010-2011 TUS-CPS. Objective: To assess differences in past-year cigarette-smoking-cessation attempts and use of counseling or medication among current cigarette-only users, cigarette and cigar users, and cigarette and ST users.	Data were analyzed for demographic differences among tobacco use groups; differences in a variety of cessation measures; and the association between tobacco use group and making a past-year cigarette-smoking-cessation attempt or using evidence-based cessation resources.	A higher percentage of combined cigarette and ST users reported trying to quit smoking cigarettes for a day or more in the past year (45.7%) than cigarette-only users (36.6%). Compared with that for cigarette-only users (5.6%), a significantly smaller percentage of those using cigarettes and ST reported they had used counseling during the last quit attempt (1.7%). Tobacco-use group was significantly associated with making a past-year quit attempt; those in cigarette and ST group had higher odds of reporting that they had tried to quit in the past year than did those in the cigarette-only group (OR = 1.31, 95% CI: 1.05, 1.64). However, after adjusting for other sociodemographic and smoking characteristics, tobacco-use group was no longer a significant correlate for attempting to quit in the past year or using counseling during a quit attempt.	Limitations: (1) The data are cross-sectional and cannot be used to assess causality or temporality; (2) sample size limitations precluded the assessment of users of other combinations of tobacco products; (3) heterogeneity may exist within the dual-use groups assessed because both cigars and ST include multiple products, each with potentially different use profiles; (4) cessation behaviors were assessed only among current smokers; (5) findings from cigarette and ST group apply primarily to males; and (6) although dual users appear to attempt to quit at rates similar to those of cigarette-only users, the study was unable to assess quit rates due to insufficient sample sizes.

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(Sung et al., 2016)	Polytobacco use of cigarettes, cigars, chewing tobacco, and snuff among US adults	Data were derived from the 1998, 2000, 2005, and 2010 Cancer Control Supplements of the National Health Interview Survey (n = 117, 816 adults; age: 18+ years; 48% male; 72.3% non-Hispanic white). Objective: To examine the prevalence, trends, and correlates of PTU among current users of cigarettes, cigars, chewing tobacco, and snuff in U.S. adults aged ≥18 years.	The study analyzed significant factors associated with PTU.	The prevalence of PTU was 8.6% among current cigarette smokers, 50.3% among current cigar users, 54.8% among current chewing tobacco users, and 42.5% among current snuff users in 2010. “Among current chewing tobacco users, polytobacco use was significantly more likely among non-Hispanic Asians and binge drinkers; however, it was significantly less likely among those aged ≥ 25, high school graduates, and college graduates.” “Among current snuff users, polytobacco use was significantly more likely among men, non-Hispanic blacks, and binge drinkers, but was significantly less likely among adults aged ≥ 25, college graduates, and the high income group.”	Strengths: The study used a large, nationally representative data set. Limitations: (1) The study did not examine new and emerging tobacco products, such as ECs, hookah, and dissolvables; (2) the study was based on cross-sectional data, with 2010 being the most recent year of available data; and (3) the sample size of certain subgroups was small.
(White, Redner, Bunn, & Higgins, 2016)	Do socioeconomic risk factors for cigarette smoking extend to smokeless tobacco use?	Data from the 2012 NSDUH were obtained from U.S. adults (n = 37,869; age: 18+ years; 48.1% male; 66.3% non-Hispanic white). Objective: To examine SES as a risk factor for ST use in a U.S. nationally representative sampling, utilizing data from the 2012 NSDUH.	Odds were generated for current cigarette smoking and ST use among adults based on SES markers after controlling for the influence of demographics and other substance dependence.	Prevalence rates of current cigarette smoking and ST use were 23.8% and 3.7%, respectively. Among current cigarette smokers, 5.7% reported current ST use; among current ST users, 37.2% reported current cigarette use.	Limitations: (1) The data set was observational, and as such it was important to acknowledge the possible influence of unobserved variables; and (2) the data were self-reported, and thus may be biased in the direction of underreporting.
(Wong et al., 2016)	Distinct motives for use among polytobacco versus cigarette only users and among single tobacco product users	The study analyzed data from past-30-day tobacco users at Wave 2 (spring of 2015) of a six-wave longitudinal study of 3,418 students aged 18-25 years from seven U.S. colleges. Among participants, 679 were past-30-day tobacco	Participants' sociodemographics, tobacco use, and tobacco use motives were compared between PTU and cigarette-only use.	Among past-30-day ST users (n = 87), 36 (41.4%) also used cigarettes, 22 (25.3%) also used LCCs, 29 (33.3%) also used ECs, and 19 (21.8%) also used hookahs in the past 30 days. The prevalence of past-30 day ST use among other past-30-day tobacco product	Limitations: (1) There is limited generalizability of the findings due to its recruitment from colleges and universities in the Southeast region of the U.S.; (2) the sample sizes for the LCCs, ST, and EC were

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		users (mean age: 20.55 years; 54.93% female; 58.6% white). Objective: To examine motives for tobacco use in relation to PTU versus cigarette-only use and motives for tobacco use in relation to levels of tobacco use across products.		users was 10.8% (cigarettes), 11.1% (LCCs), 14.2% (ECs), and 7.8% (hookahs). “Multivariate analyses found that boredom relief motives were associated with polytobacco use versus cigarette only use (p = .007).”	small; and (3) there was a relatively low response rate through the E-mail recruitment method.
(Anand et al., 2015)	E-cigarette use and beliefs among urban public high school students in North Carolina	A 47-item EC questionnaire modeled after Monitoring the Future with additional demographics, adolescent and family nicotine use, and school and health care interventions was designed, piloted, and administered to public high school students (n = 3,298; mean age: 16.4 years; 51% male; 38% white) in May 2013 in North Carolina. Objective: To examine the prevalence, attitudes, and risk factors associated with EC use among high school students in a tobacco-growing state.	Binary logistic regression was used to assess multiple variables associated with EC use.	Past-30-day dual use of EC and ST tended to increase from 9th grade to 12th grade: 4.4%, 3.6%, 4.6%, and 6.5%. The overall prevalence of EC and ST dual use in Grades 9-12 was 4.7%.	Limitations: (1) Authors could not assess if EC-use patterns lead to other tobacco use; and (2) data from one county in a tobacco-growing state may not accurately reflect adolescent EC-usage patterns of other states or the U.S. as a whole.
(Boyle et al., 2015)	Tobacco use among Minnesota adults, 2014	A surveillance of adult tobacco product use in 2014 was conducted in Minnesota through 9,304 phone interviews (age: 18+ years). Objective: To examine tobacco use over the changing landscape of tobacco, including the introduction of new products such as ST and electronic delivery devices.	Respondents who met lifetime use thresholds were defined further as current users if they reported one day or more of use in the past 30 days.	“[A]mong cigarette smokers 27.3% used [ECs], 9.5% smoked cigars, 7.4% used [ST], and 2.5% used a regular pipe.”	Strength: Large sample population. Limitations: (1) The data relied on self-reported behaviors; (2) the stratified design resulted in small sample sizes across regions and subgroups, and, therefore, the point estimates vary in precision; and (3) although the response rate was considered an acceptable random digit dial

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					response and the data were adjusted for nonresponse, the possibility of nonresponse bias remains.
(Creamer et al., 2015)	Trends in multiple tobacco product use among high school students	Trends in individual and CU of cigarettes, cigars, and ST products of high school students, Grades 9-12, were tested using repeated cross-sectional data from eight national YRBS surveys between 1999 and 2013. Objective: To determine the trends of multiple and individual tobacco-product use over time among all students and current tobacco users, and to examine sociodemographic differences in these trends.	The primary tobacco variables related to self-reported use of cigarettes (smoked cigarettes ≥ 1 day during the past 30 days); cigars and LCCs (smoked cigars ≥ 1 day during the past 30 days); and ST (used ST ≥ 1 day during the past 30 days). Tests for effect modification by race/ethnicity and sex were conducted for each trend.	<p>“There was no change in the prevalence of the dual use of cigarette and [ST] among boys who used tobacco between 1999 and 2013 ($p = 0.62$), yet girls’ concurrent use of cigarettes and [ST] increased between 1999 (1.3%) and 2013 (4.4%) ($p = 0.02$).”</p> <p>“[S]ex was identified as an effect modifier, but not race/ethnicity, for the concurrent use of cigarettes and cigars and the concurrent use of cigarettes and [ST].”</p>	<p>Strength: The study used nationally representative data from YRBS.</p> <p>Limitations: (1) The data were from repeated cross-sections, as opposed to a cohort, which limits causal implications and some analytic capabilities; and (2) the data were from self-reported measures.</p>
(Elfassy et al., 2015)	Trends in cigarette, cigar, and smokeless tobacco use among New York City public high school youth smokers, 2001-2013	Objective: To describe the recent trends in youth smoking behaviors and to examine cigar and ST use patterns among youth smokers in New York City.	Data were from the NYC YRBS, a cross-sectional survey conducted bi-annually since 1997 in a representative sample of New York City public high school students (2001-2013, $n = 59,122$).	Cigarette smoking declined 53% from 2001 to 2013 ($p < 0.001$). The proportion of cigar use increased overall, among non-cigarette smokers, and doubled among cigarette smokers ($p < 0.001$), while the proportion of ST use among smokers increased overall, among non-cigarette smokers, and quadrupled among cigarette smokers ($p < 0.001$).	<p>Strength: It showed trends in youth smoking behaviors in New York City.</p> <p>Limitations: (1) Smoking prevalence estimates from NYC YRBS are likely to be underestimated due to underrepresented white adolescents (who are more likely to smoke) in New York City public high schools; (2) the current analysis could not characterize use of OTPs; and (3) this analysis was not a formal evaluation of tobacco policies and did not</p>

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					control for secular trends, though trends in national youth smoking rates reveal different patterns.
(Kaufman et al., 2015)	Tobacco use transitions in the United States: The National Longitudinal Study of Adolescent Health	A sample of 20,774 male and female adolescents in Grades 7-12 (49.4% male) was selected to participate in an initial 1995 survey (Wave I). Follow-up surveys were administered in 1996 (n = 14,738; Wave II), 2002 (n = 15,197; Wave III), and 2008/2009 (n = 15,701; Wave IV) Objective: To evaluate and describe transitions in cigarette and ST use, including dual use, prospectively from adolescence into young adulthood.	The data were analyzed for prevalence of cigarette smoking, ST use, and dual use; patterns of tobacco use over time, including transitions between ST and cigarette use; and how the transitions differ across demographic groups.	Among the cohort (n = 20774), 7.2% reported dual (past-30-day) use of cigarettes and ST (n = 1503; 84.3% males; 84.8% white) in at least one of the four waves. Reports of dual use for the four waves were 3.7% (Wave I), 3.8% (Wave II), 2.2% (Wave III), and 2.2% (Wave IV). “Among participants reporting dual use, the [1-year] transition probability to neither product was 13%, to cigarettes only was 5.5%, to ST only was <1%, and continuance of both products was 81%.” “Among White male participants reporting dual use, the transition probability to neither product 1 year later was 15% and continuance of both products 1 year later was 80%.”	Strength: The study analyzed prospective data on cigarette and ST product use in a nationally representative cohort followed from adolescence into young adulthood. Limitations: (1) The study relied on self-reports of tobacco product use without biochemical validation; (2) the results were not weighted to provide nationally representative estimates; (3) the data were drawn from 1995 to 2009, during which changes have occurred in both tobacco control efforts and tobacco marketing and product availability; and (4) the survey did not collect data on some other forms of tobacco use.
(Kish et al., 2015)	Characterizing concurrent tobacco product use among homeless cigarette smokers	Participants (n = 178; mean age: 45.6 years; 75.3% male; 32% white) were adult cigarette smokers from a homeless shelter in Dallas, Texas. Data about participants' sociodemographic characteristics, number of homelessness episodes, tobacco dependence, and items	Sociodemographic characteristics, number of homelessness episodes, tobacco dependence, stress, readiness to quit smoking, and number of smoking quit attempts in the last	CU (n = 91 [51.1%]; mean age: 43.69 years; 81.3% male; 38.5% white) was prevalent, and 49.5% of CUs reported the use of ≥2 products in addition to cigarettes. Of CUs, 8 (8.8%) reported snus use, and 6 (6.6%) reported chewing tobacco use. The snus CUs smoked an average of 12.6 cigarettes per day, and 50% felt their	Limitations: (1) The use of a small adult sample from a single shelter in Texas; (2) CU was defined as use over the last 30 days and might not represent regular use of these products; (3) additional psychological factors related to smoking behaviors and relapse were

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		characterizing use of several tobacco products over the last 30 days, including use frequency, reasons for use, and perceived health risks, were collected. Objective: To characterize CU in a sample of homeless smokers and to compare C-OS with concurrent users on participant characteristics and factors known to be associated with smoking cessation.	year were compared between C-OS and CUs groups.	tobacco use put their health at extreme/a lot of risk. The chewing tobacco CUs smoked an average of 16.0 cigarettes per day, and 50% felt their tobacco use put their health at extreme/a lot of risk. The majority of snus and chewing tobacco CUs used to snus (75%) or chewing tobacco (50%) because it helped them cut down/quit cigarettes. “Compared with C-OS, CUs [cigarettes + at least one other tobacco product] were younger and had more homelessness episodes, higher expired breath carbon monoxide levels, and higher stress (ps < .05).”	not studied; (4) the concurrent use of other products and descriptors and discarded cigarette-butt smoking was not assessed; and (5) there was no information on the use of alternative tobacco products among homeless nonsmokers and former homeless smokers.
(Kowitt et al., 2015)	Poly-tobacco use among high school students	Data were based on the 2013 NCYTS from students in Grades 9-12 (n = 4,092; age: 14+; 51.1% male; 54.0% non-Hispanic white). Objective: To assess patterns of PTU among a representative sample of high school students and to determine how beliefs correlate with PTU.	Multivariate regression was used to examine the association between relevant predictors and use of tobacco products at three levels: non-use (i.e., no past-30-day use), single use (i.e., past-30-day use of 1 tobacco product), and polyuse (i.e., past-30-day use of 2+ tobacco products)	There were 751 (18.4%) polytobacco users in the sample population, of which 23.0% used cigarettes and EC; 18.3% used chewing tobacco, snuff, or dip and cigars/LCCs; 12.7% used chewing tobacco, snuff, or dip and EC; and 11.9% used chewing tobacco, snuff, or dip and tobacco in a pipe (note: a subject could belong to more than one group). “Positive tobacco product beliefs were found to be significantly associated with poly-tobacco use.”	Limitations: (1) The cross-sectional nature of the data limited the ability to make causal claims about relationships between beliefs and PTU; (2) results may not be generalizable to other students in the U.S. or those of other ages; (3) self-report; and (4) four of the seven belief items in the NCYTS only asked about opinions of cigarettes.
(Lee et al., 2015)	Youth tobacco product use in the United States	Data from the 2012 NYTS (n = 24,658; age: 9+ years) of U.S. middle school and high school students were evaluated. Objective: To examine multiple tobacco-product use	Data were analyzed for current use of tobacco products (cigarettes, cigars, ST, hookah, EC, pipes, bidis, kreteks,	Dual use of cigarettes and ST was reported in 53 participants (weighted % = 0.2%; 95% CI: 0.2, 0.3). By age, the weighted percent of dual users was: 0.1% (age: 9-14 years; n = 5), 0.4% (age: 15-17 years; n = 35), and 0.5% (age: 18+ years;	Strengths: (1) Data were recent; (2) large sample size; and (3) the study used a nationally represented data. Limitations: (1) The NYTS is cross-sectional data set

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		and associated risk factors among U.S. youth.	snus, and dissolvable tobacco), associations between use patterns, and demographic characteristics.	n = 13). “Among smokers, polytobacco use [cigarettes + at least 2 other tobacco products] was significantly associated with male gender (aRRR = 3.71), by using flavored products (aRRR = 6.09), nicotine dependence (aRRR = 1.91), tobacco marketing receptivity (aRRR = 2.52), and perceived prevalence of peer use of tobacco products (aRRR = 3.61, 5.73).”	and did not collect data on the use history of participants; therefore, use trajectories could not be assessed; (2) the study needed an improved measures on the emerging products such as EC; (3) the items used to measure OTP use in the NYTS might not capture the full extent of OTP use; and (4) the NYTS was a school-based sample of youth and might not adequately represent all youth.
(Meier, Tackett, Miller, Grant, & Wagener, 2015)	Which nicotine products are gateways to regular use?	Data were collected from an online survey (September 2012 to May 2013) completed by undergraduate students (n = 1,304; mean age: 19.57 years) of past/current use of cigarettes, ST, hookah, ETPs (dissolvables, snus, and EC); and NRT. Objective: To examine use of various nicotine-containing products on a tobacco-free college campus and whether the first product tried predicts subsequent tobacco use.	Students were classified as single, dual, or polytobacco users, and descriptive statistics were used to explore first-tried tobacco products and variables potentially associated with current tobacco use. Additionally, use frequency of different forms of tobacco and current and past tobacco use as a function of first product ever tried were calculated.	The sample consisted of 79.5% nonusers, 13.8% single, 4.4% dual users, and 1.5% polyusers. “Those who initiated with conventional cigarettes and [ST] were more likely to become poly tobacco users.” “[T]hose who first tried [ST] were six times more likely than those who first tried hookah to become a current poly tobacco user [OR = 6.15; 95% CI: 2.11, 17.95; p = 0.001] and four times more likely than those who first tried an ETP [OR = 4.05; 95% CI: 1.08, 15.10; p = 0.04].”	Limitations: (1) The study design is cross-sectional; (2) all data were self-reported without biochemical verification of smoking status; (3) the demographic characteristics of the sample were not nationally representative of all youth, rather just college students; (4) the authors did not assess cigar use; and (5) the authors only investigated the construct of first product tried as the mechanism for potential gateways.
(Neff et al., 2015)	Frequency of tobacco use among middle and high school students - United	Data from NYTS in 2014 were collected from 22,007 U.S. school students in Grades 6-12 who attended public and private schools.	Tobacco products use and the frequencies were assessed.	Among participants who reported using cigarettes, EC, cigars, or ST on 1-5 days during the preceding 30 days, the percentages using multiple tobacco products were 77.3% for cigar smokers,	Limitations: (1) The data were self-reported and might be subject to recall bias or social-desirability bias; (2) the data were collected from

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	States, 2014	Objective: To determine how frequently (the number of days in the preceding 30 days) U.S. middle school and high school students used cigarettes, EC, cigars, and ST products.		76.9% for cigarette smokers, 63.4% for ST users, and 54.8% for EC users. Of the participants who reported using ST on 6-19 of the previous 30 days, approximately 85% used multiple tobacco products; of the participants who reported using ST on 20-30 of the previous 30 days, approximately 80% used multiple tobacco products.	students who attended either public or private schools, and might not be generalizable to all U.S. middle school- and high school-aged youths; (3) frequency of use was estimated by the number of days the respondent reported using the tobacco product during the preceding 30 days; however, the pattern of use, primary product used, or which products were used on specific days could not be obtained from the data; and (4) frequency of use of hookahs, tobacco pipes, snus, dissolvables, and bidis was not collected.
(Nguyen et al., 2015)	State-specific prevalence of current cigarette smoking and smokeless tobacco use among adults aged ≥ 18 years - United States, 2011-2013	Data from the BRFSS derived from U.S. adults during 2011-2013, who were current cigarette users, ST users, and concurrent cigarette and ST users, were analyzed. Objective: To assess prevalence of current cigarette smoking and current ST use.	State-specific point prevalence for current cigarette smoking, ST use, and dual use was calculated for all 50 U.S. States and the District of Columbia. The relative percent change from 2011-2013 was also calculated.	The prevalence of CU of cigarettes and ST ranged from 2% to 12.5% in 2011, and from 3.1% to 13.5% in 2013. The median dual use prevalence rates in 2011, 2012, and 2013 in all U.S. states and territories were 7.1%, 6.6%, and 7.4% (which equals a 4.2% relative percent increase from 2011 to 2013). Significant (p < 0.05) increases in CU were observed in five states.	Limitations: (1) The estimates for tobacco use were self-reported; (2) the BRFSS sampling frame does not include adults without telephone service; and (3) the median state response rates were low, which can increase the potential for bias.
(Tam et al., 2015)	A systematic review of transitions between cigarette and smokeless tobacco product	A systematic review of published literature on transitions between ST and cigarette use was performed. Search was performed through PubMed, Web of Science and	Information on the study characteristics including study population, follow-up, definitions for each tobacco use	Six articles met all selection criteria. The following are findings from the selected articles: Continued Dual Use <u>Adults</u> After 1 year, 45.0% of male dual users and	Limitations: (1) Estimates from some studies are not generalizable to the U.S. population; (2) there was variability in tobacco use definitions and follow-up

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	use in the United States	EbscoHost databases from January 2000 to March 2014. Information were extracted on the proportion of the sample population transitioning from baseline to follow-up. Objective: To identify systematic information on transitions between ST and cigarette use in the U.S.	categories, and how transitions were calculated were extracted.	<p>28.4% of female dual users remained dual users; after 4 years, 44.3% of male dual users remained dual users.</p> <p><u>Adolescents</u> After 1-2 years, 37% of dual users remained dual users; after 4 years, 20.4% of male dual users remained dual users.</p> <p>Transitioned into Dual Use <u>Adults:</u> Transitioning from neither ST nor cigarette use at baseline to dual use was rare ($\leq 0.1\%$). After 1 year, 1.8% of male exclusive ST users, 0% of female exclusive ST users, 2.2% of male exclusive smokers, and 0.1% of female exclusive smokers were dual users. After 4 years, 2.5% of male exclusive ST users and 3.2% of male exclusive smokers were dual users.</p> <p><u>Adolescents:</u> After 1-2 years, 5% of exclusive smokers were dual users. After 2 years, 8.3% of male nonusers, 40.7% of male exclusive ST users, and 23.8% of male exclusive smokers were dual users. After 4 years, 1.1% of male nonusers, 14.3% of male exclusive ST users, and 3.6% of male exclusive smokers were dual users.</p> <p>Transitioned from Dual Use <u>Adults:</u> After 1 year, 13.1% of males and 0% of females were nonusers; after 4 years, 11.3% of males were nonusers. After 1 year, 4.9% of males and 0% of females were exclusive ST users; after 4 years, 17.4% of males were exclusive ST users. After 1 year, 37.0% of males and 71.6% of females were exclusive smokers; after 4 years, 27.0% of males were exclusive smokers.</p> <p><u>Adolescents:</u> After 1-2 years, 17.9% of adolescents were</p>	time; (3) there is a potential bias in estimates from some studies due to tobacco use prevention or ban; (4) there are an absence of confidence intervals; and (5) estimates for females are missing, with the exception of one article.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Dual Use	Comments ^a
				nonusers, 8.5% of adolescents were exclusive ST users, and 36.6% adolescents were exclusive smokers. After 4 years, 14.1% of males were nonusers, 34.2% of males were exclusive ST users, and 31.2% of males were exclusive smokers.	
(Pickworth, Rosenberry, Koszowski, & Gold, 2014)	Nicotine absorption from smokeless tobacco modified to adjust pH	Double-blind, within-subject design with seven male subjects (mean age: 45 years; range: 28-62 years; 57% Caucasian). Sessions (3) separated by at least 24 hours, during which ST product was used by mouth in one of the following randomized conditions: (1) ST with altered low pH (5.4) and wintergreen flavoring; (2) ST with altered high pH (8.3) and wintergreen flavoring; (3) ST with unaltered pH (7.7) and no wintergreen flavoring (referent). Objective: To measure nicotine absorption after experimentally manipulating pH and flavorings of a single referent product.	Plasma nicotine and cardiovascular measures were assessed for all three conditions. ND, tobacco use history, subjective strength of the product, and product experience were assessed via questionnaires.	About half of the participants (43%) smoked conventional cigarettes in addition to using ST products at enrollment.	Limitation: (1) The study used a small sample size, and (2) dual-use data were only collected at baseline.
(Schauer et al., 2014)	Differences in smoking and cessation characteristics among adult nondaily smokers in the United States: findings from the 2009-2010 National	Data were obtained from the 2009-2010 NATS, a stratified, national dual frame telephone survey of 118,581 interviews (participants aged 18+ years), in which 130 questions about general health, cigarette smoking, other tobacco use, cessation, secondhand smoke, attitudes related to tobacco,	Participants were categorized into daily smokers, never-daily nondaily smokers, recently converted (≤ 1 year) nondaily smokers, and established-converted (>1 year) nondaily smokers. Chi-square	“Nondaily smokers were more likely to report specifically using smokeless tobacco (7.6%) than were daily smokers (5.1%, $p < .05$; data not shown), although no significant differences existed in use of other tobacco products (snus, cigar, hookah, or pipe).” Prevalence of PTU (cigarette use plus use of at least one of the following: ST, snus,	Strength: Data were obtained from a large nationally representative surveillance system. Limitations: (1) Tobacco-use status was not verified biochemically; (2) smoking and other data were self-reported and, thus, were subject to recall and

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Dual Use	Comments ^a
	Adult Tobacco Survey	chronic diseases, and respondent demographics were asked. Objective: To use a nationally representative data set to provide updated data on smoking and cessation characteristics among nondaily versus daily smokers, and to determine whether within-group differences exist among nondaily smokers based on whether they were ever-daily smokers and the length of time since their daily smoking.	tests were used to assess differences across groups, and multivariable logistic regression was used to identify factors associated with past-year quit attempts.	cigar, hookah, or pipe use) was not significantly different among daily (24.6%) and nondaily (28.2%) smokers (p = 0.0870).	social-desirability bias; and (3) data were from a cross-sectional survey.
(Berg et al., 2012)	Correlates of NNAL levels among nondaily and daily smokers in the college student population	Urine samples were collected from 64 current cigarette smokers (37 nondaily and 27 daily; mean age: 26.3 years; 40.3% male; 72.6% non-Hispanic white) in the Southeastern U.S. Objective: To examine correlates of urine NNAL levels among nondaily and daily smokers.	Participants were also assessed for their sociodemographics, smoking-related information, and other tobacco use.	Eight (12.5%) out of 64 participants concurrently used ST products (n = 7 nondaily smokers and n = 1 daily smoker). Dual use of ST with cigarettes was significantly associated with increased NNAL levels (p < 0.001) in nondaily smokers, but there was no significant association among daily smokers (p = 0.71).	Limitations: (1) Small sample size; (2) the use of self-reported smoking behaviors; and (3) dichotomization of daily versus nondaily smoking.

7.5.2-2.4. The Likelihood that Tobacco Users Who May Have Otherwise Quit Using Tobacco Products Will Instead Use the Product

All 3 articles found in this literature review that inform the likelihood that current tobacco users would switch to the candidate product instead of stopping to use tobacco products are discussed below and summarized in [Table 7.5.2-2-3](#).

7.5.2-2.4.1. Interventional Studies

Carpenter et al. ([Carpenter et al., 2016](#)) and Burris et al. ([Burris et al., 2016](#)) presented data from a study in current cigarette smokers, who were not interested in quitting smoking and were randomized to receive samples of snus (n = 626 current smokers) or not (n = 610 current smokers) for a 6-week sampling period. After the sampling period, the groups were monitored for 1 year for tobacco use. Carpenter et al. ([Carpenter et al., 2016](#)) reported the quit attempts for cigarettes during the period and found no group difference in any measure of abstinence between the snus group and the no intervention group. Smokers in the snus group were less likely than controls to make any quit attempts (relative risk [RR] = 0.83; 95% confidence interval [CI]: 0.70, 1.00; p = 0.05) and any 24-hour quit attempt (RR = 0.77; 95% CI: 0.63, 0.95; p = 0.02).

Burris et al. ([Burris et al., 2016](#)) focused only on the snus group and how it was a close approximation of a naturalistic study of U.S. smokers and snus. At the end of the sampling period, 47.1% of the group were current users of snus, and 17.6% of the group were frequent users of snus. At Week 58, 6.5% were current users of snus, and 1.9% were frequent users of snus. The self-reported purpose of snus use was to function as an alternative to smoking in 79.3% of snus users, and as a method of coping with smoking restrictions in 58.4%.

Both of these reports are discussed also in Section [7.5.2-2.2.1](#).

7.5.2-2.4.2. Surveys

Dunbar et al. ([Dunbar et al., 2016](#)) reported on the reasons for using multiple other tobacco products in 656 daily smokers and 203 nondaily smokers. Using snus to cut down on smoking was reported for 0% of nondaily smokers and 12.70% of daily smokers. Using snuff or chew to try to cut down on smoking was reported for 9.09% of nondaily smokers and 15.69% of daily smokers.

7.5.2-2.4.3. Updated Findings

Information in the updated literature review on the likelihood that current tobacco users who may have otherwise quit using tobacco products will instead use the candidate product is consistent with that seen in the initial literature review. The conclusions from the initial literature review (Section [7.5.2-1.4.6](#)) have not changed based on the updated literature review.

A tabular summary of the literature informing the potential of would-be tobacco quitters instead initiating use with ST is presented in [Table 7.5.2-2-3](#).

Table 7.5.2-2-3: Literature Summary for Intercepting Quitters

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Intercepting Quitters	Comments ^a
(Carpenter et al., 2016)	Snus undermines quit attempts but not abstinence: a randomized clinical trial among US smokers	Adult smokers (N = 1,236) throughout U.S. who denied intention to quit in the next 30 days were randomized to receive (n = 626; mean age: 48.7 years; 70% female; 89% Caucasian) or to not receive (n = 610; mean age: 48.7 years; 65% female; 87% Caucasian) free snus during a 6-week sampling period. Subjects were then advised to quit all tobacco use and were followed for 1 year. Objective: To examine the impact of snus use within a naturalistic, noncessation context.	Primary outcomes: Self-reported quit attempts, floating abstinence, and 7-day point-prevalence abstinence at 6 months and 1 year. Secondary outcomes: Changes in smoking, motivation, and confidence to quit, and adverse events.	Compared with control participants, smokers in the snus group were less likely to make any quit attempt (RR = 0.83; 95% CI: 0.70, 1.00) and any 24-hour quit attempt (RR = 0.77; 95% CI: 0.63, 0.95). There were no statistically significant differences between the groups on any measures of abstinence. Subjects in both groups significantly reduced the number of cigarettes smoked per day (by 23%) and increased both their motivation and confidence to quit smoking. There were no statistically significant differences between the snus and control groups in both motivation and confidence to quit smoking, and motivation to quit smoking remained low at the end of the sampling period and at the final follow-up. “The present study contrasts with several prior studies that suggest use of snus may facilitate quitting”	Limitations: (1) Only one product was used; (2) study sample consisted primarily of Caucasian women; (3) participants were smokers who did not want to quit, which may create the impression that it was methodologically biased against snus; and (4) there is a lack of biochemical verification of abstinence.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Intercepting Quitters	Comments ^a
(Burris et al., 2016)	A longitudinal, naturalistic study of U.S. smokers' trial and adoption of snus	Adult smokers (N = 1,236) throughout U.S. who denied intention to quit in the next 30 days were randomized to receive (n = 626; mean age: 48.7 years; 70% female; 89% Caucasian) or not receive (n = 610; mean age: 48.7 years; 65% female; 87% Caucasian) free snus during a 6-week sampling period. Subjects were then advised to quit all tobacco use and were followed for 1 year. Objective: To advance the current literature via a detailed description of snus uptake during a longitudinal study with adult U.S. smokers who denied intention to stop smoking in the near future.	Tobacco use outcomes were collected at each follow-up assessment (Week 0 to 58). Participants in the snus group, if they decided to use snus, were asked about the reason they decided to use snus.	<p>Among participants that reported current snus use and responded to questions about its purpose, 79.3% (n = 372/469) said it functioned as an alternative to smoking, and 58.4% (n = 277/474) said it provided a means of coping with smoking restrictions.</p> <p>If snus was only used by smokers for a single purpose (n = 222), it was more likely to be as an alternative to smoking than as a means of coping with smoking restrictions (71.6% vs. 28.4%).</p> <p>"Smokers showed willingness to try snus, but product interest waned over time. Snus as currently marketed is unlikely to play a prominent role in U.S. tobacco control efforts."</p>	<p>Strength: It was a longitudinal study that described in detail the nature of snus uptake among a large group of U.S. smokers.</p> <p>Limitations: (1) Only a single snus product was offered; (2) study population consisted of smokers who reported little to no interest in smoking cessation; (3) white, non-Hispanics and females are both overrepresented in this U.S. sample.</p>

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Intercepting Quitters	Comments ^a
(Dunbar et al., 2016)	Use of and reasons for using multiple other tobacco products in daily and nondaily smokers: Associations with cigarette consumption and nicotine dependence	Data were combined from the two studies conducted through the RAND Corporation's PROMIS Smoking Initiative. Daily smokers (n = 656) and nondaily smokers (n = 203) aged at least 18 years provided information on their use of different OTPs, reasons for using OTPs, and cigarette consumption and nicotine dependence. Objective: To examine the ways in which cigarette consumption and nicotine dependence among current daily and nondaily smokers are associated with likelihood of OTP use, number of different types of tobacco products used, and reasons for OTP use.	One study measure was the reason of use for each OTP product.	0% of nondaily smokers and 12.70% of daily smokers reported using snus to try to cut down on smoking; 9.09% of nondaily smokers and 15.69% of daily smokers reported using snuff or chew to try to cut down on smoking (OR = 0.53; 95% CI: 0.13, 2.09).	Strength: The study conducted a detailed analysis of multiple tobacco product use and reasons for use in relation to cigarette consumption and nicotine dependence in both daily and nondaily smokers. Limitations: (1) The authors did not collect biochemical measures of nicotine intake to validate self-reported data on tobacco consumption; (2) data were collected from 2013-2014, and the availability and use of OTP have only become more prevalent in recent years; and (3) data on smoking history were not available for this study.

7.5.2-2.5. The Expected Rates of Use of the Product among Current Tobacco Users

The Centers for Disease Control and Prevention used federal excise tax data to estimate total and per capita (among U.S. persons aged ≥ 18 years) consumption from 2000 to 2015 for combustible tobacco and ST to provide the most recently available tobacco consumption estimates in the U.S. (Wang, Kenemer, Tynan, Singh, & King, 2016). During that period, total ST consumption increased 23.1% ($p < 0.05$), which cannot solely be explained by the increase in U.S. adults aged ≥ 18 years over the same period: per capita ST consumption increased by 4.2% from 2000 to 2015. Total chewing tobacco consumption decreased 55.8% from 45.6 to 20.2 billion pounds ($p < 0.05$), and total snuff consumption increased 77.5% from 66.2 to 117.4 billion pounds ($p < 0.05$). The authors state that the increase may be due to advertising and promotion of snuff products; tobacco companies spent \$410.9 million promoting moist snuff in 2013. In the same year, \$11.8 million was spent on loose leaf chewing tobacco, \$234,000 for plug/twist chewing tobacco, \$485,000 for scotch/dry snuff, and \$51.2 million for snus.

Noteworthy or representative articles that address patterns of and factors associated with ST use are presented in the following sections, and all 63 articles are summarized in [Table 7.5.2-2-4](#).

7.5.2-2.5.1. Patterns of Smokeless Tobacco Use among Adolescents

Researchers have examined patterns of ST use among adolescents in the U.S. with respect to factors such as age, past-30-day usage, and race/ethnicity.

There was no clear trend of increasing ST use with increasing age in the updated literature review. Harrell et al. (Harrell et al., 2016) analyzed data from the 2012-2013 NYTS, completed by a representative sample of middle school and high school students in the U.S. They found that, among youths, 25.8% and 10% used ST and snus in the past 30 days, respectively. With the age group 9 to 13 years as referent, the odds ratio (OR) for ST use in the age group 19 to 21 years (OR = 0.77, 95% CI: 0.33, 1.84) was lower than in the age group 14 to 18 years (OR = 1.01, 95% CI: 0.68, 1.49), but neither was statistically significant. Lynne-Landsman et al. (Lynne-Landsman, Maldonado-Molina, Komro, Kominsky, & Boyd, 2016) performed a longitudinal study over 1 year in adolescents in Grades 9 through 10. They evaluated 684 adolescents (50% female and 51% American Indian) from six rural towns within the Cherokee Nation, a nonreservation tribal jurisdiction that includes a high population of American Indian persons embedded within the predominantly white population, between December 2011 and December 2012. The authors used growth mixture modeling and found that the majority of the youth (87%) followed a trajectory of no chewing tobacco use. The estimated probability of past-month chewing tobacco use was near zero across all waves of the nonuser class. About 9% followed a trajectory of moderate/increasing chewing tobacco use. These youths' estimated probability of past-month chewing tobacco use at the first assessment in early Grade 9 was 0.25 and increased to 0.50 by the final assessment in Grade 10. About 4% of youth belong to the

smallest user class, which consisted of youths with a high estimated probability of past-month chewing tobacco use (0.97 or greater across waves).

Two studies published during the review period assessed past-30 day ST use in adolescents. Neff et al. (Neff et al., 2015) analyzed data from the 2014 NYTS to determine the frequency of tobacco products use among U.S. middle school (Grades 6-8) and high school (Grades 9-12) students. The authors reported a higher percentage of frequent ST users (ST use on ≥ 20 days of the preceding 30 days) among high school ST users (42%) compared with middle school ST users (29.2%). However, a greater proportion of middle school ST users (38.4%) than of high school ST users (26.6%) used ST on 1-2 days of the preceding 30 days. Morean et al. (Morean et al., 2016) examined tobacco, marijuana, and alcohol use in 2,241 adolescents attending four high schools in southeastern Connecticut. In total, 2.8% of students reported using ST, with a mean ST use of 9.69 days per month.

Both females and non-Hispanic blacks were shown to have greater increases in ST use prevalence than males and other racial/ethnic groups, respectively, in a study of high school students. Creamer et al. (Creamer et al., 2015) analyzed data derived from the 1999-2013 national Youth Risk Behavior Survey (YRBS) and found that, among students in Grades 9 through 12, the prevalence of ST use significantly increased among females ($p = 0.01$), but not among males. Additionally, there was a significant increase among non-Hispanic black students ($p = 0.01$), but not among non-Hispanic whites and Hispanic students. Among tobacco users, the prevalence of ST use increased significantly from 19 percent in 1999 to 36 percent in 2013 ($p < 0.001$). Furthermore, the prevalence of ST use increased significantly among both male and female tobacco users (both p -values < 0.001), but the rate of increase was greater for females than for males.

Agaku et al. (Agaku et al., 2015) analyzed data from the 2001-2013 national YRBS of students that were in Grades 9 through 12. They reported that overall current ST use increased slightly from 8.2% (2001) to 8.8% (2013). There was a statistically significant increase in the prevalence of current ST use from 10% to 11.1% among athletes. Among athletes, there were statistically significant increases in current ST use among males (16.8% to 17.4%), females (2.2% to 3.4%), Grade 11 students (11.8% to 13.6%), Grade 12 students (11.1% to 12.2%), and Hispanic students (6.3% to 8%). Among nonathletes, a statistically significant increase was observed among Hispanic students (1.9% to 3.1%).

Finally, Ambrose et al. (Ambrose et al., 2015) analyzed data from youth (age: 12-17 years) enrolled in Wave I of the PATH study, which was a nationally representative longitudinal cohort study in the U.S. They showed that 68.9% of youth ST users reported their first ST product was flavored. The proportions of flavored ST use among past-30-day youth tobacco users was 81.0% for ST users (excluding snus users) and 80.4% for snus users.

7.5.2-2.5.2. Patterns of Smokeless Tobacco Use among Young Adults

The studies from the literature review update that are discussed in this section provide data on patterns of ST use among young adults in the U.S.

One longitudinal study examined ST use in men from adolescence to midlife. Macy et al. (Macy et al., 2016) analyzed data from the Indiana University Smoking Survey, which

followed subjects (n = 2,230; mean age of 20.1 years in 1987) who were male ST users or cigarette smokers from 1987 to 2011. The study found that 20.8% of subjects followed the “early onset then cessation” trajectory, 38.6% followed the “consistent abstinence from ST” trajectory, 10.9% followed the “late onset, escalating” trajectory, and 29.7% followed the “consistent regular” trajectory.

Mays et al. (Mays et al., 2016) analyzed data from young adults (age: 18-29 years) who completed the 2012-2013 NATS among U.S. adults. They found that 5.9%, 2.2%, and 0.1% of young adults were current chew/snuff/dip, snus, and dissolvables users, respectively.

Five studies assessed ST use in college-aged populations. In one, Loukas et al. (Loukas, Batanova, Fernandez, & Agarwal, 2015) analyzed a longitudinal study conducted across two waves in spring 2012 (Wave 1) and spring 2013 (Wave 2) among students in seven colleges within the University of Texas system. The study showed that the use of ST and snus increased from Wave 1 to Wave 2. There were 1.9% and 0.9% of students who used ST and snus in Wave 1, respectively. In Wave 2, about 2.2% and 1% of subjects used ST and snus, respectively.

Berg et al. (Berg et al., 2016) analyzed data from Project Documenting Experiences with Cigarettes and Other tobacco in Young adults (DECOY), which was a 2-year longitudinal study that examined risk for tobacco use among 3,418 young adults across seven Georgia colleges or universities. Data collection began in fall 2014 and consisted of individual assessments every 4 months for 2 years. They reported that past-30-day ST use was 3.6% among young adults in the study. Wong et al. (Wong et al., 2016) also analyzed data from Project DECOY; however, the authors only examined data from Wave 2 of the study (n = 2,969), which was conducted during March and April of 2015. They reported that 3.9% of all participants used ST within the past 4 months; among all tobacco users (n = 679), the prevalence of past-30-day ST use was 12.8%.

Meier et al. (2015) analyzed data from a voluntary online survey completed by undergraduate students enrolled in psychology and speech courses at a large university in Oklahoma during the 2012-2013 academic calendar. They reported that 13.2% of young adults who participated in the survey had ever tried ST and that 15.1% of young adults who had tried a tobacco product used ST as their first tobacco product. Additionally, 40.2% of subjects who first tried ST were current ST users.

Cooke et al. (Cooke et al., 2016) conducted a longitudinal study among freshman at Virginia Commonwealth University in 2011 and 2012. They reported that in fall 2011, there were 1.6%, 1.3% and 0.9% of subjects that used ST only once or twice, between three to 11 days, and between 26 to 30 days in a month, respectively. In spring 2012, there was a slight decrease of the percentage of subjects that used ST only once or twice (1.5%) and between 3 to 11 days in a month (1.1%), but there was an increase in subjects that used ST between 26 and 30 days in a month (1.2%).

Berg et al. (Berg et al., 2012) reported ST use in 62 college students who were cigarette smokers. In total, 12.5 percent (8 of 62 subjects) of the young adults concurrently used ST. Of these ST users, the mean number of days of ST use in the prior 30 days was 8.4 days.

7.5.2-2.5.3. Patterns of Smokeless Tobacco Use among Adults

The four studies selected for discussion in this section provide representative data on the patterns of ST use among adults in the U.S. Overall, there is a large range of prevalence rates when data are examined by state. Nationally, studies found the prevalence of ST use declined in the late 1990s and early 2000s before increasing or remaining constant.

Nguyen et al. (2015) analyzed the 2011-2013 Behavioral Risk Factor Surveillance System data among U.S. adults aged 18 years and older and demonstrated that current ST use ranged from 1.4% (California and Rhode Island) to 9.8% (Wyoming) in 2011, whereas in 2013, the current ST use range from 1.5% (District of Columbia and Massachusetts) to 9.4% (West Virginia). Statistically significant ($p < 0.05$) relative percent changes were observed in Louisiana (26.7%), Montana (12.7%), South Carolina (22.2%), West Virginia (25.3%), Ohio (-16%), and Tennessee (-25.0%). In 2016, Nguyen et al. (2016) performed a similar study by analyzing data from the 2014 Behavioral Risk Factor Surveillance System among U.S. adults. They demonstrated that the prevalence for ST use among U.S. adults in 2014 ranged from 1.4% (Hawaii) to 8.8% (Wyoming).

Chang et al. (Chang et al., 2016) performed a study that was based on data collected from nine waves of TUS-CPS among U.S. adults aged 18 years and older from 1992 until 2011. They found that total adult ST use significantly decreased at an annual percentage change (APC) rate of 4.5 percent per year from 1992 until 2003, but remained steady since 2003. They also found a similar trend in males aged 18-24 years, with an APC rate of -9.5 percent from 1992 until 2003 ($p < 0.05$). Additionally, they reported that males aged 18 to 24 years had the highest prevalence of ST use based on TUS-CPS conducted in 1992-1993.

Sung et al. (Sung et al., 2016) analyzed pooled data from the 1998, 2000, 2005, and 2010 Cancer Control Supplements of the NHIS collected from U.S. adults aged 18 years and older. They showed that the prevalence of current snuff use was 1.8% in 1998, decreased to 1.3% in 2000, but increased to 2% in 2010. Additionally, among current chewing tobacco users, the proportion of polytobacco users who used cigarettes increased from 19.2% (1998) to 37.2% in 2000, then declined to 19.1% in 2010.

7.5.2-2.5.4. Comparison of Smokeless Tobacco Use Patterns among Adolescents, Young Adults, and Adults

There were several articles in the updated literature review that compared ST usage patterns between adolescents, young adults, and adults.

Studies found that the percentages of ST and snus users were higher in adults, especially young adults, than in adolescents. One example is the study conducted by Kasza et al. (Kasza et al., 2017), which surveyed the prevalence of various tobacco products use among adolescents (age: 12-17 years) and adults (age: 18 years and older) in 2013 and 2014. The authors found that, among adolescents overall, 4.8% and 1.7% were ever-ST and ever-snus users, respectively. When stratified by age, 2.1% of adolescents aged 12 to 14 years and 7.5% of adolescents aged 15 to 17 years were ever-ST users; 0.6% of adolescents aged 12 to 14 years and 2.8% of adolescents aged 15 to 17 years were ever-snus users. The authors reported that 1.6% of adolescents and 3.3% of adults were past-30-day ST users; the authors

reported that 0.5% of adolescents and 0.6% of adults were past-30-day snus users. The percentage of daily ST users was also higher among adults than among adolescents (1.8% versus 0.4%). The prevalence rate of snus use was 1.8% in the age group 18 to 24 years and 0.6% in those greater than 25 years old. Additionally, daily ST use was reported in 2.1% of adults aged 18 to 24 years and 1.7% of adults aged greater than 25 years. Moreover, daily snus use was reported in 0.2% of adults aged 18 to 24 years and 0.1% of adults aged greater than 25 years. Liu et al. (Liu et al., 2015) analyzed data from a survey completed by adolescents (age: 15-17 years) and adults (age: 18 years and older) in four Ohio Appalachian counties and conducted between February 2009 and May 2010. They showed that 43.4 percent of adolescents and 60.3 percent of adults reported daily use of chew and/or snuff.

Some articles reported that young adults had higher prevalence rates of ST use than older adults. Brown-Johnson et al. (Brown-Johnson & Popova, 2016) analyzed a national sample comprising 1,812 U.S. adults aged 18 years and older recruited by a survey and research company in 2013. The authors found that 41.1 percent of ST users were 18 to 29 years of age and 37.5 percent were 30 to 44 years. Syamlal et al. (Syamlal, Jamal, & Mazurek, 2016) analyzed data from the 2012-2014 NHIS completed by U.S. adults aged 18 years and older and reported that the prevalence of ST use was highest in the 18- to 24-year age group among all adults.

7.5.2-2.5.5. The Association between Smokeless Tobacco Use and Sex

The prevalence of ST use was consistently found to be higher among males than among females in publications included in the literature review update (Agaku et al., 2016; Agaku et al., 2015; Berg et al., 2016; Johnson et al., 2016; Linde et al., 2016; Lynne-Landsman et al., 2016; Nguyen et al., 2016; Parent, Bradstreet, Piper, Brace, & Parkman, 2016; Reichenberger, Hilmert, Irish, Secor-Turner, & Randall, 2016; Wilkinson et al., 2015).

7.5.2-2.5.6. The Association between Smokeless Tobacco Use and Race and Ethnicity

Most articles in the updated literature review reported that prevalence of ST use was positively associated with the subgroup of non-Hispanic whites, regardless of age. Studies in nationally representative sample populations or large, diverse sample populations are presented here.

Harrell et al. (Harrell et al., 2016) reported that, among U.S. middle school and high school students in 2012-2013, African Americans were less likely to be ST users than white non-Hispanics (OR = 0.67, 95% CI: 0.51, 0.95). When compared with white non-Hispanics, the OR for ST use for Asians was 0.97 (95% CI: 0.48, 1.95) and the OR for Hispanics was 0.81 (95% CI: 0.6, 1.09). Agaku et al. (Agaku et al., 2015) reported that among U.S. middle school and high school students in 2001-2013, non-Hispanic black and Hispanic subjects have significantly lower odds for current use of ST than non-Hispanic white subjects. Parent et al. (Parent et al., 2016) analyzed data from the 2013 YRBS among U.S. students in Grades 9 through 12. The authors showed that, among black or African Americans, 3% used chew/dip, whereas, among whites, 12% used chew/dip. Among Hispanic/Latinos, 4% used

chew/dip. Whites also had a higher prevalence of chew/dip use than both multiracial Hispanics (7%) and multiracial non-Hispanics (9%).

Brown-Johnson et al. (Brown-Johnson & Popova, 2016) found that, in 2013, 56.9% of U.S. adult ST users were white, 19.1% were black or African American, 14.7% were Asian, and 12.6% were Hispanic. Another study (Syamlal et al., 2016) that examined patterns of ST use among U.S. adults showed that the prevalence of using ST was significantly higher among non-Hispanic whites (4.6%, 95% CI: 4.3, 4.9) than among other races and ethnicities, based on the 2012-2014 NHIS. Using data from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions, Fu et al. (Fu, Vaughn, Wu, & Heath, 2014) showed that, among U.S. adults, ST use was significantly more common in Caucasians than in African Americans or Hispanics. Using data from the 2012 National Survey on Drug Use and Health (NSDUH), White et al. (White et al., 2016) reported that, among U.S. adults, individuals who identified as black, Hispanic, Asian, or multiracial were less likely to use ST than individuals who identified as non-Hispanic white, but individuals who identified as Native Americans were more likely to use ST.

Berg et al. (Berg et al., 2016) analyzed data from the 2014-2015 DECOY study, which included subjects of diverse race/ethnicity, geographic location (urban versus rural), and socioeconomic background. They reported prevalence by race of past-30-day ST use among students attending seven Georgia colleges/universities: prevalence rates were 5.1% among whites, 1.2% among Hispanics, 0.7% among blacks, and 2.8% among Asians. A study by Wong et al. (Wong et al., 2016), in which the authors only analyzed the second wave of the 2014-2015 DECOY study, showed that being Asian was associated with lower levels of ST use than being white.

7.5.2-2.5.7. The Association between Smokeless Tobacco Use and Cigarette Smoking

Ambrose et al. (Ambrose et al., 2015) analyzed youth data from Wave 1 of the 2013-2014 PATH study and reported that one of the leading reasons given by participants for ST use was its potential to be used at times when or in places where smoking cigarettes is not allowed. In addition, Mays et al. (Mays et al., 2016), using data from the 2012-2013 NATS data among U.S. adults (age: 18 years and older), demonstrated that there was a significant, positive association between openness to using noncigarette products and cigarette smoking. They showed that noncurrent ever-smokers, current smokers, and former smokers reported significantly higher openness to using chew/snuff/dip and snus than never-smokers (all p-values < 0.001).

The updated literature review largely supports the notion that there is a positive association between current or past cigarette smoking and ST use. For example, Sung et al. (Sung et al., 2016) analyzed pooled data from the 1998-2010 Cancer Control Supplements of the NHIS among U.S. adults aged 18 years and older. They found that the prevalence of current chewing tobacco use and current snuff use varied by cigarette-smoking status (1.5% and 2.2%, respectively, among current smokers; 0.9% and 1.3%, respectively, among never-smokers). However, compared with never-smokers, current smokers had significantly lower adjusted odds of being a current chewing tobacco user (AOR = 0.80, 95% CI: 0.65, 0.99) and of being a current snuff user (AOR = 0.78, 95% CI: 0.65, 0.93). Conversely, but still

compared with never-smokers, former smokers had nonsignificantly higher odds of being a current chewing tobacco user (AOR = 1.17, 95% CI: 0.97, 1.40) and significantly higher odds of being a current snuff users (AOR = 1.39, 95% CI: 1.19, 1.62). A study by Syamlal et al. (Syamlal et al., 2016) among U.S. adults aged 18 years and older (data from the 2012-2014 NHIS) showed that the prevalence of ST use was 6.7% among current cigarette smokers, 4.8% among former smokers, and 2.1% among never-smokers. Furthermore, White et al. (White et al., 2016) reported that, among U.S. adults aged 18 years and older (data from the 2012 NSDUH), 5.7% of current cigarette smokers currently used ST. Among current ST users, about 37.2% reported current cigarette use. Additionally, the authors' results showed that being a cigarette smoker was associated with increased odds of ST use (OR = 1.95, 95% CI: 1.66, 2.28, $p < 0.0001$).

Spangler et al. (Spangler et al., 2014) analyzed data from surveys completed by young adults at eleven colleges in North Carolina and Virginia in 2011. They found that current cigarette smokers were over five times more likely than nonsmokers to have used ST during the past 30 days (adjusted OR = 5.5, 95% CI: 4.21, 7.1, $p < 0.0001$). Boyle et al. (Boyle et al., 2015) analyzed data from the adult tobacco survey in 2014 among adult Minnesota population. The authors demonstrated that the prevalence of ST use was 7.4% among current smokers, 4.9% among former smokers, and 2.0% among never-smokers.

7.5.2-2.5.8. The Association between Smokeless Tobacco Use and Occupation

White et al. (White et al., 2016) analyzed data from the 2012 NSDUH among U.S. adults aged 18 years and older, and reported that working in a blue-collar industry was positively associated with ST use. Three studies in the updated literature review provide representative data to support this association.

Graber et al. (Graber et al., 2016) analyzed data from the 2006-2012 NSDUH completed by U.S. adults aged 18 to 64 years. They reported that the prevalence and odds of ST use were significantly higher among all three groups of dusty industry workers (i.e., workers in the industries of agriculture, construction, and extraction) than other workers and particularly high among extraction workers (OR = 3.3, 95% CI: 2.4, 4.6). The OR for ST use among agricultural workers and construction workers were 2.1 (95% CI: 1.6, 2.6) and 1.4 (95% CI: 1.3, 1.6), respectively, compared to other workers. The prevalence of current ST use was 15.8% in agriculture, 10.9% in construction, 28% in mining/extraction, and 7.9% in other work. A study by Syamlal et al. (Syamlal et al., 2016) that analyzed the 2012-2014 NHIS data among U.S. adults aged 18 years and older showed that the prevalence of ST use was highest among subjects who worked in the mining industry (15.1%, 95% CI: 9.0, 21.1) or those who had occupations in farming, fishing, and forestry (11.0%, 95% CI: 6.8, 15.1). Jitnarin et al. (Jitnarin et al., 2016) analyzed data from two different firefighter surveillance studies: (1) The Firefighter Injury and Risk Evaluation study, and (2) The Fuel 2 Fight study. They found that 14% of firefighters reported using ST and 15.9% of them initiated ST use after joining the service.

7.5.2-2.5.9. The Likelihood that Consumers Will Use the Product as Intended or Designed

ST is a consumer product without specific directions for use or application; therefore, the likelihood that consumers will or will not use the product as intended or designed cannot be effectively assessed. However, the topography of ST consumption has been reviewed thoroughly in the literature and is summarized in Section 7.5.8-1 and Section 7.5.8-2 of this MRTPA. Briefly, the available published literature indicates the “average” user of ST uses about 7 to 8 dips per day and 3 to 4 cans per week. An average dip size is between 1 to 2 g. A typical dip lasts about 40 to 50 minutes, and over an entire day, a user keeps dip in his or her mouth for approximately 5 to 6 hours.

7.5.2-2.5.10. Updated Findings

Key or new findings from articles in the updated literature review addressing patterns of ST use are below:

- When comparisons were made between adolescents and adults, adults (particularly young adults) showed higher prevalence of ST use (Section 7.5.2-2.5.4). Being male (Section 7.5.2-2.5.5) or non-Hispanic white (Section 7.5.2-2.5.6) were strongly associated with higher ST use when compared with being female or of other race/ethnicities.
- Although most articles suggested that cigarette smoking was associated with ST use, there was one article that found that noncigarette smokers had higher prevalence of ST use than did cigarette smokers (Section 7.5.2-2.5.7).

Information in the updated literature review on the likelihood that consumers will use the candidate product as intended or designed is consistent with that seen in the initial literature review. The conclusions from the initial literature review (Section 7.5.2-1.5.1) have not changed based on the updated literature review.

A tabular summary of the literature informing the effects the candidate product may have on tobacco use behavior among current tobacco users is presented in Table 7.5.2-2-4.

Table 7.5.2-2-4: Literature Summary for Patterns of Use of Smokeless Tobacco Products

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Arimilli, Madahian, Chen, Prasad, & Marano, 2017)	Gene expression profiles associated with cigarette smoking and moist snuff consumption	Data are from a single-blind, cross-sectional study of healthy volunteers. A total of 120 healthy subjects completed the study with 40 subjects in each group (MSC, SMK, and NTC). Majority of subjects were Caucasian, with a mean age ranging from 45 to 47.2 years. Objective: To characterize gene expression in PBMCs from MSC compared with that from SMK and NTC.	PBMCs from 120 subjects were collected under fasting condition and before tobacco consumption. Microarray assay was performed, and qPCR was conducted on 44 selected target genes to confirm results from microarray analysis.	"The mean years of product use were 25.1 and 20.6 in the SMK and MSC groups, respectively. During the month prior to the study, the mean number of cigarettes per day consumed by the SMK group was 21.5, while the MSC group consumed a mean 6.3 cans per week of moist snuff."	Strength: The study used two assays to confirm findings in this study and previous studies. Limitations: (1) Analysis based on microarray may not be sensitive enough for expressions of some genes, and the study only confirmed the results of the microarray analysis with 44 target genes using qPCR analysis; and (2) there may be other genes not detected for their change in expressions by microarray and qPCR analysis.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Braverman, Hoogesteger, Johnson, & Aaro, 2017)	Supportive of a smoke-free campus but opposed to a 100% tobacco-free campus: Identification of predictors among university students, faculty, and staff	Data are from a cross-sectional study. Subjects (4,138 students and 1,582 faculty/staff) expressed support for the 100% tobacco-free policy at Oregon State University. Objective: To identify variables that distinguish between levels of support for the two kinds of policy, including potentially, the use of cigarettes, EC, and other tobacco products; exposure to secondhand smoke on campus; campus-life factors; perceptions of the extent of policy support and tobacco use; demographics; and other variables.	Data derived from a web-based survey conducted in May 2013 were assessed for the following measures: support for a smoke-free campus, opposition to a tobacco-free campus; tobacco use, exposure to secondhand smoke on campus, perceptions of smoking-related norms, and demographics and campus life variables. Analyses were conducted separately for students and faculty/staff. Bivariate association with policy opposition and multivariate logistic regression model were performed.	In the student sample, 2.9% had used ST within the past month, whereas 0.8% of faculty/staff used ST. Based on bivariate analysis, tobacco-free opposition was associated ($p < 0.001$) with sex, cigarette-smoking status, ST use (users more opposed), and weaker support for the existing smoke-free policy. Out of 81 occasional ST users, 48.1% were not opposed to the policy, whereas out of 34 regular ST users, 14.7% were not opposed to the policy. Out of 3,862 of ST nonusers, 87.3% were not opposed to the policy. Based on logistic regression analysis for students, the odds of being opposed to the tobacco-free policy were significantly higher for ST users; likewise, for faculty/staff, the odds were higher for current ST users.	Limitations: (1) It was a cross-sectional study; (2) the study was based on self-report; (3) there were small number populations of faculty/staff who were ST users; (4) the survey was based on population in a single university; and (5) data were collected less than 1 year after the implementation of the smoke-free policy.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Courtemanche et al., 2017)	Influence of the flavored cigarette ban on adolescent tobacco use	Data are from repeated cross-sectional studies, in which subjects (n = 197,834; age: 11-19 years) were part of a nationally representative sample of middle school and high school students and were asked about their use of cigarettes, cigars, ST, and pipe in the past 30 days as part of the 1999-2013 NYTS. Objective: To estimate the association between the U.S. Food and Drug Administration's 2009 ban on flavored cigarettes and adolescents' tobacco use.	Subjects were asked about initiation and current use of a variety of tobacco products. Variables including age, sex, race, tobacco price index, and unemployment rate for teens were measured.	There was an insignificant reduction in the use of ST after the ban (p = 0.806). The ban was associated with statistically significant (p < 0.001) increases in the prevalence of cigar and pipe use, and was positively but insignificantly associated with ST use. The ban was associated with an increase in the use of NCTP (cigars, ST, or pipes) of 14.2% (p < 0.001). However, the ban was associated with a statistically significant 6.1% reduction (p < 0.001) in the probability of using any tobacco. All types of tobacco use increased significantly with age, and men were more likely to use all forms of tobacco. ST use was on an inverted U-shaped trajectory. Rising cigarette prices were associated with increases in the use of ST products.	Strengths: (1) Large sample population and (2) nationally representative sample. Limitations: (1) Study design was cross-sectional; and (2) estimating the causal effect of any national law is difficult because only time-series variation is available for identification.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Kasza et al., 2017)	Tobacco-product use by adults and youths in the United States in 2013 and 2014	Data are from Wave 1 of a longitudinal study (PATH), in which subjects consisted of 32,320 adults (age: 18+ years, 48.1% male, 66.0% non-Hispanic white) and 13,651 youths (age: 12-17, 51.3% male, 54.6% non-Hispanic white). Tobacco products surveyed included cigarettes, EC, traditional cigars, cigarillos, filtered cigars, pipe tobacco, hookah, snus pouches, other ST (i.e., loose snus, moist snuff, dip, spit, or chewing tobacco), dissolvable tobacco, bidis, and kreteks. Objectives: To examine the prevalence of use of various tobacco products and the prevalence of current use (among adults) or use in the previous 30 days (among youths) for each tobacco product according to demographic subgroup, and the prevalence of multiple-product use or single-product use.	Subjects were asked questions about types of tobacco products and categories of tobacco use.	Among youths overall, 4.8% of youths were ever-ST users (2.1% for 12-14 years of age and 7.5% for 15-17 years of age) and 1.7% of youths were ever snus use (0.6% for 12-14 years of age and 2.8% for 15-17 years of age). Among youths overall, 1.6% of youths used ST in the past 30 days (0.5% for 12-14 years of age and 2.7% for 15-17 years of age) and 0.5% of youths used snus in the past 30 days (0.8% for 15-17 years of age). Among adults overall, 3.3% of adults used ST in the past 30 days (5.3% for 18-24 years of age and 3.0% for ≥25 years of age). Among adults overall, 0.6% used snus in the past 30 days (1.6% for 18-24 years of age and 0.5% for ≥25 years of age). Among adults overall, 3.4% were current users of ST (5.2% for 18-24 years of age and 3.1% for ≥25 years of age). Among adults overall, 0.8% were current snus users (1.8% for 18-24 years of age and 0.6% for ≥25 years of age). Among youths overall, 0.4% of youths were daily ST users (0.7% for 15-17 years of age). For adults overall, 1.8% of adults were daily ST users (2.1% for 18-24 years of age and 1.7% for ≥25 years of age). Among adults overall, 0.1% of adults were daily snus users (0.2% for 18-24 years of age and 0.1% for ≥25 years of age).	Strengths: The study used a large and nationally representative sample. Limitations: (1) The data came from only the first wave of the PATH study; and (2) the study was based on self-report.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Owusu et al., 2017)	The use of e-cigarettes among school-going adolescents in a predominantly rural environment of central Appalachia	Data are from a cross-sectional study. Subjects (n = 894; age: 14-22 years, 57.8% female) were high school students in northeast Tennessee. Objective: To estimate the prevalence of EC use and examine association of EC use with two tobacco products among school-going adolescents.	Subjects provided information regarding their use of tobacco products, age of initiation, intention to quit, age, and sex.	Of the total study subjects, 8.3% were current ST users, and 20.4% were ever-ST users. Among EC users, 2.8% subjects were current users of cigarettes and ST. Additionally, 16.8% had ever used EC and ST products concurrently. The ever-use of all three products simultaneously was reported by 15% of the subjects. In the bivariate analysis, EC use was associated with current ST use (OR = 14.92, 95% CI: 8.8, 25.2) and being male (OR = 2.94, 95% CI: 1.9, 4.6). After adjusting for covariates, odds of EC use were elevated in current ST users (OR = 7.92, 95% CI: 3.8, 16.5).	Strength: The study had a large sample size. Limitations: (1) Institutional constraints limited the ability to generate a representative sample; (2) the study was based on self-report; (3) the results need to be interpreted in the context that the majority of subjects were under the age of 18 years; and (4) the study could not adjust for school differences.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Stein, Koffarnus, Judd, Bickel, & Wilson, 2017)	Naturalistic assessment of demand for cigarettes, snus, and nicotine gum	Data are from a cross-sectional study. Subjects (snus group: n = 22, mean age: 39.5 years, 45.45% female, 59.09% Caucasian; gum group: n = 20, mean age: 39.7 years, 50%, 55% Caucasian) were cigarette smokers. Objective: To examine the demand for snus in comparison to both cigarettes and medicinal nicotine [gum].	Subjects were assigned to self-administer and purchase their usual brand of cigarettes and either Camel Winterchill snus or Nicorette Fresh Mint polacrilex gum. Progressive ratio and purchase measurements were analyzed.	There was a significant main effect of product on progressive ratio breakpoint ($p < 0.001$). Post hoc tests showed significantly lower breakpoints in gum than in cigarettes ($p < 0.001$). However, only marginally significant differences observed between cigarettes and snus ($p = 0.064$) and snus and gum ($p = 0.054$). Five of 22 subjects never purchased snus, and four of 20 subjects never purchased gum. Therefore, the frequency of these null demand functions did not differ significantly ($OR = 0.85$, $CI: 0.19, 3.74$, $p > 0.999$). Null demand functions for snus were significantly more frequent in females than in males ($OR = 25$, $CI: 1.17, 535.6$, $p = 0.010$), but not for nicotine gum ($OR = 0.26$, $CI: 0.02, 3.07$, $p = 0.582$). Values of R^2 of the intersubject variability in purchasing snus were 0.201 with all subjects included and 0.309 with null demand subjects excluded. There was a significantly greater elasticity for snus than for cigarettes ($p < 0.001$). When considering only data from subjects who purchased snus or gum at least once, there was a significantly greater elasticity for snus than for cigarettes ($p < 0.001$). There was significantly lower demand intensity for gum than for cigarettes ($p < 0.001$), but there were no significant differences in demand intensity between snus and cigarettes, or snus and gum (including when considering only data from subjects who purchased snus or gum at least once).	Strength: The use of progressive ratio assessments. Limitations: (1) This was a cross-sectional study; (2) findings were limited to the population recruited, which is smokers who did not use snus or nicotine gum regularly; and (3) findings were limited to specific varieties of snus and nicotine gum used in this study.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Agaku et al., 2016)	Exposure and response to current text-only smokeless tobacco health warnings among smokeless tobacco users aged ≥ 18 years, United States, 2012-2013	Data are from a cross-sectional study. Subjects (age: ≥18 years residing in 50 U.S. states) were past-30-day ST users (n = 1,626). Most past-30-day ST users were male (93.7%) and non-Hispanic white (72.3%), with the following age distribution: 18-24 years (25%), 25-44 years (45.1%), 45-64 years (24.7%), or ≥65 years (5.2%). Objective: To assess U.S. adult ST users' exposure and response to ST health warnings.	Data from the 2012-2013 NATS were measured for tobacco use status, exposure variables (primary exposure was recent exposure to health warnings on ST packages; and second exposure was cumulative exposure to health warnings from different sources), outcome variables (primary outcome was cognitive or behavioral response to ST health warning labels and secondary outcomes were perceptions of respondents regarding the harmfulness and addictiveness of ST products), and sociodemographic variables (sex, age, race/ethnicity, education, annual household income, and U.S. Census region).	Prevalence of exposure to ST health warning labels among ST users was 77.5%. Prevalence was lower among subjects who used novel ST products (snus/dissolvables, 58.3%) than among users of traditional ST products (chewing tobacco/snuff/dip, 78.9%), or combined users (80.5%) (all p < 0.05). Prevalence was higher among ST users who did not smoke cigarettes (84.6%) than among those who also smoked cigarettes (67.7%) (p < 0.001). Prevalence was higher among males (78.7%) than among females (57.9%) (p = 0.0002). By census, prevalence was highest among subjects living in the Northeast (82%) and lowest among those in the South (72.2%) (p = 0.0167). Prevalence increased linearly with increasing education, from 64.8% among subjects with less than a high school education, to 84.6% among subjects with a postgraduate degree (p = 0.0097). Prevalence also increased linearly with increasing annual household income, from 64.4% among persons earning ≤\$19,999 to 81.4% among those earning ≥100,000 (p = 0.0019).	Strength: Data came from a recent nationally representative survey. Limitations: (1) This was a cross-sectional study; (2) the study was based on self-report; and (3) there was a low NATS response rate (44.9%).

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Alcala, von, & Tomiyama, 2016)	Adverse childhood experiences and use of cigarettes and smokeless tobacco products	Data are from a cross-sectional study. Subjects (n = 102,716, 50.53% female, 84.46% white, 2.98% black, 6.08% Hispanic, 2.63% Asian, and 3.85% other) were noninstitutionalized adults (age: 18 years and over) who lived in Maine, Minnesota, Montana, Nebraska, Nevada, Oregon, Vermont, Washington, or Wisconsin. On average, subjects had completed some college, and less than 7% of the subjects had ever been diagnosed with cancer. ST includes chewing tobacco, snuff, and snus. Objective: To examine associations between ACEs and smoking behaviors, specifically, whether or not ACEs were associated with ever smoking, current smoking, and current ST use.	Data from the 2011 BRFSS were analyzed for independent variables measured using the ACE scale, dependent variables that measured tobacco use behaviors (lifetime/ever-smokers, current smokers, or current ST users), and other variables (age, race/ethnicity, state of residence, educational attainment, and cancer status)	About 3.96% of subjects were current ST users. In unadjusted model (Model 1), physical abuse (OR = 1.40, 95% CI: 1.14, 1.72), emotional abuse (OR = 1.41, 95% CI: 1.19, 1.67), living with a drug user (OR = 1.50, 95% CI: 1.17, 1.93), living with someone who was jailed (OR = 1.50, 95% CI: 1.11, 2.02), and having parents who were separated or divorced (OR = 1.31, 95% CI: 1.09, 1.57) were associated with current ST use. Sexual abuse was associated with lower odds of current ST use (OR = 0.70, 95% CI: 0.51, 0.95). In Model 2 with confounders, physical abuse (OR = 1.43, 95% CI: 1.16, 1.78), emotional abuse (OR = 1.32, 95% CI: 1.10, 1.57), living with a problem drinker (OR = 1.30, 95% CI: 1.08, 1.58), living with a drug user (OR = 1.31, 95% CI: 1.00, 1.72), and living with adults who treated each other violently (OR = 1.30, 95% CI: 1.05, 1.62) were associated with current ST use. In Model 3 with ACE measures and confounders, living with someone who was mentally ill was associated with lower odds of currently using ST (OR = 0.70, 95% CI: 0.53, 0.92).	Strength: Large sample population. Limitations: (1) This was a cross-sectional study; (2) the study population was not nationally representative; and (3) there were low representative data of ST users that might not adequately detect all associations between ACEs and ST use.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Berg et al., 2016)	DECOY - Documenting experiences with cigarettes and other tobacco in young adults	Data are from a 2-year longitudinal mixed-methods study examining risk for tobacco use among 3,418 young adults across seven Georgia colleges/universities. Subjects (age: 18-25 years, mean = 20.55 years) were mostly female (64.3%) and white (62.4%). Objective: To examine the psychographic characteristics associated with tobacco use among DECOY subjects.	Baseline measures for this study included sociodemographics, tobacco use, and psychographics using the Values, Attitudes, and Lifestyle scale. Bivariate and multivariable analyses were conducted to identify correlates of tobacco use.	Past-30-day use prevalence was 3.6% for ST, with the average number of days of use was 14.28 (SD = 11.81). Mean age for ST users was 20.59 (SD = 2). About 9.6% of males, 0.3% of females, 5.1% of whites, 1.2% of Hispanics, 0.7% of blacks, and 2.8% of Asians used ST. Of ST users, 3.5% went to private school, 5.0% went to public school, 3.9% went to technical college, and 0.2% went to historically black college/university. Controlling for sociodemographics, correlates of ST use included greater novelty seeking ($p = 0.006$) and less intellectual curiosity ($p < 0.001$).	Strengths: (1) Longitudinal data; and (2) subjects were diverse in terms of race/ethnicity, geographic location (urban vs. rural), and socioeconomic background. Limitations: (1) Data were from colleges and universities in Georgia, were subject to selection bias, and may not be generalizable to all young adults; (2) there were slightly higher female populations; and (3) the study was based on self-report.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Bonhomme et al., 2016)	Flavoured non-cigarette tobacco product use among US adults: 2013-2014	Data are from a cross-sectional study. Subjects (n = 75,233) were U.S. adults aged ≥18 years. ST used includes chewing tobacco/snuff/dip, snus, and dissolvables. Objectives: (1) To describe the proportion of current NCTP users reporting past-30-day flavored product use by product type and demographic and tobacco-use characteristics; (2) to identify flavor types most commonly used by U.S. adults for each NCTP type, both overall and by age, and (3) to characterize associations between flavors used and other demographic characteristics, frequency of product-use and cigarette-smoking status.	Data were from the NATS collected from October 2013 to October 2014. The survey assessed tobacco product types, the use of flavored and nonflavored NCTPs, types of flavors used, demographic characteristics, and cigarette-smoking status.	Among U.S. adults, prevalence of past-30-day use of any (at least one) NCTP was 14.5%, including 3.4% for ST. Among current ST users, 96.1% (95% CI: 94.4, 97.3) used ST in the past 30 days. The proportion of any flavored product use among past-30-day users of any NCTP was 61.1%. The proportion of past-30-day flavored ST use was 50.6%. Among 18- to 24-year-old NCTP users, flavored product use by NCTP type was 68.9% for ST. Among 45- to 64-year-old NCTP users, flavored product use was 37.2% for ST. The vast majority of flavored ST users reported using a menthol/mint-flavored product (76.9%), followed by clove/spice/herb-flavored (12.3%), fruit-flavored (10.8%), candy/chocolate/other sweet-flavored (4.5%) products, flavored with alcohol (1.6%), and other flavors (1.4%). There were no meaningful differences in the distribution of demographic characteristics among users of different flavor types for flavored ST use.	Strengths: (1) Large sample population; and (2) nationally representative data. Limitations: (1) This was a cross-sectional study; (2) the study was based on self-report; and (3) there was a low response rate.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Brown-Johnson & Popova, 2016)	Exploring smoking stigma, alternative tobacco product use, and quit attempts	Data are from a cross-sectional study. Subjects (n = 1,812, 47% women, 15% Hispanic, 42% white, mean age: 41 years) were U.S. adults aged 18+ years. ST used includes chewing tobacco, snuff, dip, or snus. Objective: To investigate smoking stigma among different tobacco user types.	Subjects provided information regarding the type of ST used, the frequency of ST and/or cigarette used, smoking stigma, and quit attempts.	Among subjects, 483 were nonsmokers, 341 were ST users, 488 were conventional cigarette smokers, and 500 were ST and conventional cigarette dual users. Among ST users, 72.7% were men, 41.1% were aged 18-29 years, and 37.5% were aged 30-44 years. Additionally, 56.9% of ST users were white, 19.1% were black or African American, 14.7% were Asian, and 87.4% were not Hispanic. Among ST users, 38.7% had some college education, 38.7% had an income of \$25-59,900/year, and 43.7% lived in the South.	Strength: This was a nationally representative study. Limitation: This was a cross-sectional study.
(Buzzell et al., 2016)	Using electrophysiological measures to assess the consumer acceptability of smokeless tobacco products	Data are from an interventional study. Subjects were exposed to one of four ST products (Camel snus, Verve chewable disc, Skoal snuff, Ariva dissolvable tablet) or a Nicorette nicotine lozenge as a control. Objective: To explore the viability of using EEG, in combination with traditional subjective measures, to assess consumer acceptability of five ST products.	Measurements in the study included the subjective measures (demographic and tobacco use history) and behavioral data from cognitive task using EEG.	At baseline, the 30 male ST users (28 Caucasian, one African American, and one Asian American) ranged in age from 19 to 61 years (mean age: 22.2 years) and had a mean score on the modified version of the Fägerstrom Test for Nicotine Dependence of 1.27 (1.23). On average, the subjects had been using ST for 21.72 (15.01) months.	Strength: The study combined the electrophysiological and subjective measures. Limitations: (1) This study had a small data population; (2) subjects were all males; and (3) there were limited ST products available to try.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Chang et al., 2016)	Trends and factors related to smokeless tobacco use in the United States	Data collected from nine waves of TUS-CPS from 1992-2011. Subjects' ages were grouped as follows: 18-24 years, 25-34 years, 35-44 years, 45-54 years, 55-64 years, 65-74 years, and 75 years and older. Objective: To investigate the time trends of ST use and to examine the factors associated with ST prevalence in the U.S.	The study analyzed trends in tobacco use, ST use by demographics (age, race, sex, education, residence, smoking status, and unemployment status), frequency of ST use, and factors associated with ST use.	Total adult ST use significantly decreased at an APC of 4.5% per year from 1992 to 2003. The ST use prevalence has remained constant since 2003. Similar patterns were also found in males aged 18-24 years with APC of -9.5% from 1992 to 2003 ($p < 0.05$). Age-specific ST prevalence is the highest for males aged 18-24 years in 1992 and 1995 surveys. ST prevalence is highest among whites, those living in rural areas, those with lower education, and nondaily smokers ($p < 0.01$). Those who earn less than \$14,999 per year, although the decrease stopped in 1993, and lived in the South had the largest significant decline in ST prevalence (APC = -6.3% and -5.6%, respectively). Former smokers and never-smokers also had significant declines in ST use (APCs = -2.4%, 1992-2011 and -5.2%, 1992-2003, respectively).	Strengths: (1) The data came from nationally representative surveys; and (2) the study compared between self-reported data and market sales. Limitations: (1) This study was based on self-report; (2) This was a cross-sectional study; (3) the changes of ST use definitions across survey years might have introduced bias; and (4) introduction of new ST products made it difficult to interpret trends, given the variability in available products each year.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Cooke et al., 2016)	Predicting tobacco use across the first year of college	Data are from a longitudinal study. Subjects (n = 4,073, 39% male, 60.1% female, 51% white, 18.2% black/African American, 15.9% Asian, 5.9% Hispanic/Latino, 5.4% more than one race) were from the incoming freshman classes of 2011 (Cohort 1 only) and 2012 (Cohort 2; 68% response rate across both cohorts) at Virginia Commonwealth University. Surveys were administered in the fall and spring semesters. Objective: To assess patterns of tobacco use across the first year of college, transitions in use, and associated predictors.	The study analyzed the frequency of tobacco use, subjects' demographics (sex and race/ethnicity), anxiety, depression, peer deviance, and stressful life events.	In the fall, 96.1% of subjects did not use ST, 1.6% used ST once or twice, 1.3% used ST in between 3 to 11 days per month, and 0.9% used ST in between 26 and 30 days per month. In the spring, 96.2% of subjects did not use ST, 1.5% used ST once or twice, 1.1% used ST in between 3 and 11 days per month, and 1.2% used ST in between 26 to 30 days per month. Endorsement frequencies for ST products for Cohort 1 were 3.8% in the spring (no ST prevalence reported for the fall); and 3.7% (fall) and 3.8% (spring) for Cohort 2.	Strength: Data are from a longitudinal study. Limitations: (1) The study focused on the transitional period of starting college; (2) there was a small sample size in the frequently using class; (3) the data cannot be generalizable to all tobacco users; and (4) there was the potential for recall bias, leading to either inflated or deflated reports of tobacco use.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Ebbert, Schroeder, Severson, Danaher, & Benowitz, 2016)	Nicotine metabolite ratio is associated with lozenge use but not quitting in smokeless tobacco users	This is a secondary analysis of data from a large trial that randomized ST users to one of three conditions (Assisted Self-Help, Lozenge-Assisted Self-Help, or Lozenge Self-Help). Subjects (n = 152; age: ≥18 y) were using ST as a primary tobacco product, had been using it daily for at least 1 year, and were willing to quit in the next month. Objective: To evaluate whether the NMR can be used to predict self-reported nicotine lozenge use and tobacco abstinence among ST users treated for tobacco dependence.	The level of tobacco dependence at baseline was measured with the Severson ST Dependency Scale. Tobacco use outcomes were self-reported and measured at 3 and 6 months after enrollment. Subjects provided information for analysis of lozenge use at 3-month follow-up.	At baseline, the mean age of subjects was 36.5 (10.7) years. Subjects were largely male (97%) and white/non-Hispanic (96%). The subjects who were not white/non-Hispanic were comprised of one Indian/Alaska Native, one Asian, three African Americans, one white Hispanic, and two subjects who did not have a report a race/ethnicity. The mean Severson ST Dependency Scale score among subjects was 11.6 (4.0), and subjects had been using ST for an average of 15.0 (9.3) years.	Limitations: (1) The study had a small sample size; (2) self-reported abstinence and lozenge use and the timing for the assessment at 3 months when reporting may be influenced by outcome; (3) the study had limited generalizability; (4) the magnitude of the effect of the association between the NMR and the amount of self-reported lozenge use during the day was small.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Flanagan et al., 2016)	Fetal exposures to carcinogens with tobacco use in pregnancy: phase 1 MAW study findings	A cross-sectional study. Subjects (n = 148) were Alaskan native pregnant women (mean age: 27.1 years). ST used include <i>iqmik</i> and commercial ST. Objective: To study the correlation of maternal cotinine levels with fetal exposure to a tobacco-specific carcinogen in an effort to incorporate in a biomarker feedback intervention to motivate tobacco cessation during pregnancy.	The study analyzed the type of tobacco product use, sociodemographic factors, length of gestation, number of children, spouse/partner tobacco use status, number of household tobacco users, and household restrictions on tobacco use. Postdelivery specimen collection included maternal and infant urine samples that were analyzed for cotinine and total NNAL.	Among subjects, 30 were ST users (20 <i>iqmik</i> and 10 commercial ST users). Five ST users were <24 years old, 15 ST users were between 24 and 32 years old, and 10 ST users were ≥33 years old. Six ST users lived in urban area, whereas 24 lived in rural area. Seven ST users lived in southcentral region, and 23 lived in other regional areas of Alaska.	Limitations: (1) The study was based on self-report; (2) The study had a small sample size for ST users.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Fu & Vaughn, 2016)	A latent class analysis of smokeless tobacco use in the United States	Data are from a cross-sectional study. Subjects (n = 43,093) were noninstitutionalized civilians aged 18 years and older. Among subjects, 2,504 used snuff or chewing tobacco at least 20 times in their lifetime. The survey oversampled young adults, Hispanics, and African Americans. ST used includes snuff and chewing tobacco. Objectives: (1) To examine differences between lifetime ST users and nonusers of ST in relation to psychiatric disorders; and (2) to delineate exclusive snuff use or exclusive chewing tobacco from dual use with respect to psychiatric disorders.	Data derived from the NESARC Wave 1 conducted in 2001 and 2002 were analyzed for antisocial behaviors, sociodemographic variables, and psychiatric diagnoses.	The prevalence of antisocial behaviors of subjects who ever used snuff or chewing tobacco ranged from 3.3% to 42.3%. The most prevalent behavior was “ever stayed out late night even though parents told to stay at home,” and the least prevalent behavior was “forged a signature.” Four subtypes of ST use emerged: Normative class (50.2%), deviant class (21.9%), disengaging class (17.2%), and antisocial class (10.5%). Major depression, alcohol use disorder, and marijuana use disorder were associated with greater odds of membership in the deviant, disengaging, and antisocial latent classes with uniformly larger effects found for the antisocial class. Bipolar disorder was associated with disengaging and antisocial classes, which differentiates the deviant latent class from the disengaging latent class. All psychiatric disorders were associated with greater odds of membership in the antisocial latent class. General anxiety disorder and illicit drug use disorder were associated with greater odds of membership in the antisocial latent class.	Strength: The data was weighted and adjusted to reflect the U.S. population from the 2000 Decennial Census. Limitations: (1) Sample size was not large enough to identify subtypes of ST use; (2) antisocial behaviors were based on retrospective recall; (3) cigarette use was often comorbid with ST use, and (4) data were from 2001-2002 survey.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Graber et al., 2016)	Cigarettes, smokeless tobacco, and poly-tobacco among workers in three dusty industries	Data are from a cross-sectional study. Subjects (18 to 64 years old, all male) in three blue-collar industries with a potential for significant occupational dust exposure were compared with those in other industries (agriculture, n = 2,031; construction, n = 12,708; extraction/mining, n = 990; other work, n = 72,853). Objective: To assess and compare tobacco-use prevalence and risk factors among workers in three dusty industries: agriculture, construction, and extraction; and to explore trends over time and the frequency of product use among single and dual tobacco product users.	Data from the 2006 through 2012 NSDUH were analyzed for tobacco use prevalence among male blue-collar workers in "dusty" industries compared with all other employed men.	The prevalence and odds of ST and dual use were significantly higher among all three groups of dusty industry workers than among other workers and were particularly high among extraction workers (OR _{ST} = 3.3, 95% CI: 2.4, 4.6; OR _{DUAL} = 2.6, 95% CI: 1.8, 3.6). Among agriculture workers, the OR for ST use was 2.1 (95% CI: 1.6, 2.6) and for dual use was 1.8 (95% CI: 1.3, 2.5). Among construction workers, the OR for ST use was 1.4 (95% CI: 1.3, 1.6) and for dual use was 1.5 (95% CI: 1.3, 1.8). The prevalence of current ST use was 15.8% in agriculture, 10.9% in construction, 28% in mining/extraction, and 7.9% in other work. The prevalence of dual cigarette/ST use was 5% in agriculture, 4.9% in construction, 10.1% in mining/extraction, and 3.1% in other work. ST and dual use rates did not decline over the study period. However, there was a nonsignificant 25% increase in the prevalence of dual use among extraction workers.	Limitations: (1) This was a cross-sectional study; (2) the data were based on self-report; (3) there was a paucity of information on the reliability and validity of survey questions for other types of tobacco use, including ST; (4) prevalence estimates may vary between national surveys and between studies; and (5) the analysis was not able to address tobacco use among unemployed workers from specific industries.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Haardorfer et al., 2016)	Polytobacco, marijuana, and alcohol use patterns in college students: A latent class analysis	Data are from a baseline survey of a multiwave longitudinal study entitled Project DECOY. Subjects (n = 3,418) were recruited from seven college campuses in Georgia. Objectives: To examine (1) profiles of substance-use behaviors among young adult college students, with particular focus on use of various tobacco products, marijuana, and alcohol; and (2) sociodemographic, individual-level, and sociocontextual-level factors associated with use profiles among this sample.	Data derived from the fall of 2014 self-report assessment. The study analyzed use patterns of various tobacco products, sociodemographics, individual-level factors (depression; perceptions of harm and addictiveness), and sociocontextual factors (parental/friend use).	Subjects were between 18 and 25 years old. Subjects were mostly female (64.3%) and white (63.2%). The prevalence of ST use for the past 4 months was 4.9% and for the past 30 days was 3.6%.	Limitations: (1) The study sample is subject to selection bias and might not be generalizable to all young adults; (2) this was a cross-sectional study; and (3) the data were based on self-report.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Harrell et al., 2016)	Patterns of youth tobacco and polytobacco usage: the shift to alternative tobacco products	Data are from a cross-sectional study. Subjects (n = 6,841, 40.1% female, age ≥ 9 years old, 47.7% non-Hispanic white) were middle school and high school students, and all were tobacco users. ST was defined as chewing tobacco, snuff, or dip. Objective: To identify patterns of youth tobacco use and to examine associations with sociodemographic characteristics and nicotine dependence.	Data derived from the 2012-2013 NYTS were analyzed for past-30-day tobacco product use (based on latent class analysis) and its relationship with sociodemographics and nicotine dependence variables.	Of tobacco users, only 25.8% of subjects reported past-30-day ST use. About 10% of subjects used snus in the past 30 days and 90% reported no use of snus in the past 30 days. African Americans were 1.6 times more likely than whites to be cigar smokers, but less likely to be ST users (OR = 0.67, 95% CI: 0.51, 0.95). The OR for an ST user to be Asian was 0.97 (95% CI: 0.48, 1.95) and to be Hispanic was 0.81 (95% CI: 0.60, 1.09), compared to being white. When compared with that for age group 9-13 years, the OR for age group 14-18 years was 1.01 (95% CI: 0.68, 1.49), whereas the OR for age group 19-21 years was 0.77 (95% CI: 0.33, 1.84).	Strength: The study had a large sample size that allowed for latent analysis. Limitations: The study had a cross-sectional design.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Jitnarin et al., 2016)	Prevalence and correlates of late initiation of smokeless tobacco in US firefighters	This was a secondary analysis of the baseline assessments from two different firefighter surveillance studies: of firefighters from (1) the International Association of Fire Chief's Missouri Valley Region and (2) 20 career departments across 14 U.S. states and territories. Subjects (n = 207, mean age between 36 and 37 years) were male firefighters. Objective: To examine characteristics associated with late ST initiation in a sample comprising male career firefighters from two large cohort studies.	Age-standardized prevalence of ST use before and after joining the fire service was computed in the combined sample to facilitate comparison with the U.S. adult males in the general population and males in the U.S. military. The study also analyzed demographics and occupational history and physical and behavioral health.	Of firefighters in the joint sample, 14% reported using ST, and 15.9% of firefighters initiated ST use after joining the fire service. Mean age of subjects reported using ST before or after joining the service were 36.4 or 36.8 years old. Most (91.7%) of subjects who initiated ST before joining the service had higher education than high school, whereas 87.5% of subjects who initiated ST after joining the service had higher education than high school. Among subjects, 89% of those who initiated ST before joining the service were white, whereas 80% of those who initiated ST after joining the service were white.	Strengths: The study used (1) a large sample size and (2) standardized and validated health measures. Limitation: This was a cross-sectional study.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Johnson et al., 2016)	Tobacco product use among sexual minority adults: Findings from the 2012-2013 National Adult Tobacco Survey	Data are from a cross-sectional study. Subjects (n = 60,192) were noninstitutionalized adults aged ≥18 years. Overall, 2% of subjects identified as lesbian/gay, 1.7% identified as bisexual, 95.8% identified as heterosexual/straight, and 0.6% reported something else. Objective: To examine the prevalence of tobacco use by sexual identity in the context of sex and other characteristics.	Data derived from the 2012-2013 NATS were measured for sexual identity, and current use and ever-use of tobacco products (cigarettes, cigars, regular pipes, hookah, EC, and ST).	The prevalence of ST use among sexual minority males was 3.8% (95% CI: 2.4, 6.0) and among heterosexual/straight males was 7.4% (95% CI: 6.9, 7.9; p < 0.05). The prevalence of ST use among heterosexual/straight females was 0.4% (95% CI: 0.3, 0.5).	Strength: The study was based on nationally representative data. Limitations: (1) It was a cross-sectional study; (2) the data are not inclusive of the entire LGBT population; (3) the prevalence of sexual minorities in this sample was still lower than might be expected based on more comprehensive demographic surveys; and (4) small sample sizes limited the ability to examine patterns of use of certain demographic characteristics.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Linde et al., 2016)	Smokeless tobacco use among United States Air Force trainees	Data are from a cross-sectional study. Forty-six percent of the subjects were younger than 20 years old. Subjects (n = 14,810, 74% male, 26% female, 68% white, 85% non-Hispanic, 90% single, 52% had a high school education, 10% regular ST user) were USAF technical training students. ST includes chewing tobacco and snuff. Objective: To assess the prevalence of ST use and the sociodemographic correlates of ST use among individuals entering the USAF.	Data collected from March 2011 to March 2013 were analyzed for demographics, frequency of ST use, tobacco use among family and friends, ownership of items with tobacco advertising, perceived harm of ST relative to cigarettes, sports participation in high school, and intentions to return to tobacco use.	Non-Hispanic white males were more likely to be ST users. Playing high school sports, smoking cigarettes at least once per month, having friends or living with someone who used tobacco products, owning at least one item that had tobacco advertising on it, and being willing to try a tobacco product that claimed to be safer than cigarettes were associated with both infrequent and regular ST use (all ps ≤ 0.02). Male sex, playing sports, cigarette smoking, having friends who used ST, willingness to try a tobacco product claiming to be safer than cigarettes, and living with someone who uses ST were all positively associated with infrequent and regular ST use (all ps < 0.001). Black or African American race, having friends who smoke cigarettes (p < 0.001), and living with somebody who smoked cigarettes (p < 0.001) were associated with a lower odds of both infrequent and regular ST use.	Strengths: The study had a (1) large sample population and (2) included a population of interest (i.e., non-college-bound young adults aged 18–24 years). Limitations: (1) The study only included subjects who were early on their careers; (2) ST use in USAF is not representative of ST use across the service branches; (3) the study was based on self-report; and (4) this was a cross-sectional study.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Lisha, Jordan, & Ling, 2016)	Peer crowd affiliation as a segmentation tool for young adult tobacco use.	Data are from a cross-sectional study. Subjects (n = 3,366; mean age: 24 years; fairly evenly divided between men and women; 36% non-Hispanic whites, 36.1% Hispanics, 13.3% non-Hispanic Asians, 4.3% non-Hispanic blacks, and 10.3% non-Hispanic other) were young adults who were bar patrons in Los Angeles, San Diego, and San Francisco. The largest peer crowd was Hipsters at 29%. ST was used by 7.5% of subjects. Objective: To examine social affiliation with "peer crowd" as an innovative way to identify high-risk tobacco users.	Data derived from survey conducted in 2014 were analyzed for demographics (age, sex, sexual orientation, race/ethnicity, and education), peer crowds, and tobacco use.	Those affiliated with Country had a higher ST use rate than that of Hipsters, Partiers or Young Professionals, and the Hip Hop crowd had the highest ST use rate. Hip Hop and Hipster groups had the highest overall use of any product compared with the four other groups. Hispanics had a higher ST prevalence than all other groups, except non-Hispanic blacks. Overall, Asians had the lower use rates of all products. Peer crowd was a significant predictor for four products; including cigarettes, EC, cigars, and ST; as well as any tobacco use. Degree of Hipster affiliation was associated with decreased risk of ST use, and Young Professional affiliation was associated with decreased risk of any tobacco use.	Limitations: (1) This was a cross-sectional study; (2) subjects were specific to bar-goers in California in metropolitan cities and, therefore, not generalizable; (3) there were very little data on peer crowds and ATP use; (4) bars selected in the study reflected the Hipster population; (5) bar owner or patron refusal could lead to bias; and (6) the study was based on self-report.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Little et al., 2016)	Prevalence and correlates of tobacco and nicotine containing product use in a sample of United States Air Force trainees.	Data are from a cross-sectional study. Subjects (n = 13,685, 78.2% male, mean age: 20.5 years, 89.4% single, 43.1% had some college education, 16% Hispanic, 61.3% non-Hispanic white) were airmen trained at the four advanced major Technical Training Air Force Bases in the U.S in 2013 and the first quarter of 2014. Objective: To determine the prevalence and correlates of TNCPs, including cigarettes, new and ETPs, and EC, in young military trainees; and to assess two important correlates of use, including intentions to use and perceptions of harm associated with TNCPs to assist future work in identifying areas for intervention.	Data were analyzed for demographics (age, sex, education, race/ethnicity, and marital status), prevalence of tobacco and EC use, and correlates of tobacco and EC use.	Among subjects, 26.9% reported regular use of a TNCP, of whom 8.5% used ST. Among ST users, 26 were females and 1,142 were males; 1,014 were non-Hispanic white; 754 had a high school diploma or general equivalency diploma, and 1,078 were single. Among current TNCP users, 29.1% reported intentions to use ST.	Strength: The study had a large sample size. Limitations: (1) This was a cross-sectional survey; (2) the study was based on self-report; (3) there were differences in sample sizes of the recruitment classes; (4) subjects were airmen and could not be generalized for other service branches; and (5) airmen with missing TNCP data were excluded from analysis and were more likely to be of Hispanic descent.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Lynne-Landsman et al., 2016)	Early trajectories of alcohol and other substance use among youth from rural communities within the Cherokee nation	Data are from a large longitudinal randomized controlled trial. Subjects (n = 684) were adolescents (50% female, 51% American Indian) who were in 9th (three waves in Study Year 1) and 10th (two waves in Study Year 2) grades. At the first assessment, 41% of subjects were aged 14 years or younger, 52% were aged 15 years, and 7% were aged 16 years. Objective: To examine sex and racial/ethnic differences in substance use trajectories during early adolescence among American Indian and non-American Indian adolescents.	Data from the 2013 YRBS of ninth to 10th grade students were analyzed for demographics (race, ethnicity, sex, parental education, age, and whether they received free or reduced-price lunch) and substance use (past-month frequency of alcohol use, heavy drinking, cigarette smoking, chewing tobacco use, marijuana use, prescription drug misuse, and other illicit drug use.	At each of the five longitudinal assessments, males (10%-16%) consistently reported significantly higher rates of chewing tobacco use than females (2%-5%). The majority of youth followed a trajectory of no chewing tobacco use (87%). Nine percent of chewing tobacco users followed a trajectory of moderate/increasing chewing tobacco use. These youth had a 0.25 estimated probability of past-month chewing tobacco use at the first assessment in early 9th grade, increasing to 0.5 by the final assessment in 10th grade. The smallest user class (4% of subjects) consisted of youth with a high estimated probability of past-month chewing tobacco use (0.97 or greater across waves). Significantly, more males followed trajectories of moderate/increasing or high chewing tobacco use (13% and 7%, respectively) compared with females (5% and 1%, respectively). There were no significant differences in chewing tobacco trajectory class membership by race/ethnicity.	Strengths: This was a longitudinal study of an under-studied population. Limitation: (1) The data were not generalizable to youth in general or other American Indian youth from different tribal communities; and (2) the study was based on self-reported data.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Macy et al., 2016)	Dual trajectories of cigarette smoking and smokeless tobacco use from adolescence to midlife among males in a midwestern US community sample	Data are from a longitudinal study. Subjects (n = 2,230) were men who reported cigarette smoking or ST use in 1987, 1993, 1999, 2005, or 2011. Objective: To identify tobacco-use trajectories from adolescence to midlife and to test correlates of trajectory group membership.	Data were analyzed for cigarette smoking and ST use, parent education, personally relevant health beliefs, personalized risk of addiction, general health beliefs, normative beliefs, perceived prevalence, and health dangers of smoking versus ST.	Those in the early-onset, then cessation ST trajectory group were significantly younger in 1987 than those in other ST groups. Those in the regular use groups for cigarette smoking and ST were the least likely to have at least one parent with a college education. ST trajectory groups: early onset, then cessation (20.8%); consistent abstinence from ST (38.6%); late onset and escalating (10.9%); and consistent regular (29.7%). For dual trajectory analysis, the cells with the highest proportion of participants were those indicating consistent regular smoking and abstinence from ST (26.8%) and consistent regular ST use and abstinence from smoking (20.6%).	Strength: This was a longitudinal study. Limitations: (1) Subjects were mostly non-Hispanic white from the Midwest; and (2) any short-term changes in tobacco use behaviors could not be detected due to 6-year lag in between waves.
(Mays et al., 2016)	Openness using non-cigarette tobacco products among U.S. young adults	Data are from a cross-sectional study. Subjects (n = 5,985, 51.5% male, 55.9% non-Hispanic white, 20.5% Hispanic, 10.7% non-Hispanic black, mean age: 23.3, 39.9% never-smoker, 28.4% noncurrent ever-smoker, 22.8% current smoker, 8.9% former smoker) were adults aged 18-29 years. In this study, ST includes chew, snuff, dip, snus, and dissolvable tobacco. Objective: To characterize openness to using NCTPs and associated factors among U.S. young adults.	Data derived from the 2012-2013 NATS were analyzed for demographic characteristics (age, sex, race/ethnicity, education, and marital status), current cigarette smoking, and current use of noncigarette products.	About 5.9%, 2.2%, and 0.1% of subjects were current chew/snuff/dip, snus, and dissolvables users, respectively. Among subjects, 91.3%, 26.9%, and 8% would not use chew/snuff/dip, snus, and dissolvables, respectively. About 8.3%, 11.1%, and 1.5% of subjects were open to using chew/snuff/dip, snus, and dissolvables, respectively. The odds of being open to using chew/snuff/dip, snus, and dissolvables were significantly higher among men (all ps < 0.001); odds were significantly higher for young adults aged 18-24 years for snus (p < 0.01). Minority racial/ethnic respondents were significantly less likely to report openness to using chew/snuff/dip and snus (all ps < 0.05). Noncurrent smokers/ever-smokers, current smokers, and former smokers reported significantly higher openness to use chew/snuff/dip and snus than never-smokers (all ps < 0.001).	Strengths: (1) The study had a large sample population; and (2) the study used nationally representative data. Limitations: (1) Findings may not generalize to other populations; (2) definitions of openness and use behaviors varied across products owing to the survey questions, which may affect findings, and (3) this was a cross-sectional study.

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(Meier et al., 2016)	Perceptions of snus among US adult smokers given free product	Data are from a longitudinal study. Subjects were adult smokers (n = 543; 69.2% female, median age: 49.3 years, 89.4% non-Hispanic white; 64.7% with at least some college education) who were uninterested in quitting and received free snus for ad libitum use. During the 6-week sampling period, subjects were grouped into never-users (18.4%, n = 100), experimenters (33.1%, n = 180), and persistent users (48.4%, n = 263). In this study, snus is categorized as ATP, whereas traditional ST is categorized as ST. Objective: To examine perceptions of snus among U.S. smokers given free snus for 6 weeks and a method for assessment of an ATP at the population level.	Subjects provided information regarding use of Camel snus, attitudes and risk perceptions of ATPs, snus outcome expectancies, and product preference for snus versus cigarettes.	The percentage of subjects that tried Camel snus were 2% (never users), 5.6% (experimenters), and 5.7% (persistent users). The percentages of subjects who tried Marlboro snus were 0% (never users), 5% (experimenters), and 5.7% (persistent users). The percentages of subjects who tried ST were 2% (never users), 6.1% (experimenters), and 9.9% (persistent users). There were significant differences between groups in cigarettes per day (p = 0.05) and nicotine dependence (p < 0.01).	Strength: This was a novel design of a longitudinal assessment of naturalistic use among a group of smokers uninterested in quitting. Limitations: (1) This study did not provide information of snus use in other countries; (2) subjects were uninterested in quitting and, therefore, the result should not be generalized to all smokers; and (3) subjects were only informed of the manufacturers' claim that snus and other ATPs provide lowered risk than cigarettes and not told about research also supporting the claim.

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(Meier et al., 2016)	Preference for flavored noncombustible nicotine products among smokers motivated to switch from cigarettes	Data are from a randomized study. Subjects (n = 195 received 4 mg nicotine gum, n = 196 received Camel snus, 81.8% non-Hispanic white, 52.9% males, mean age: 43.9 [12.5] years) were smokers from Minneapolis/St. Paul, MN, and Eugene, OR. Average number of cigarettes per day was 18 (6.5), average age of first tobacco use was 14.3 (4.2) years, and 76.5% of subjects smoked nonmenthol cigarettes. Objective: To test whether smokers willing to switch to an alternative product would prefer flavored versus nonflavored products.	Subjects were randomized to receive either Camel snus or 4-mg nicotine gum for 12 weeks. Subjects were free to choose any flavor of their assigned product during the intervention period. Demographic variables, smoking history, and switching between flavored and nonflavored tobacco were measured.	Among subjects, 17.4% (n = 67) tried snus before the study, with 16% (n = 31) of them assigned to be in the nicotine group and 18.8% (n = 36) in assigned to be in the snus group. Among subjects assigned to the nicotine group, 1 (0.5%) participant chose original flavor and 78 (40%) chose mint, 69 (35.4%) chose fruit, and 47 (24.1%) chose cinnamon. Of these individuals, 25 (12.8%) switched from one flavored product to another and none switched from flavored to a nonflavored gum during the treatment period. Among subjects assigned to the snus group, 140 (71.4%) chose Winterchill, 15 (7.7%) chose Frost, 9 (4.6%) chose Mellow (no flavor), and 32 chose (16.3%) Robust (no flavor). Of these individuals, 26 (13.3%) switched from one flavored product to another, 5 (2.6%) switched from flavored to nonflavored, 10 (5.2%) switched from nonflavored to flavored, and 12 (6.1%) made multiple switches.	Limitation: The study did not compare flavored versus nonflavored products using an intrasubject design.

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(Morean et al., 2016)	Latent class analysis of current e-cigarette and other substance use in high school students	The study was cross-sectional. Subjects (n = 2,241; mean age: 15.6 years; 45.6% male; 65.1% white) were adolescents attending four high schools in southeastern Connecticut. Objective: To examine high school students' current use of EC, cigarettes, cigars, ST, hookah, blunts, marijuana, and alcohol.	The study analyzed demographic information (age, sex, and race/ethnicity), EC, cigar, ST, hookah, and blunt use, cigarette use, and alcohol and marijuana use.	The proportion of participants who self-reported using ST was 2.8%. The conditional probabilities of current ST use were 0% for abstainers, 0.2% for EC and alcohol users, 0.01% for marijuana and alcohol users, and 0.22% for all product users. The mean number of days of ST use per month was 9.69.	Limitations: (1) The study was based on an adolescent self-study report; (2) data were collected from four high schools in Connecticut; (3) the study was cross-sectional; and (4) the study placed a premium on having complete past-month substance use data from subjects rather than imputing missing past-month substance use data.

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(Mushtaq & Beebe, 2016)	Assessment of the tobacco dependence screener among smokeless tobacco users	Data are from a cross-sectional study. Subjects (n = 95, mean age: 31.93 [12.20]; 100% male) were exclusive ST users for at least 1 year and lived in Oklahoma. The average consumption of ST was 3.6 (2.2) cans per week. Objective: To evaluate the TDS as a measure of tobacco dependence among ST users.	Subjects were recruited through email distribution lists and community referrals from May 2010 to December 2010. Data were analyzed for sociodemographic, tobacco use characteristics and for saliva cotinine levels.	The mean TDS score was 5.4 (2.61). TDS item "Feeling dependent on tobacco" had the highest prevalence (80%), whereas only 10% of the subjects reported giving up important activities to use ST. The mean score of FTND-ST was 3.84 (2.54), and the median cotinine level was 350.53 ng/mL. Mean TDS score was higher among those who had quit attempts in the past 12 months, those with higher frequency of ST use, and those who used ST soon after waking up. TDS score was positively associated with increasing age (p < 0.009); FTND-ST total score (p < 0.0001); salivary cotinine concentration (p < 0.018); tobacco use characteristics, such as time to first chew/dip, (p = 0.0002); and frequency of ST use (p = 0.013). The amount of ST use was not significantly associated with TDS score (p = 0.168). Based on the best TDS cut point, 50.5% of subjects had TDS-based dependence diagnosis. ST users who placed their first dip within 30 minutes of waking were 3.57 times more likely to have TDS-based dependence diagnosis than those who used ST after 60 minutes of waking. Similar association was observed when ST users dipping more than six times a day were compared with ST users not dipping more than three times a day (OR = 3.3, 95% CI: 1.06, 10.27). Among everyday ST users, those with higher cotinine concentration were 1.06 times more likely to be screened as dependent by TDS. Years of ST use and quit attempt had significant relationship with TDS-based dependence diagnosis (OR = 1.06, 95% CI: 1.01, 1.1 and OR = 3.99, 95% CI: 1.5, 10.6).	Strengths: (1) Subjects were recruited without regard to their intention to quit; and (2) the study is generalizable. Limitations: (1) The predictive validity of TDS was not able to be evaluated due to lack of cessation information; (2) the study lacked representation of all the racial ethnic groups; and (3) all subjects were males.

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(Nguyen et al., 2016)	State-specific prevalence of current cigarette smoking and smokeless tobacco use among adults, United States, 2014	Data are from a cross-sectional study (2014 BRFSS). Subjects were noninstitutionalized U.S. adults aged ≥18 years. Objective: To assess prevalence of current cigarette smoking and current ST use.	State-specific prevalence for cigarette smoking, ST use, and dual use was calculated for all 50 U.S. States, territories, and the District of Columbia in 2014. Demographic (sex and race/ethnicity) or subjects were also measured.	Prevalence for ST use ranged from 1.4% (Hawaii) to 8.8% (Wyoming). ST use was significantly higher among males than females in 44 states. Among males, the prevalence of ST use ranged from 2.3% (Hawaii) to 16.5% (West Virginia), whereas among females ranged from 0.4% (Maryland) to 3.4% (Mississippi).	Limitations: (1) The estimates for tobacco use were self-reported; (2) the BRFSS sampling frame does not include adults without telephone service; (3) the median state response rates were low, which can increase the potential for bias; and (4) this was a cross-sectional study.

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(Parent et al., 2016)	Racial disparities in substance use by sport participation among high school students	Data are from a cross-sectional study. Subjects (6,721 male and 6,761 female) were high school students. About 60% of males and 46% of females reported that they played team sports. The study evaluated differences in use of smoked tobacco, chew/dip, steroids, alcohol, marijuana, cocaine, inhalants, methamphetamine, diet pills, and prescription drugs. The study also conducted exploratory analysis with other substances and examined racial/ethnic disparities. Objective: To evaluate differences in substance use patterns among adolescents who did and did not participate in team sports.	The study analyzed subjects participation in sport teams, use of substances, and demographic (race/ethnicity and sex).	About 15% of males used chew/dip and 3% of females used chew/dip. Among black or African Americans, 3% used chew/dip. Among whites, 12% used chew/dip. Among Hispanic/Latinos, 4% used chew/dip. Among multiracial Hispanics, 7% used chew/dip. Among multiracial non-Hispanics, 9% used chew/dip. Female athletes reported higher use of chew/dip (OR = 1.49, 95% CI: 1.03, 2.18). Among Asian adolescent males, athletes were not more likely to report use of chew/dip (OR = 2.54, 95% CI: 0.41, 15.73). Among multiracial Hispanic adolescent males, athletes were more likely to report use of chew/dip (OR = 2.14, 95% CI: 1.12, 4.11), but multiracial non-Hispanic adolescent male athletes were not more likely to report use of chew/dip (OR = 2.02; 95% CI: 0.69, 5.93). Among white females, athletes were not more likely to report use of chew/dip (OR = 1.22, 95% CI: 0.77, 1.92).	Strengths: (1) Data were from nationally representative survey; and (2) the study had a large sample population. Limitations: (1) Substance use was assessed using single items, which did not allow for detailed analysis of frequency and intensity use of the substances; (2) this was a cross-sectional study; (3) although it is unlikely that substance use precipitates sport participation, other third variables might affect the relationship between sport participation and substance use; (4) sport participation was assessed broadly in the survey, and differences by type of and commitment to a sport were not detailed; and (5) the YRBS relied on students who were enrolled in schools and did not include those in nontraditional education systems.

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(Reichenberger et al., 2016)	Associations between sleep and health-risk behavior in a rural adolescent population	Data are from a cross-sectional study. Subjects (n = 322) were rural adolescents (age: 14-19 years; 54.7% male). Objective: To develop a better understanding of sleep and health behavior associations, sleep associations with tobacco use, alcohol use, illicit drug use, and risky sexual activity.	Data from Rural Adolescent Health Survey were analyzed for measures of sleep and health-risk behaviors. For sleep measurements, subjects were asked for the amount of sleep. For tobacco use behaviors, subjects were asked for frequency of tobacco use.	Sex was associated with use of chewing tobacco, with a greater percentage of males (28.6%) reporting use compared with females (5.6%, $p < 0.001$). Sleep appeared to be unrelated to chewing tobacco. Hours of sleep experienced by those who did not use chewing tobacco and those who used chewing tobacco 20 to 29 days or all 30 of the past 30 days were 8.04 and 7.67 hours ($p = 0.08$), respectively.	Limitations: (1) This was a cross-sectional study; (2) The amounts of sleep reported may not accurately reflect the actual amount of sleep; and (3) there was not a nonrural sample for comparison.

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(Roberts et al., 2016)	Rural tobacco use across the United States: How rural and urban areas differ, broken down by census regions and divisions	Data are from cross-sectional studies. Subjects (n = 136,147 total, n = 68,309 in 2012 and n = 67,838 in 2013, 51.5% female) lived in the U.S. and were over the age of 12 years. Among subjects, 17.4% lived in the rural area, and 13% lived in poverty. ST in this study included chew and snuff. Objective: To examine rural vs. nonrural differences in use of cigarettes and other tobacco products, and to investigate how these differences vary across regions and divisions of the country.	Data came from the pooled 2012 and 2013 U.S. NSDUH. Data were analyzed for tobacco use (any past-30-day use for chew and snuff), poverty levels, urban/rural area, and regions and division within the U.S.	Nationally, cigarette use, chew, and snuff were significantly more prevalent in rural areas than in urban areas (all ps < 0.001). In the West, the prevalence rates for chew and snuff in the rural area (2.4% and 4.9%, respectively) were significantly higher (all ps < 0.01) than in the urban area (1.0% and 2.0%, respectively). In the Midwest overall, the prevalence rates of chew and snuff were significantly higher (all ps < 0.01) in the rural area (2.8% and 5.8%, respectively) than in the urban area (1.2% and 2.7%, respectively). In the Northeast overall, the prevalence rates for chew and snuff were significantly higher (all ps < 0.01) in the rural area (1.8% and 3.7%, respectively) than in the urban area (0.6% and 1.5%, respectively). In the South, the prevalence rates for chew and snuff were significantly higher (all ps < 0.01) in the rural area (1.9% and 6.1%, respectively) than in the urban area (0.8% and 2.8%, respectively). Specifically, in the West North Central, East North Central, Middle Atlantic, New England, South Atlantic, and West South Central, the prevalence rates of chew were significantly higher (all ps < 0.01) in the rural area than in the urban area. In the Pacific, West North Central, East North Central, Middle Atlantic, South Atlantic, East South Central, and West South Central, the prevalence rates of snuff were significantly higher (all ps < 0.01) in the rural area than in the urban area.	Strengths: (1) The study had a large sample population; and (2) nationally representative data. Limitations: (1) The study relied on U.S. census regions that were based on political boundaries, which cut across other types of boundaries and obscured the high tobacco-use rates that are known to exist in certain places; (2) the study also relied on U.S. census definition of "rural" and analysis using alternative definitions that may lead to different results; and (3) the rural-versus-urban dichotomy in this study belies more gradual, continuous distinctions in population density and distance from urban centers; and (4) this was a cross-sectional study.

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(Sapra et al., 2016)	Time-to-pregnancy associated with couples' use of tobacco products	Data are from a cross-sectional study. Couples (n = 501; males aged 18+ years, females aged 18-40 years) resided in 16 counties in Michigan and Texas. Objective: To assess the relationship between paternal preconception tobacco use (ST and combustible) and prospective TTP; and to evaluate blood heavy metal and serum cotinine concentrations among various tobacco-product users and nonusers to determine if specific chemicals may contribute to changes in TTP.	Subjects discontinuing contraception to become pregnant were followed until positive pregnancy test or 12 months of trying. They were interviewed on lifetime and current cigarette, cigar, and ST (chew/snuff) use and provided blood samples for quantification of heavy metals and cotinine. FORs were estimated and adjusted for demographics and lifestyle (FOR < 1 indicates a longer TPP).	Among male partners who exclusively used snuff/chew (n = 28), mean age at enrollment was 32.6, 96% were non-Hispanic white and 4% were other, 15% had a high school education or below, and 58% had an annual income of \$50,000-100,000.	Strengths: Recall bias was minimized. Limitations: The study had a small numbers of ST users.

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(Smith et al., 2016)	Association between use of flavoured tobacco products and quit behaviours: findings from a cross-sectional survey of US adult tobacco users	Data are from a cross-sectional study. Subjects (n = 1,443, 61% male, 24% aged 55+, 62% with less than a high school education, 45% never married, 62% white, non-Hispanic, and 41% with a household income <US\$30,000 annually) were adult tobacco users. Objective: To examine associations between first use and current use of flavored tobacco products, and between current flavored tobacco use and quit behaviors.	Data were collected from a nationally representative survey from November 2012 through April 2013. Data were analyzed for use of flavored tobacco at product trial, current use of flavored tobacco products, current tobacco product use, and quit attempts.	About 87% of subjects reported use of one or more tobacco products, with 70% reporting use of only one product. Sixty-six percent of ever users of snus/ST reported using a flavored product at trial. Among subjects, 58% reported snus/ST use.	Strength: This study represented a sample of U.S. adult tobacco users. Limitations: (1) This was a cross-sectional study; (2) the study was based on self-report; (3) there was a low response rate; (4) the study used a landline-based random-digit-dial sampling method; (5) the study did not speak to the specific tobacco product used first by respondents and whether the very first product used was flavored; and (6) sample size was limited.

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(Stanton et al., 2016)	Trends in tobacco use among US adults with chronic health conditions: National Survey on Drug Use and Health 2005-2013	Data are from cross-sectional studies. Subjects (n = 335,080) were adults (age: ≥18 years). ST includes chewing tobacco and snuff. Objectives: (1) To compare trends in adult tobacco use among adults with versus without chronic health conditions; and (2) to examine cigarette smoking and trends in the use of NCTPs (i.e., cigars, pipes, and ST products) within each chronic condition subgroup.	Data derived from the 2005-2013 NSDUH were analyzed for past-30-day use of cigarettes, cigars, pipes, and ST, and chronic health conditions.	Among subjects, 29.6% used tobacco in the past 30 days. Among tobacco users, 15.2% used multiple tobacco products. Rates of ST use were higher among adults with at least one chronic condition (3.1% - 3.49%) than among those with none (2.36%-2.66%, AOR = 1.32 [95% CI: 1.24, 1.41], p < 0.01). There was a significant increase in ST use over time among those with and without chronic conditions (AOR = 1.02 [95% CI: 1, 1.03], p = 0.02). ST use among those with anxiety, substance abuse disorders, asthma, and hypertension was significantly higher across years than it was among those without a chronic condition (AOR = 1.17 [95% CI: 1.04, 1.32], p = 0.01; AOR = 1.70 [95% CI: 1.58, 1.84], p < 0.01; AOR = 1.28 [95% CI: 1.13, 1.45], p < 0.01; AOR = 1.24 [95% CI: 1.11, 1.39], p < 0.01, respectively), while those with heart disease showed decreases in ST use (AOR = 0.81 [95% CI: 0.66, 0.98], p = 0.03). There was an increase in ST use among subjects with any of the chronic health conditions between 2005 and 2013.	Strength: (1) The study used a large sample population from 2005 until 2013; and (2) the study used nationally representative data. Limitations: (1) The study was based on cross-sectional studies; (2) the study was based on self-report; (3) it was limited to studying only the chronic conditions measured in the NSDUH; and (4) findings were limited to 2005-2013 since not all the smoking and chronic condition questions were administered in the previous years.

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(Sung et al., 2016)	Polytobacco use of cigarettes, cigars, chewing tobacco, and snuff among US adults	Data are from four cross-sectional studies. Subjects (n = 117,816 adults; age: 18+ years; 48% male; 72.3% non-Hispanic white, 35.9% lived in the South) participated in in-person surveys. Objective: To examine the prevalence, trends, and correlates of polytobacco use among current users of cigarettes, cigars, chewing tobacco, and snuff in U.S. adults aged ≥18 years.	Data from the most recent Cancer Control Supplements were conducted in 1998, 2000, 2005, and 2010 were analyzed for current single use of four tobacco products (cigarette, cigar, chewing tobacco, and snuff), current polytobacco use, sociodemographic characteristics, and other health-risk behaviors.	Prevalence of current snuff use was 1.8% in 1998, dropped to 1.3% in 2000, and increased to 2% in 2010. The prevalence of current chewing tobacco and snuff use varied by cigarette smoking status (1.5% and 2.2%, respectively, among current smokers; and 0.9% and 1.3%, respectively, among never-smokers). About 60.8% of current snuff users consumed snuff daily, and 44.3% of current chewing tobacco users consumed chewing tobacco daily. About 54.8% and 42.5% of current chewing tobacco users and snuff users, respectively, were polytobacco users. The prevalence rates of polytobacco users were in the range of 47.4%-57.4% among chewing tobacco users and 42.1%-47.4% among snuff users between 1998-2010. Among current chewing tobacco users, the proportion of polyusers who concurrently used cigarettes increased from 19.2% in 1998 to 37.2% in 2000 and then declined to 19.1% in 2010, and the proportion of polyusers who concurrently used cigarettes and other forms of NCTPs fluctuated in the range of 22.2%-36.8%; in 2010, more than half of polyusers concurrently used only other forms of NCTPs. Of the polyusers among current snuff users, more than one-third concurrently used cigarettes only, 23.5%-30% concurrently used both cigarettes and other forms of NCTPs, and 30.2%-40.6% concurrently used only other forms of NCTPs.	Strengths: (1) The study was used a large sample population; and (2) the data were nationally representative. Limitations: (1) The study did not examine new and ETPs, such as EC, hookah, and dissolvables; (2) the study was based on cross-sectional data, with 2010 being the most recent year of available data; and (3) the sample size of certain subgroups was small.

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(Syamlal et al., 2016)	Combustible tobacco and smokeless tobacco use among working adults—United States, 2012 to 2014	Data are from three cross-sectional studies. Subjects (n = 105,779, aged ≥18 years, 53% men, 66.5% non-Hispanic white) were noninstitutionalized U.S. civilian population. ST products used in this study include chewing tobacco, dip, snuff, snus, or dissolvable tobacco. Objective: To examine tobacco use among working adults of at least 18 years of age.	Data derived from 2012-2014 National Health Interview Survey were analyzed for current tobacco use, employment status, and demographics (age, sex, race/ethnicity, education, health insurance status, household income, physical health status, and chronic disease status).	During 2012-2014, an estimated 23.1% of working adults currently used any tobacco. The prevalence of using ST was significantly higher than comparators among the 18- to 24-year-old age group (OR = 5.4, 95% CI 4.5 ,6.2), males (OR = 6.1, 95% CI: 5.7, 6.5), non-Hispanic whites (OR = 4.6, 95% CI: 4.3, 4.9), those with less than a high school education (OR = 4.8, 95% CI: 4.3, 5.2), and those without health insurance (OR = 4, 95% CI: 3.4,4.5) (all ps < 0.05). The prevalence of using ST was the highest among subjects with household income of \$35,000-\$74,999, (OR = 3.7, 95% CI: 3.4, 4.1), among current cigarette smokers (OR = 6.7, 95% CI: 6.0, 7.4), very good/good physical health (OR = 3.5, 95% CI: 3.2, 3.7), with chronic obstructive pulmonary disease (OR = 3.6, 95% CI: 2.5, 4.7), worked in the mining industry (OR = 15.1, 95% CI: 9.0, 21.1), and had occupations in farming, fishing, and forestry (OR = 11, 95% CI: 6.8, 15.1).	Strengths: (1) The study used a large sample population; and (2) nationally representative data. Limitations: (1) The study was based on cross-sectional studies; (2) the study was based on self-report; (3) it was based on employment information collected applied only on the week before the interview; and (4) no detailed data about specific type of tobacco product was used.
(Wang et al., 2016)	Consumption of combustible and smokeless tobacco – United States, 2000-2015	Tobacco consumption was estimated by analyzing Federal excise tax data from 2000 to 2015. ST category includes chewing tobacco and dry snuff. Objective: To provide the most recently available tobacco consumption estimates in the U.S. during 2000-2015 period for combustible tobacco and ST.	Data derived from the federal excise tax data were analyzed to provide estimate total and per capita consumption during 2000-2015 for combustible tobacco and ST.	During 2000-2015, total ST consumption increased 23.1% (p < 0.05), or 4.2% per capita. However, chewing tobacco and snuff consumption patterns diverged; total chewing tobacco consumption decreased 55.8% from 45.6 to 20.2 billion pounds (p < 0.05), whereas total snuff consumption increased 77.5% from 66.2 to 117.4 billion pounds (p < 0.05).	Limitations: (1) Sales data did not provide information on consumer demographics; and (2) sales data might not reflect actual consumption since all purchased products might not be used by the consumer as a result of loss, damage, or tobacco cessation.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(White et al., 2016)	Do socioeconomic risk factors for cigarette smoking extend to smokeless tobacco use?	Data are from a cross-sectional study. Subjects were (n = 37,869; age: 18+ years; 48.1% male; 66.3% non-Hispanic white) U.S. adults who were selected from the civilian noninstitutionalized population. Objective: To examine socioeconomic status as a risk factor for ST use in a U.S. nationally representative sampling.	Data obtained from the 2012 NSDUH were analyzed for four socioeconomic status variables (educational attainment, household income, industry, and current unemployment), four demographic characteristics (age, sex, marital status, and race), and smoking and ST use in the past 30 days.	The prevalence of current ST use in the general population of adults were estimated at 3.7% (7.1% among males, 0.5% among females). Among current cigarette smokers, 5.7% reported current ST use; among current ST users, 37.2% reported current cigarette use. Odds of ST use were negatively associated with educational attainment, although only one comparison (college graduates vs. less than a high school education reference group) achieved significance. Working in a blue-collar industry was significantly associated with ST use. Younger age, being male, and being a current cigarette smoker were each associated with increased odds of ST use. Compared with non-Hispanic whites, individuals who identified as black, Hispanic, Asian, or multiracial were less likely to use ST, and Native Americans were more likely to use ST. Dependences on alcohol, marijuana, and heroin were associated with ST use. Increasing the lower age limit to 26 years eliminated heroin dependence as a predictor of cigarette and ST use, and retained current smoking as a predictor of ST use. Also, being black no longer was related to lower risk of ST use. Changing the definition of current smoker resulted in the retention of current smoking status a predictor of ST use.	Strengths: (1) The study used a large sample population and (2) nationally representative data. Limitations: (1) The data set was observational, and as such it was important to acknowledge the possible influence of unobserved variables; (2) the data were based on self-report; and (3) cross-sectional study.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Wong et al., 2016)	Distinct motives for use among polytobacco versus cigarette only users and among single tobacco product users	The study analyzed data from past-30-day tobacco users at Wave 2 (spring, 2015) of a six-wave longitudinal study of 3,418 students aged 18-25 years from seven U.S. colleges. Among subjects, 679 were past-30-day tobacco users (mean age: 20.55 years; 54.93% female; 58.6% white). Objective: To examine motives for tobacco use in relation to polytobacco versus cigarette-only use and motives for tobacco use in relation to levels of tobacco use across products.	Information regarding subjects' sociodemographics, tobacco use, and tobacco use motives were compared between polytobacco and cigarette-only use.	Among subjects, 12.8% (n = 87) used ST in the past 30 days. The prevalence of past-30-day ST use among other past-30-day tobacco product users was 10.8% (cigarettes), 11.1% (LCCs), 14.2% (ECs), and 7.8% (hookahs). Higher levels of ST consumption were associated with being male, not being Asian, lower social motives subscale scores, and higher self-enhancement and boredom-relief motives.	Limitations: (1) Samples were from the Southeast region of the U.S.; (2) the sample sizes for the LCCs, ST, and EC were small; (3) there was a relatively low response rate; and (4) the study was based on cross-sectional data.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Agaku et al., 2015)	Combustible and smokeless tobacco use among high school athletes - United States, 2001-2013	Data are from a cross-sectional study. Subjects (during 2001-2013, sample sizes ranged from 13,583 to 16,410 with overall response rates ranged from 63% to 71%) were students in Grades 9-12 who attended public and private schools. Objective: To examine prevalence and trends in current use of combustible tobacco (cigarettes, cigars) and ST (chewing tobacco, snuff, or dip) products among athlete and nonathlete high school students.	Data from the 2001-2013 National YRBS were analyzed for current use of combustible tobacco products, ST products, any tobacco products, and sociodemographic variables (grade, sex, race/ethnicity, and athlete status). Logistic regression models were fit, controlling for grade, sex, and race/ethnicity, to assess linear trends in tobacco use during 2001-2013.	Current ST use overall was slightly increased from 8.2% (95% CI: 6.8, 9.9) in 2001 to 8.8% (95% CI: 7.3, 10.6) in 2013. Current ST use significantly increased ($p < 0.05$) from 10.0% to 11.1% among athletes and did not change (5.9%) among nonathletes. Among athletes, significant increases in current ST use were observed among male (16.8% to 17.4%) and female (2.2% to 3.4%) students, 11th (11.8% to 13.6%) and 12th (11.1% to 12.2%) grade students, and Hispanic students (6.3% to 8%) ($ps < 0.05$); among nonathletes, a significant increase was observed among Hispanic (1.9% to 3.1%) students only ($p < 0.05$). In 2013, athletes had significantly higher odds of being current ST (AOR = 1.77, $p < 0.05$). In 2013, the AORs of current use of ST were significantly higher among male students than among female students, overall, and among athletes ($p < 0.05$). Among nonathletes, the odds of current use of any ST were significantly higher among male students. Students in 11th grade did not differ significantly in current use of ST when compared with 12th grade students ($ps < 0.05$). Overall and among athletes and nonathletes, non-Hispanic black and Hispanic students had significantly lower odds of current use of ST when compared with non-Hispanic white students. During 2013, the prevalence of ST use was 5.9%, 10.2%, 11.5%, and 12.5% among students participating in zero, one, two, or three or more sports teams, respectively ($p < 0.05$).	Strengths: (1) The study used a large sample population and (2) nationally representative data. Limitations: (1) It was a cross-sectional study; (2) the study was based on self-report; (3) the prevalence rates of snus and other ETPs were not assessed; (4) differential time frames and sports team participation might miss seasonal patterns of tobacco use; (5) the study did not collect tobacco use by type of sport; (6) nonresponse bias might have affected the results; and (7) the findings only applied to youth who attend school, which was not representative of all youth.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Ambrose et al., 2015)	Flavored tobacco product use among US youth aged 12-17 years, 2013-2014	Data are from Wave I of the PATH longitudinal cohort study of 13,651 youths (age: 12-17 years, mean = 14.5 years). Subjects were 51.3% male, 54.5% non-Hispanic white, 13.7% non-Hispanic black, and 22.5% Hispanic. ST types studied include snus and other ST besides snus. Objective: To examine flavored tobacco use among a nationally representative sample of U.S. youth.	Data collected from September 2013 through December 2014 were assessed for ever- and past-30-day use of tobacco products, including cigarettes, hookahs, cigars, pipe tobacco, all types of ST, dissolvable tobacco, bidis, and kreteks; and leading reasons for noncigarette tobacco-product use among past-30-day tobacco users.	The majority of youth ever-users reported that the first product they had used was flavored, including 68.9% of ST users (excluding snus) and 81.2% of snus users. The prevalence of ever product use (excluding snus) was 4.4% of ST users and 1.7% of snus users. The prevalence of past-30-day product use was 1.4% of ST users (excluding snus) and 0.5% of snus users. The proportion of flavored use among past-30-day youth tobacco users was 81% of ST users (excluding snus) and 80.4% of snus users. Leading reasons for ST use (excluding snus) were because of the flavors, affordable, could be used at times when or in places where smoking cigarettes were not allowed, and they might be less harmful than cigarettes. The leading reason for snus use was that snus could be used at times or in places where smoking is not allowed (69.7%); the next most cited reason for snus use was the flavors (69.3%).	Strengths: (1) The study used a large sample population and (2) nationally representative data. Limitations: (1) It was a cross-sectional study; (2) there was a potential difficulty with recall because youth often experiment with many products; and (3) mode differences in household- vs. school-based youth tobacco surveys.
(Boyle et al., 2015)	Tobacco use among Minnesota adults, 2014	Data are from surveillance series conducted since 1999. Subjects (n = 9,304) were adults aged ≥18 years in Minnesota. ST used includes chewing tobacco, snuff, and snus. Objective: To assess the changing landscape of tobacco, including the introduction of new products such as ST and electronic delivery devices.	Data from the Minnesota Adult Tobacco Survey studies (from 1999 until 2014) were assessed for tobacco products use.	In 2014, 3.6% of subjects used ST, 0.2% were women, and 7.2% were men. Subjects who were 25 to 44 years old, American Indians or Alaska Natives, Non-Hispanics, high school graduates, or current cigarette smokers, and those that had an annual household income between \$35,001 and \$50,000, had the highest prevalence rates of ST use. Among subjects who used ST, 7% lived in the Northeast, 6% lived in the Northwest, 5.3% lived in the Southeast, 5.1% lived in the Southwest, and 5% lived in the South Central region of Minnesota. In 2010, there was an increase in ST use (+1.2 percentage points since 2007) but in 2014 ST use dropped (-0.7 points). Concurrent use of ST among smokers also dropped in 2014 compared with 2010 (-2.2 points).	Strength: The study used a large population sample. Limitations: (1) The study was based on self-report; (2) the stratified design resulted in small sample sizes across regions and subgroups; and (3) there was a possibility of nonresponse bias.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Creamer et al., 2015)	Trends in multiple tobacco product use among high school students	Data are from a repeated cross-sectional study. Subjects were high school students, Grades 9-12, in public and private schools. Between 1999 and 2013, the number of usable questionnaires ranged from 13,601 to 16,460. Objectives: (1) To determine the trends of multiple and individual tobacco-product use over time among all students and current tobacco users; and (2) to examine sociodemographic differences in these trends.	Data from eight national YRBS (1999 -2013) were assessed for self-reported use of cigarettes, cigars, little cigars and cigarillos, and ST; and for sociodemographic variables of interest including race/ethnicity and sex.	The prevalence of cigarettes and ST and the concurrent use of cigars and ST did not significantly change between 1999 and 2013. However, there was a significant increase among Hispanic white students between 1999 and 2013 ($p = 0.02$). ST use did not significantly change among boys, but significantly increased among girls ($p = 0.01$). There were no significant changes in the prevalence of ST use among non-Hispanic white and Hispanic students, but there was a significant increase among non-Hispanic black students ($p = 0.01$). The prevalence of ST use increased from 19% in 1999 to 36% in 2013. ST use also increased in both boys ($p < 0.001$) and girls ($p < 0.001$) who used tobacco; however, the increased rate of ST use reported by girls was greater than that for boys.	Strengths: (1) The study examined trends in multiple tobacco product use; (2) the data were nationally representative; (3) the measures of tobacco use behaviors are standard in tobacco literature; and (4) the study used large sample population. Limitations: (1) The data came from repeated cross-section surveys; (2) self-report; and (3) there were no data on ETPs.
(Liu et al., 2015)	Risk perceptions of smokeless tobacco among adolescent and adult users and nonusers	Data are from a cross-sectional study. Subjects were adolescents ($n = 53$; median age: 17 years; 66% male; 84.9% white) and adults ($n = 63$; median age: 34; 79.4% male; 98.4% white) from four Ohio Appalachian counties. ST includes chew and snuff. Objective: To examine risk perceptions of ST among adolescent and adult users and nonusers in Ohio Appalachia.	Subjects were asked about their perceptions of ST-related health risks, ST safety, and the relative safety of ST compared with cigarettes.	In this study, 43.4% of adolescents and 60.3% of adults reported daily use of chew and/or snuff or use on most days. Nearly half of adolescent ST users (47.8%) used both snuff and chew products, whereas 60.5% of adult ST users used only snuff products.	Limitations: (1) This was a cross-sectional study; (2) findings may not be generalizable to other counties or the Ohio Appalachian region; (3) the study was limited to male ST users; and (4) participants were not asked about the relative risks of the various types of ST products such as chew, snus, and dissolvable tobacco available.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Loukas et al., 2015)	Changes in use of cigarettes and non-cigarette alternative products among college students	Data are from a longitudinal study. Subjects (n = 698, mean age: 22.98, 10.7% freshmen, 18.5% sophomores, 25.9% juniors, 29.4% seniors, 15.5% graduate students, 56% female, 42.5% non-Hispanic white) were from seven urban 4-year colleges within the University of Texas System. Subjects participated in the study at two waves, with 14 months between each wave. Among subjects, 138-140 were current cigarette smokers, and 530-533 were noncurrent cigarette smokers. Objective: To examine the change in use of smoked and smokeless non-cigarette alternatives (i.e., cigars/cigarillos/little cigars, hookah, chew/snuff/dip, snus, EC) by 18- to 35-year-old college students.	Data from Wave 1 (spring 2012) and Wave 2 (spring 2013) of college students participated in a two-wave study were analyzed for current tobacco and EC use.	Among subjects, less than 2.2% used snus and chew/snuff/dip for the entire study. The use of these products did not change across time with both products being used by less than 4.3% of current cigarette smokers. Among ST users, the prevalence was 1.9% at Wave 1 and 2.2% at Wave 2. Among snus users, the prevalence was 0.9% at Wave 1 and 1% at Wave 2. At Wave 1, 93.6% and 93.5% of current cigarette smokers were persistent nonusers of snus and ST, respectively. About 0.7% of current cigarette smokers were persistent users of snus and ST. At Wave 2, 2.9% and 3.6% of current cigarette smokers reported cessation of snus and ST use, respectively. New use of snus and ST only at Wave 2 were 2.9% and 2.2%, respectively. Persistent nonuse among nonsmokers of cigarettes was 99.4% and 97.7% for snus and ST, respectively. Persistent current use among non-cigarette smokers was 0% for snus and 0.8% for ST, respectively. Fewer than 6.6% of non-cigarette smokers reported use of any one product (snus: 0.4%, ST: 1.1%) for the first time in the study at Wave 2. Desistance among noncurrent smokers of cigarettes was 0.2% for snus and 0.4% for ST.	Strength: This was a longitudinal study. Limitations: (1) The study was limited to only two waves separated by 14 months; (2) data are not generalizable to populations outside the current sample; and (3) this study was based on self-report.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Meier et al., 2015)	Which nicotine products are gateways to regular use	Data are from a cross-sectional study. Subjects (n = 1,304; mean age: 19.57 years; 65.2% female; 80.1% white) were undergraduate students at a large university. Objective: To examine use of various nicotine-containing products on a tobacco-free college campus and whether the first product tried predicts subsequent tobacco use.	Data from the online survey conducted during the 2012-2013 academic semesters were analyzed for nicotine-containing product that subjects first tried and current use of tobacco products.	About 49.4% of subjects reported ever trying a tobacco product, with 13.2% ever tried ST. About 15% of subjects used ST as their first tobacco product. About 40.2% of individuals who first tried ST were current ST users, and 52.5% were current tobacco users (n = 51); and 3.4% of subjects who first tried ETPs were current ETP users and 28.8% were tobacco users (n = 17). Individuals who first used cigarettes were more likely than those who first used ETPs to be current polyusers (OR = 3.29, 95% CI: 0.97, 11.12, p = 0.06). Those who first tried ST were approximately six times more likely than those who first tried hookah to be current users of multiple tobacco products (OR = 6.15, 95% CI: 2.11, 17.95, p = 0.001), and they were four times more likely than those who first tried ETPs to be current users of multiple products (OR = 4.05, 95% CI: 1.08, 15.10, p = 0.04).	Limitations: (1) This was a cross-sectional study; (2) the study was based on self-report; (3) the data were not nationally representative of all youths, just college students; (4) the study only investigated the construct of first product tried as the mechanism for potential gateways; and (5) subjects were mostly white.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Mushtaq, Boeckman, & Beebe, 2015)	Predictors of smokeless tobacco cessation among telephone quitline participants	Data are from a longitudinal study. Subjects (n = 374, 100% male, mean age: 41.3 years, 83% white) were exclusive ST users (61% used ST for ≥20 years, 68% used three or more cans/pouches per week, 89% attempted to quit tobacco use). Subjects who attempted to quit had a high level of motivation (73%) and high level of confidence to quit (53%) at registration. The mean number of completed scheduled Helpline calls was 2.4, and >85% subjects received NRT for either 2-4 weeks (65%) or 8 weeks (20%). Objective: To examine factors related to tobacco abstinence among exclusive ST users registering for services with the Oklahoma Tobacco Helpline.	Data collected from ST users who registered with the Oklahoma Tobacco Helpline and completed the 7-month follow-up survey from 2004 to 2013, were analyzed for sociodemographic factors, tobacco use behavioral factors, and presence of any chronic disease.	Subjects (exclusive ST users) with higher income were 1.74 times more likely to quit tobacco use than participants with lower income (OR = 1.74, 95% CI: 1.04, 2.9). Level of motivation and income were significantly associated with abstinence (OR = 2.1, 95% CI: 1.17, 3.75 and OR = 1.79, 95% CI: 1.04, 3.09). There was a moderately strong positive association between number of completed scheduled calls and tobacco abstinence. Each additional Helpline call resulted in a 20% increase in the odds of tobacco cessation (OR = 1.2, 95% CI: 1.04, 1.38). ST users who completed more than one call were 1.77 times more likely to quit tobacco use than those who completed one call. Tobacco abstinence exhibited a positive NRT gradient: ST users who received 8 weeks of NRT were more likely to quit tobacco than non-NRT users. However, there was no statistical significance in abstinence rates between those who received 2-4 weeks of NRT and non-NRT users. (crude OR = 1.3, 95% CI: 0.7, 2.43). The observed positive association between NRT and tobacco abstinence did not remain significant after the model was corrected for level of motivation, income, and number of completed scheduled calls.	Strength: This was a longitudinal study. Limitations: (1) The study was based on self-report, with no biochemical verification of abstinence; (2) the study was based on 39% of subjects who completed the 7-month follow-up survey, which made the findings prone to selection bias; (3) all subjects were male, and majority were white; (4) subjects were assumed to have a high likelihood of progressing to the action stage with delivery of the intervention; and (5) the study was not generalizable.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Neff et al., 2015)	Frequency of tobacco use among middle and high school students - United States, 2014	Data are from a cross-sectional study. Subjects (n = 22,007) were middle school (Grades 6-8) and high school (Grades 9-12) students. ST includes chewing tobacco, snuff, or dip. Objective: To determine how frequently U.S. middle school and high school students used cigarettes, EC, cigars, and ST products.	Data from the 2014 NYTS were analyzed for current use of nine products (cigarettes, cigars, ST, EC, hookahs, tobacco pipes, snus, dissolvables, and bidis) and frequency of use.	Among current users in high school, frequent use was most prevalent among ST users (42%). Among current users in middle school, frequent use was greatest among ST users (29.2%). Most (63.4%) of ST users were current users of two or more types of tobacco products. In 2014, among middle school and high school students, an estimated 390,000 used ST. Among high school students, 42% of ST users reported using ST during ≥20 days of the preceding 30 days, and 26.6% of ST users used ST during 1-2 days of the preceding 30 days. Among middle school students, 29.2% of ST users reported using ST during ≥20 days of the preceding 30 days, and 38.4% of ST users used ST during 1-2 days of the preceding 30 days. Among middle school and high school students, 63.4% reported ST use on 1-5 days during the preceding 30 days.	Strengths: (1) The study used a large sample population. Limitations: (1) This was a cross-sectional study; (2) the study was based on self-report and may be subject to recall bias or social-desirability bias; (3) data were from public and private school students and may not be generalizable to all middle school- and high school-aged youth; (4) data about patterns of use, primary product used, or which products were used on specific days could not be obtained; and (5) frequency of use of hookahs, tobacco pipes, snus, dissolvables, and bidis was not collected.
(Nguyen et al., 2015)	State-specific prevalence of current cigarette smoking and smokeless tobacco use among adults aged ≥18 years — United States, 2011–2013	Data are from several surveys (2011-2013 BRFSS). Subjects were noninstitutionalized U.S. adults aged ≥18 years. Objective: To assess prevalence of current cigarette smoking and current ST use.	State-specific prevalence for current cigarette smoking, ST use, and dual use was calculated for all 50 U.S. States and the District of Columbia. The relative percent change from 2011-2013 was also calculated.	Current ST use ranged from 1.4% (California and Rhode Island) to 9.8% (Wyoming) in 2011 and from 1.5% (District of Columbia and Massachusetts) to 9.4% (West Virginia) in 2013. Increases in relative percent change were observed in Louisiana (26.7%), Montana (12.7%), South Carolina (22.2%), and West Virginia (25.3%), while declines were observed in Ohio (-16%) and Tennessee (-25%).	Limitations: (1) The estimates for tobacco use were self-reported; (2) the BRFSS sampling frame did not include adults without telephone service; and (3) the median state response rates were low, which can increase the potential for bias.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Redner, White, Higgins, & Harder, 2015)	Examining vulnerability to smokeless tobacco use among adolescents and adults with major depressive disorder	Objective: To examine ST use among adolescents and adults with major depressive disorder in the NSDUH.	Data derived from the 2011 NSDUH were analyzed for current cigarette smoking and ST use among adolescents and adults meeting criteria for past-year major depressive disorder to the general population, after adjusting for potential confounding influences of sociodemographic and other substance use characteristics.	"Odds for current ST use did not differ among adolescents (OR = 0.90 [0.46, 1.76], p = 0.678) and were lower among adults (OR = 0.68 [0.46, 1.00], p = 0.01)."	Limitations: Study methodology and reports are only reported in an abstract.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Warren, Smalley, & Barefoot, 2015)	Perceived ease of access to alcohol, tobacco, and other substances in rural and urban US students	Data are from a cross-sectional study. Subjects (n = 513,909) were middle school (252,403) and high school (261,506) students (18.2% rural). Objective: To examine rural-urban differences in perceived ease of access to alcohol, smoking and chewing tobacco, marijuana, and seven other substances in order to better inform and promote future substance-use prevention and programming efforts in rural areas.	Data from the 2013 Georgia Student Health Survey II were analyzed for perceived ease of access to substances.	For middle school students, a significant difference in perceived ease of access was found for each substance, with rural students reporting greater access to predominantly “legal” substance including chewing tobacco (OR = 1.46, $p < 0.001$). The largest magnitudes of difference were found in access to chewing tobacco (with rural students 46% more likely to report ease of access). For high school students, there was a significant difference in perceived ease of access chewing tobacco (OR = 1.51, $p < 0.001$), with rural students reporting higher access.	Strength: The study used a large sample population. Limitations: (1) This was a cross-sectional study; (2) the study was based on self-report; (3) study data came from a single state; and (4) information on sex and race/ethnicity was withheld in the data set, which precluded analyses that incorporated these factors.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Wilkinson et al., 2015)	Demographic, psychosocial, and genetic risk associated with smokeless tobacco use among Mexican heritage youth	Data are from three waves of the MATCH cohort, with 1328 subjects participated at baseline in 2005-2006 (Wave 1), 1154 subjects participated in 2008-2009 (Wave 2), and 1000 subjects participated in 2010-2011 (Wave 3). Subjects (n = 1087, mean age: 14.3 years, 50.5% girls) reported psychosocial risk factors in 2009-2009 and ST use in 2010-2011 (mean age: 16.7 years). Objective: To examine demographic, psychosocial, and genetic risks associated with ST use among Mexican heritage youth.	Data derived from the MATCH cohort were analyzed for lifetime ST use, demographic, and psychosocial risk factors. The demographic variables include age, socioeconomic status, and sex. Psychosocial covariates examined included anxiety, sensation seeking, and subjective social status. Additionally, subjects provided a saliva sample that was genotyped for genes in the dopamine, serotonin, and opioid pathways.	Increasing numbers of subjects reported lifetime ST use at each wave: 22 subjects at Wave 1, 45 subjects at Wave 2, and 62 subjects at Wave 3. Males reported higher ST use than females (p = 0.003). Obese youth reported higher ST use than overweight, normal weight, or underweight youths (p = 0.002). Ever-users of ST reported higher levels of anxiety (p < 0.001), lower subjective social status than never users (p < 0.005), and higher levels of social disinhibition than never users (p < 0.001). Five single nucleotide polymorphisms that increased the risk for lifetime use were identified, specifically, rs2023902 on SERGEF, rs16941667 on ALDH2, and rs17721739 on tryptophan hydroxylase 1 in the dopamine pathway, rs514912 on TRH-DE in the serotonin pathway, and rs42451417 on the serotonin transporter gene, SLC6A4. After controlling for genetic risk, being male (OR = 1.86, 95% CI: 1.02, 3.41), obesity status (OR = 2.22, 95% CI: 1.21, 4.09), and both higher levels of anxiety (OR = 1.04, 95% CI: 1.01-1.08) and social disinhibition (OR = 1.26, 95% CI: 1.07, 1.48) were associated with increased use. High subjective social status (OR = 0.78, 95% CI: 0.64, 0.93) was negatively associated with ST use, while higher parental education (OR = 2.01, 95% CI: 1.03, 3.93) was positively associated with ST use.	Strengths: (1) Sample represented an ethnically homogeneous population that is largely understudied and underserved; and (2) the study used personal digital assistant to ensure that subjects responded to the questions without concern for their parents hearing or seeing their responses. Limitations: (1) There was a lack of independent replication sample; (2) subjects were all of Mexican origin; (3) there was a small number of subjects who reported lifetime ST use; and (4) the study relied on self-report.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Fu et al., 2014)	Psychiatric correlates of snuff and chewing tobacco use	Data are from NESARC Wave 1 study (cross-sectional study). Subjects (n = 43,093) were noninstitutionalized civilians aged 18 years and older selected from U.S. population. Objective: To examine differences between lifetime ST users and nonusers of ST in relation to psychiatric disorders; and to delineate exclusive snuff use or exclusive chewing tobacco from dual use with respect to psychiatric disorders.	Data collected in 2001 and 2002 were assessed for ST use and sociodemographic variables that include age, sex, race/ethnicity, marital status, household income, educational attainment, metropolitan area, regions, and birth in the U.S. Psychiatric diagnoses were made using the Alcohol Use Disorder and Associated Disabilities Interview Schedule (Fourth Edition).	ST use was significantly more common in Caucasians, men, people aged 18 to 34 years old, those born in the U.S., and residents of suburban and rural areas. ST use were less common among African Americans and Hispanics. Smaller proportions of exclusive chewing tobacco users and chewing tobacco and snuff dual users were aged 50 years or older than were non-ST users. Exclusive chewing tobacco was more common in subjects who were married, but less common in those who were never married, than it was in non-ST users. Those who were divorced, separated, widowed, or with household incomes <\$20,000 were less likely to use only snuff or to use both snuff and chewing tobacco. High school graduates were more likely to use any ST products, but subjects with greater than a college education were less likely to use snuff and chewing tobacco or use only chewing tobacco. The following were associated with snuff use, chewing tobacco use, or dual use of snuff and chewing tobacco: being antisocial; used alcohol, nicotine, cannabis, amphetamine, opiates, sedatives, cocaine, hallucinogens; and smoked cigarettes Use of tranquilizers, inhalant/solvents, or heroin was associated with chewing tobacco use and dual use of snuff and chewing tobacco. AORs of alcohol use were 1.97 for snuff use, 2.01 for chewing tobacco use, and 2.99 for snuff and chewing tobacco use. Snuff use was significantly ($p < 0.05$) associated with schizoid and alcohol use, whereas chewing tobacco use was significantly ($p < 0.05$) associated with panic disorder, specific phobia, being antisocial, alcohol use, and inhalant/solvent use.	Strengths (1) This study used a large sample population; and (2) nationally representative study. Limitations: (1) This was a cross-sectional study; (2) lifetime diagnoses of psychiatric disorders and lifetime ST use used in this study may obscure some true relationships between ST use and psychiatric disorders; (3) the findings were not generalizable to adolescents; (4) the study could not examine the subtypes of ST use in relation to heroin use disorder; and (5) data were from 2001-2002 survey.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Pickworth et al., 2014)	Nicotine absorption from smokeless tobacco modified to adjust pH	Double-blind, within-subject design with seven male subjects (mean age: 45 years; range: 28-62 years; 57% Caucasian). Sessions (3) separated by at least 24 hours, during which ST product was used by mouth in one of the following randomized conditions: (1) ST with altered low pH (5.4) and wintergreen flavoring; (2) ST with altered high pH (8.3) and wintergreen flavoring; (3) ST with unaltered pH (7.7) and no wintergreen flavoring (referent). Objective: To measure nicotine absorption after experimentally manipulating pH and flavorings of a single referent product.	Dependent measures include plasma nicotine, cardiovascular measures (heart rate and blood pressure), whereas subjective measures include nicotine dependence, tobacco use history, subjective strength of the product, and product experience.	Subjects were 100% male, consisted of 4 whites and 3 African Americans, and had an average age of 45 years. Subjects were regular ST users (for an average of 15 [17] years), and the number of tins used per day was 1.1 (0.7). About 43% of subjects were also cigarette smokers.	Limitation: The study used a small sample size.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Spangler et al., 2014)	Correlates of smokeless tobacco use among first year college students	Data are the first year of an ongoing longitudinal study. Subjects (n = 10,520, 92.5% were 18 years old, 63% female, 90% never used ST, 7% reported ST ever use, and 3% reported ST past-30-day use) were first-year students at 11 colleges and universities in North Carolina and Virginia in fall of 2010. Objective: To assess trajectories and correlates of ST use in a cohort of college students by surveying them each semester, beginning in their freshmen year and continuing through the fall of their senior year.	Data were from survey of a cohort of freshman in fall of 2010. Subjects provided information regarding type of tobacco product use, frequency of ST use, use of alcoholic energy drink, physical activity, and hours of sleep.	Among subjects, 7.2% of men and 0.6% of women had used ST in the past 30 days ($p < 0.001$). Being a man greatly increased the risk of past-30-day ST use (AOR = 11.6, 95% CI: 8.16, 16.59). Current cigarette smokers were over five times more likely to have used ST during the past 30 days (AOR = 5.5, 95% CI: 4.21, 7.1). Students who had ever used alcoholic energy drinks were nearly five times more likely to be past-30-day ST users (AOR = 4.8, 95% CI: 3.62, 6.43). Also, students who participated in five or more days per week of physical activity were 1.5 times more likely to have used ST during the past 30 days (AOR = 1.5, 95% CI: 1.07, 2.01). There were no associations between ST use and age, hours of sleep, or school size.	Strength: The study used a large sample population. Limitations: (1) There was a low response rate; (2) the study excluded colleges that likely had low prevalence of tobacco use; (3) lower rate of tobacco use in these colleges compared with the NSDUH; (4) the study was based only on two states; and (5) this was a cross-sectional study.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to Patterns of Use	Comments ^a
(Berg et al., 2012)	Correlates of NNAL levels among nondaily and daily smokers in the college student population	Objective: To examine correlates of urine NNAL levels among nondaily and daily smokers. This was a cross-sectional study. Subjects (n = 62, mean age: 26.3 years, 40.3% male, and 72.6% non-Hispanic white) were college students from three colleges in the southeastern U.S. who were nondaily (n = 35) or daily (n = 27) cigarette smokers.	Sociodemographic information, and smoking related and other tobacco use information were collected by questionnaire. Urine NNAL levels were assessed by LCMS.	Eight (12.5%) of the 62 subjects concurrently used ST products (n = 7 nondaily smokers and n = 1 daily smoker). Among the ST users, the mean number of days ST was used in the prior 30 days was 8.4 days.	Limitation: Small sample size.

7.5.2-2.6. The Abuse Liability and the Potential for Misuse of the Product as Compared with Other Tobacco Products on the Market

The four noteworthy articles found in this literature review that inform the abuse liability and potential for misuse of the candidate product are highlighted below, and all five articles are summarized in [Table 7.5.2-2-5](#).

7.5.2-2.6.1. Nicotine Pharmacokinetic Data

To evaluate the effect of pH on nicotine pharmacokinetics, Pickworth et al. ([Pickworth et al., 2014](#)) compared nicotine absorption of a single unflavored referent ST product (pH 7.7) and two additional formulations that were flavored with wintergreen and had the pH amended to either high (8.3) or low (5.4) pH with sodium carbonate or citric acid, respectively. Seven male ST users were exposed to each of the three conditions (pH 5.4, 7.7, or 8.3) for 30 minutes over three study visits. After product exposure, blood samples were collected to assess serum nicotine concentrations. In all three conditions, peak plasma nicotine levels occurred between 20 and 35 minutes from the initial time in which the product was placed into the participant's mouth. After adjusting for baseline nicotine concentrations, the maximal average was higher in the altered high pH condition (mean = 20.0 ng/mL; SD = 4.2 ng/mL) compared with the unaltered medium pH condition (mean = 19.5 ng/mL; SD = 6.5 ng/mL), and altered low pH condition (mean = 6.6 ng/mL; SD = 3.9 ng/mL).

7.5.2-2.6.2. Smokeless Tobacco Dependence

Strong et al. ([Strong et al., 2015](#)) examined past-year symptoms of nicotine dependence in a large U.S. longitudinal study cohort in two study waves: Wave 1 (n = 43,093) conducted in 2001–2002, and Wave 2 (n = 34,653) conducted in 2004–2005. The 22 symptoms assessed in the study were organized into groups reflecting specific Diagnostic and Statistical Mental Disorders (Fourth Edition) criteria or similar content. Tobacco users identified in Wave 1 were assigned to one of four mutually exclusive tobacco user groups: cigarette-only users (n = 9305), cigarette and cigar users (n = 581), cigar-only users (n = 538), and ST users with or without other forms of tobacco (n = 615). Wave 2 included 8,289 tobacco users of whom 356 were successful quitters. Nicotine dependence scores were higher in cigarette and cigar users (0.14) and cigarette-only users (0.06) compared with ST users (−0.36) and cigar only users (−0.85), where higher scores may either reflect real differences in levels of nicotine dependence or the higher likelihood of reporting particular dependence symptoms. Consistent with these findings, cigar-only users and ST users had significantly higher odds of quitting at Wave 2 than exclusive cigarette users.

7.5.2-2.6.3. Subjective Effects Associated with Smokeless Tobacco Use

Consumer acceptability of five ST products was assessed by Buzzell et al. ([Buzzell et al., 2016](#)) using an electroencephalographic (EEG) approach in combination with traditional subjective measures. Thirty male ST users (five current cigarette smokers [smoking four or less cigarettes per day], 21 previous cigarette smokers, and four never-smokers), ranging from 19 to 61 years in age were exposed to one of four ST products (Camel Snus, Verve®

chewable disc, Skoal® snuff, Ariva dissolvable tablet) or a Nicorette nicotine lozenge as a control over five study visits. At each study visit, subjects completed questionnaires that subjectively assessed smoking urges (before and after product use) and evaluated the product (after product use). A resting-state EEG recording was taken prior and after product use to assess cortical arousal. Subjects were exposed to the product for 30 minutes, and an EEG recording was taken every 6 minutes.

Subjective product analysis following use showed an effect of product type. Paired comparisons revealed that Skoal was rated statistically significantly higher in psychological reward than Verve, and that Skoal was rated statistically significantly higher in aversion than Ariva. Analyses of EEG measures, particularly the alpha suppression measure, revealed robust differences between products. Skoal elicited significantly enhanced alpha suppression indicating increased attention and arousal compared with all four other products tested, which correlated positively with subjective measures of satisfaction and psychological reward, but was unrelated to perceived aversion.

Krautter et al. ([Krautter, Chen, & Borgerding, 2015](#)) conducted a randomized, controlled, open-label, parallel group study to evaluate changes in tobacco product use behavior and levels of selected biomarkers of exposure in smokers who switched to one of six conditions (Camel Snus, Sticks, Strips or Orbs, controlled dual use of cigarettes and Camel snus, or tobacco abstinence). Healthy U.S. male and female smokers (n = 167), ranging from 21 to 65 years in age, were randomized to the six groups (n = 25–30/group). Subjects smoked their usual brand of cigarette for 1 day before switching to their designated intervention condition. Subjects completed questionnaires to subjectively rate nicotine dependence and withdrawal discomfort at baseline and on Days 1, 3, and 5 of product exposure. At baseline, questionnaire scores were not significantly different between treatment groups, except for the lowest Orbs and highest Strips groups. After product exposure (Day 5), scores were lowest (indicating less withdrawal discomfort) for the dual use group and highest (indicating greater withdrawal discomfort) for the abstinent group.

Pickworth et al. ([Pickworth et al., 2014](#)), in the study described in Section 7.5.2-2.6.1, showed that there was no significant difference in subjective strength of a product when the pH was altered, as measured by questionnaires completed after 30 minutes of product exposure. Similarly, subjective product experience was not different between the three pH conditions.

7.5.2-2.6.4. Updated Findings

Information in the updated literature review on the abuse liability and the potential for misuse of the candidate product as compared with those for other tobacco products on the market is consistent with that seen in the initial literature review. Although the conclusions from the initial literature review (Section 7.5.2-1.6.9) have not changed, the updated literature review did add additional information. Pickworth et al ([Pickworth et al., 2014](#)) showed that, while the pH of a ST product does not alter subjective measures of product strength or experience, it does influence nicotine absorption and, therefore, has the potential to alter abuse liability.

A tabular summary of the literature informing the abuse liability of ST is presented in [Table 7.5.2-2-5](#).

Table 7.5.2-2-5: Literature Summary for Abuse Liability of Smokeless Tobacco Products

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to ST Abuse Liability	Comments ^a
(Buzzell et al., 2016)	Using electrophysiologic al measures to assess the consumer acceptability of smokeless tobacco products	A methods development study that tested the use of EEG, in combination with traditional subjective measures, as an objective method to assess consumer acceptability (liking) of five products. During five visits, subjects (30 male ST users 19 to 61 years of age [mean 22.2 years] with a mean mFTND score of 1.27) were exposed to one of four ST products (Verve discs, Ariva dissolvables, Skoal snuff, Camel snus) or Nicorette lozenges. Objective: To objectively characterize cognitive changes associated with tobacco product use by focusing on EEG measures of attention/arousal.	Subjects completed subjective scales (mFTND, mCES mQSU-brief), and EEG was performed (n = 23) while subjects completed attention-based tasks. EEG study endpoints were N2, P3b, and alpha suppression before and after use of ST products.	<p>Analysis of the mQSU-brief yielded no significant product type effect for either the “relief from withdrawal” (p = 0.514) or “intention to use ST” (p = 0.138) factors.</p> <p>Analysis of the mCES “satisfaction” factor revealed a product type effect (p = 0.018); however, none of the follow-up comparisons remained significant after multiple comparisons correction.</p> <p>Analysis of the mCES “psychological reward” factor revealed a product type effect. Paired comparisons revealed that Skoal was rated higher in psychological reward than Verve (corrected p = 0.023).</p> <p>Analysis of the mCES “aversion” factor revealed a main effect of product type. Paired comparisons revealed that Skoal was rated higher in aversion than Ariva (corrected p = 0.003), Snus (corrected p = 0.0002), Verve (corrected p = 0.002), and Nicorette (corrected p = 0.0001).</p> <p>Analysis of EEG global alpha difference scores revealed a significant product type effect. Follow-up paired comparisons revealed that Skoal exhibited enhanced alpha suppression relative to Ariva (corrected p = 0.001), Snus (corrected p = 0.007), Verve (corrected p = 0.001), and Nicorette (corrected p = 0.001). Additionally, Snus exhibited enhanced alpha suppression relative to Ariva (corrected p = 0.014).</p>	Limitation: Small sample size, only five ST products tested, females were excluded.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to ST Abuse Liability	Comments ^a
(Ebbert et al., 2016)	Nicotine metabolite ratio is associated with lozenge use but not quitting in ST users	ST users (n = 152) were 18-65 years old (mean 36.5 years), 97% male, and 96% white/non-Hispanic. They had a mean Severson ST Dependency Scale score of 11.6 (4.0) with a range of 1-19. ST users enrolled in one arm of a large randomized trial were included in this secondary analysis. Subjects received quitting support materials and lozenges plus three coaching phone calls. Objective: To evaluate whether NMR (higher NMR corresponds to faster nicotine clearance) correlates with nicotine lozenge use and tobacco abstinence.	Severson ST Dependency Scale, self-reported lozenge use, and NMR were assessed.	The level of tobacco dependence did not differ between fast and slow metabolizers. “Fast metabolizers may need to self-administer more nicotine replacement in the form of nicotine lozenges to achieve the same clinical response achieved by slower metabolizers using fewer lozenges.”	Limitation: The authors did not ask the subjects to record the timing of the last tobacco use before sample collection, which could lead to unknown intrinsic variability in the NMRs. The study had a small sample size and, therefore, has low generalizability.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to ST Abuse Liability	Comments ^a
(Krautter et al., 2015)	Consumption patterns and biomarkers of exposure in cigarette smokers switched to Snus, various dissolvable tobacco products, dual use, or tobacco abstinence	Randomized, controlled, open-label, parallel group study, in which subjects (aged 21-64 years [mean = 40.6 years], 53.9% male, 94.6% not Hispanic or Latino) who successfully completed the trial were included in the statistical analysis, n = 167 (n = 25-30 per group). Objective: To characterize tobacco product use patterns and subjective responses, estimate daily mouth-level exposure to 'tar' and/or nicotine, and to quantify levels of select biomarkers of tobacco or tobacco smoke exposure (32 biomarkers) after smokers are switched for a 5-day period to one of 6 groups: exclusive use of Camel Snus, sticks, strips, or orbs, dual use of cigarettes and snus (dual use), or smoking/tobacco abstinence.	Daily smoking behavior measures of cigarettes per day, 'tar' and nicotine mouth-level exposures, butt lengths, and daily test product usage rates were collected at baseline and during study days for applicable groups.	<p>When baseline total nicotine equivalents in urine on Day 5 were compared with baseline, every group had a significant decrease. The abstinent group had a significantly greater percent decrease (-97.6%) than all other groups, including dual use (-31.8%) and snus (-47.6%) groups. While the percent decrease in total nicotine equivalents in the snus group was greater than in the dual use group, the difference was not significant.</p> <p>"Results demonstrate that when active smokers switch to exclusive use of Snus, Sticks, Strips, or Orbs, after 5 days their biomarkers of exposure to toxicants in cigarette smoke were substantially and significantly reduced, usually comparable in magnitude to being tobacco abstinent. Similarly, when smoking rates are reduced by 60% in Dual users, significant but less robust toxicant reductions are still evident."</p> <p>The abstinent group had a significantly higher score in the self-reported 15-Item-MNWS-R questionnaire than the dual-use and snus groups, indicating heightened withdrawal discomfort.</p>	<p>Strength: The study included use of a controlled diet low in potentially confounding biomarkers, and there is good compliance inherent in a confinement trial.</p> <p>Limitations: Limited sample size, short intervention period.</p> <p>Mandated 60% reduction in cigarettes per day (from baseline) in the dual use group during intervention may or may not accurately reflect the way subjects actually dual use.</p>

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to ST Abuse Liability	Comments ^a
(Strong et al., 2015)	Measurement of multiple nicotine dependence domains among cigarette, non-cigarette and poly-tobacco users: insights from item response theory	Organized the 22 ND symptoms assessed by the NESARC AUDADIS into groups that either reflected specific DSM-IV criteria or had similar content. Examined past-year symptoms of ND in NESARC data from two United States waves. Wave 1 (n = 43,093; 43.0% male, 80.7% non-Hispanic/Latino; aged 18+ years; n = 615 ST users [1.4%]) conducted 2001-2002. Wave 2 (n = 34,653; aged 18+ years; n = 513 ST users) conducted 2004-2005 with 21.4% and 18.3% of males and females, respectively, missing from Wave 1. Objective: To establish a set of symptoms that efficiently and effectively measures ND across users of different tobacco products.	Primary endpoint was a report of no tobacco use in 12 months before the Wave 2 interview.	Cigar-only users (OR = 4.85; 95% CI: 3.93, 5.99; p < 0.01) and ST users (OR = 1.72; 95% CI: 1.39, 2.12; p < 0.01) had significantly higher odds of quitting at Wave 2 than exclusive cigarette users (reference group).	Strengths: The study (1) was longitudinal; (2) had very large sample cohort; (3) compared multiple tobacco types; and (4) compared and combined DSM-IV criteria with NESARC AUDADIS criteria for ND. Limitations: The study (1) used small sample sizes for analysis of groups other than smokers, (2) did not have a biological marker of nicotine exposure that could be linked to levels of reported tobacco use, and (3) was limited by the poor representation of symptoms at the lower range of the ND continuum. (4) The available symptoms may best measure ND among established tobacco users and may not be sensitive to early progression to regular tobacco use or escalating use patterns.

Author	Title	Study Methods	Primary Study Measurements and Endpoints	Author's Findings Related to ST Abuse Liability	Comments ^a
(Pickworth et al., 2014)	Nicotine absorption from ST modified to adjust pH	Double-blind, within-subject design with seven male subjects (mean age: 45 years; range: 28-62 years; 57% Caucasian). Sessions (3) separated by at least 24 hours, during which ST product was used by mouth in one of the following randomized conditions: (1) ST with altered low pH (5.4) and wintergreen flavoring; (2) ST with altered high pH (8.3) and wintergreen flavoring; (3) ST with unaltered pH (7.7) and no wintergreen flavoring (referent). Objective: To measure differences in nicotine absorption in ST products after pH and ST flavoring changes.	ST ND using FTND-ST and tobacco use history were collected. Subjective strength of the product was measured using visual analog scale, and total nicotine absorption and speed of nicotine absorption were assessed.	At baseline, the ST users had a mean FTND-ST score of 4.3 (1.6), which indicates moderate dependency on nicotine. The referent product and the high pH flavored product delivered significantly more nicotine than the low pH flavored product. “The addition of the small amount of wintergreen flavoring did not seem to increase nicotine absorption – comparing the high pH flavored product with the unflavored referent product.”	Strength: Well-controlled use of a single tobacco product, which mitigates inherent differences in nicotine content present in different ST products Limitation: Small sample size, males only. Hard to generalize to a large population.

7.5.2-2.7.Literature Cited

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