

Cancer incidence among a cohort of smokeless tobacco users (United States)

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Abstract

Objective: Smokeless tobacco (ST) use remains a prevalent form of tobacco use among certain US populations. The purpose of this paper is to clarify its role in cancer development.

Methods: Using data from a prospective cohort of the US population, we categorized 6779 subjects 45–75 years of age as ST users or non-ST users. Subjects were further stratified by cigarette smoking status in order to differentiate ‘exclusive’ ST users (n = 414) from never tobacco users (n = 2979).

Results: In this cohort, exclusive ST use was not associated with increased incidence of all cancer in males (hazard ratio = 0.8, 95% CI: 0.4, 1.6) or females (HR = 1.2, 95% CI: 0.7–2.1) or oral cancer (standardized incidence ratio = 30, 95% CI: 3, 95). No synergistic effect was observed between ST and cigarette smoking among male combined users (females were not analyzed for combined use) for the major cancers.

Conclusions: In contrast to the well-known deleterious effects of cigarette smoking, ST use did not substantially increase the risk for cancer incidence above that of non-tobacco users, particularly among males. Although the use of tobacco in any form is to be discouraged, our data suggests that cancer risks are much lower from ST use than from cigarette smoking.

Introduction

Tobacco use remains prevalent in the United States, yet the literature focused on smokeless tobacco (ST) use and cancer is rather limited, especially when compared to the cigarette smoking literature. The role of ST use in cancer development has yet to be clearly defined. Several national reports have concluded that ST use is associated with increased disease risk [1, 2]. In 1986, the American Medical Association pointed out that, though evidence of an association between ST use and adverse health effects was increasing, few studies demonstrated the link [1]. The International Agency for Research on Cancer recently concluded that there is ‘sufficient evidence’ that the oral use of ST is carcinogenic to humans [3]. How-

ever, when reviewing studies of ST and specific cancers, it is difficult to reach definitive conclusions.

Several studies have found that ST use can increase the risk of oral cancer [4–6], although a recent review states that the increased risk for oral cancer among ST users is minimal [7]. Other cancers for which at least one epidemiologic study has found an increased risk of morbidity or mortality among ST users include stomach [8], rectal [9], prostate [10], breast [11], and pancreatic cancers [12]. However, results from these studies have not been verified by other epidemiologic studies, and in fact, the breast cancer study was later retracted [13]. Cancers for which epidemiologic evidence suggests there is no association with ST use include esophagus [14, 15], bladder [16, 17], and colon [9] cancers.

The prevalence of ST use is increasing among young adult white males [18, 19]. ST use has also been proposed by some as a nicotine replacement therapy for cigarette smokers [20]. For these reasons, it is now more

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important than ever to fully understand the contribution of ST use to cancer incidence. This is the first study of which we are aware to describe and quantify the health effects of ST use for cancer incidence among a representative adult US population. This paper serves to further this understanding by presenting the incidence of cancer among a cohort of ST users who were followed for approximately 20 years.

Materials and methods

The National Health and Nutrition Examination Survey (NHANES I) assessed ST use and exposure to other known and suspected cancer risk factors between 1971 and 1975 [21, 22]. Information on cancer incidence, including self-reports, health care facility (HCF) records, and death certificates, was obtained from the NHANES I Epidemiologic Followup Study (NHEFS) conducted in 1982–1984, 1986, 1987 and 1992. The design of the NHEFS offers the opportunity to assess the association between ST use and cancer incidence over an extended follow-up period. Detailed descriptions of the NHEFS have been published elsewhere [23–26].

NHANES I assessed ST use among a sub-sample of 3847 subjects, using questions concerning their current use of either snuff or chewing tobacco. The entire NHANES I cohort was reassessed in the 1982–1984 survey, when all successfully traced subjects or their proxies ($n = 12,220$) were asked questions concerning the 'ever use' of snuff or chewing tobacco. In our study, 'ever use' was defined as reported use of ST (snuff or chewing tobacco) in either of these surveys. Of the 14,407 subjects 25–75 years of age in this cohort, 12,451 (86%) provided information on ST use.

Most of our analyses compare those participants reporting the use of ST as their sole tobacco exposure ('exclusive' ST) to those participants who reported no tobacco exposure. 'Combined use' was defined as use of both ST and cigarettes, though these behaviors did not necessarily occur concomitantly. Non-tobacco use was defined as never use of ST and smoking fewer than 100 cigarettes. Pipe and cigar use was not accounted for in this analysis.

Incident cases of cancer were identified from the four follow-up assessments. During each follow-up interview, subjects or their proxies were asked about disease conditions that had developed since the prior interview. For each reported cancer case requiring an overnight HCF stay, an attempt was made to obtain a medical records abstract from the appropriate facility. For some reported conditions, no HCF record was retrieved (subject did not grant permission, hospital had closed, or record

was otherwise unavailable), and the self-report could not be validated. For some subjects, diagnoses were found during the abstract review process for cancers that the subject did not report during the interview. These additional cancers were counted as cases, because they were confirmed by a medical record. For deceased subjects, any cancer listed as an underlying or contributing cause-of-death from the death certificate was considered a confirmed diagnosis. All analyses considered only those conditions for which a HCF record or death certificate with an ICD-9 code was available in the data set.

A small group of non-white and non-black subjects ($n = 172$) were excluded from all analyses, because their numbers were too small to permit precise cancer risk estimates. Additionally, 527 participants who were not traced in any of the four follow-up periods were excluded. Also, because the cancers of interest were unlikely to occur in young subjects, our analyses were restricted to the remaining 7787 subjects ≥ 45 years of age at baseline, of whom 6779 (87%) furnished information on both ST use and cigarette smoking.

Distributions of potential confounding variables were calculated across categories of ST and cigarette use. The Cox proportional hazards model was used to estimate both the crude and adjusted hazard ratios (HR). Follow-up time was measured from the date of baseline examination to the date of diagnosis of the condition of interest (date of hospital admission or date of death) for cases and to the date of last contact or the date of death from another condition for non-cases.

Because we were interested in only incident cancers, all subjects with a pre-existing cancer (as determined from the NHANES I interview) were excluded when estimating the HR for that particular cancer. Our analyses required a definitive diagnosis of each incident case, and all incident events with 'questionable' diagnostic status (i.e., those coded as probable, possible, suspected, question of, suggestive of, compatible with, questionable, and history of) and 'recurrent' malignancy codes were not considered incident cases.

In order to account for the complex survey design and the oversampling of certain populations used in NHANES I [21], we used SUDAAN to conduct the majority of analyses. SUDAAN is a software package specifically designed to analyze data from complex sample surveys that incorporate multi-stage sampling and unequally weighted designs [27].

The HR for oral cancer associated with exclusive ST use was 0.0 because there were no observed cases among exclusive ST users. Because of this, we estimated standardized incidence ratios (SIR) to compare the observed number of oral cancer cases to the number of oral

cancer cases that would have been expected in the general US population based on the size of the cohort and duration of follow-up. The SIR is the ratio of the number of observed cases to the number of expected cases (times 100) based on a referent population. In this analysis, expected numbers were based on incidence rates from Surveillance, Epidemiology, and End Results statistics for 1982 [28], the approximate midpoint of the follow-up period.

Results

Table 1 displays several demographic variables categorized by ST use and smoking. Exclusive ST users were older than subjects in the other tobacco use categories. The ratio of white to black subjects was smallest among exclusive ST users compared to the other three groups. Nearly half of the exclusive ST users were females, 60% of them being black females. Exclusive ST users were poorer than other subjects (lower poverty index ratio) and more likely to reside in the south.

Exclusive male ST users drank more often than non-tobacco users but less often than smokers

(Table 2). Exclusive female ST users drank less and exercised less than non-ST users (smokers and non-smokers). All ST users ate fewer fruits and vegetables than non-ST users. ST users had higher systolic blood pressures and lower blood cholesterol levels than did non-ST users.

We found no statistically significant increases in cancer risk for male exclusive ST users compared to non-tobacco users (Table 3). A non-significant increase was found for all digestive cancer (HR = 1.5, 95% CI: 0.6, 3.6) among exclusive male ST users 65 years of age and older (Table 3).

Among females, we found a significantly increased risk of lung cancer among exclusive ST users (HR = 6.8, 95% CI: 1.6, 28.5) (Table 4). This finding was restricted to females 65 years of age and older (HR = 9.6, 95% CI: 1.8, 51.2). We also found a modest, though non-significant increase among all females for breast cancer (HR = 1.8, 95% CI: 0.5, 6.5).

Analyses investigating the combined use of ST and cigarettes were limited to males because of the small number of female combined users ($n = 62$). As shown in Table 5, higher rates of lung cancer (HR = 22.3, 95% CI: 7.5, 66.3) were observed among combined users of

Table 1. Demographic profile of subjects according to ST use and cigarette smoking

	ST users				Non-ST users			
	Non-smokers		Smokers		Non-smokers		Smokers	
	No.	%	No.	%	No.	%	No.	%
Total	414	100.0	653	100.0	2979	100.0	2733	100.0
Age								
45–54	52	26.8	179	40.7	729	36.0	1067	50.1
55–64	77	34.7	172	39.9	671	35.7	716	35.5
65+	285	38.5	302	19.4	1579	28.4	950	14.4
Race								
White	248	66.6	550	90.7	2623	92.0	2434	93.1
Black	166	33.5	103	9.3	356	8.0	299	6.9
Sex								
Male	225	56.0	591	92.7	719	24.1	1583	55.8
Female	189	44.0	62	7.3	2260	75.9	1150	44.2
PIR ^a								
< 1.0	153	35.3	122	20.5	412	12.1	246	7.3
1.0–2.0	111	31.7	153	24.3	714	26.5	458	20.7
> 2.0	78	32.9	221	55.2	1158	61.4	1170	72.0
Residences								
Northeast	42	11.5	91	13.8	674	26.8	655	25.3
Midwest	60	17.7	135	23.3	758	26.8	656	24.7
South	239	50.9	265	38.7	755	21.7	668	23.1
West	73	19.9	162	24.2	792	24.8	754	27.0

^a Poverty index ratio.

Table 2. Distribution of potential confounders stratified by tobacco status and gender

	Males				Females											
	ST users		Non-ST users		ST users		Non-ST users									
	Non-smokers	Smokers	Non-smokers	Smokers	Non-smokers	Smokers	Non-smokers	Smokers								
	No.	%	No.	%	No.	%	No.	%								
Alcohol frequency																
None	80	25.8	167	25.1	263	29.6	331	25.1	138	63.5	26	37.9	1187	45.4	282	22.3
Less than 12 times/year	28	17.3	92	14.9	147	21.1	254	14.7	26	19.5	21	37.8	544	26.7	312	26.9
About 13–48 times/year	55	23.4	123	20.5	129	21.2	368	23.6	17	14.5	9	16.4	300	14.7	265	23.1
At least 104–156 times/year	62	33.5	207	39.5	177	28.1	628	45.1	6	2.5	4	7.9	228	13.3	287	27.7
Fruit and vegetable intake																
None or < 1 serving/day	45	25.6	73	15.5	76	8.5	168	9.1	43	31.4	10	15.0	125	4.9	72	7.4
1 or 1.5 servings/day	62	24.7	174	35.5	144	26.3	349	29.1	61	32.5	19	38.8	439	24.1	218	26.0
2 or 2.5 servings/day	59	37.4	139	31.7	216	35.8	434	42.7	39	23.6	17	37.7	697	39.9	300	39.8
≥3 servings/day	17	12.4	57	17.3	146	29.4	191	19.1	13	12.5	6	8.5	490	31.1	187	26.8
Recreational physical activity																
Little	113	37.3	242	39.8	277	36.3	637	38.9	122	65.0	38	64.2	1193	50.1	583	49.7
Moderate	74	38.4	222	40.6	293	40.1	627	39.4	53	27.5	14	18.1	792	36.9	418	37.7
Much	38	24.3	126	19.6	148	23.6	318	21.6	13	7.5	10	17.8	275	13.0	149	12.6
Pack-years of smoking ^a				44.2				43.3				24.6				26.7
Blood cholesterol (mg/dl) ^a		223.1		226.0		227.7		230.1		235.8		237.1		240.9		241.5
Systolic blood pressure (mmHg) ^a		145.7		138.2		139.6		137.7		150.6		152.7		143.2		135.4
Body mass index (kg/m ²) ^a		26.6		25.5		27.0		25.7		28.6		28.6		26.7		25.3
Vitamin A intake (IU) ^a		6466.9		4470.9		6082.2		5498.2		3682.7		3306.0		5574.2		5783.4
Vitamin C intake (mg) ^a		83.7		80.5		103.2		88.5		66.9		40.9		91.5		88.4
Dietary fat intake (g) ^a		90.7		85.8		81.6		91.2		49.7		71.0		56.1		59.6

^a Mean.

Table 3. HR for exclusive ST users relative to non-tobacco users for selected diseases: males stratified by age

	Observed cases ^a	45–64 years			> 65 years			Overall					
		Crude HR	95% CI	Adjusted HR ^b	95% CI	Crude HR	95% CI	Adjusted HR ^b	95% CI	Crude HR	95% CI	Adjusted HR ^c	95% CI
Lung cancer	0	0.0	0/1	0.0	0/1	0.0	0/9	0.0	0/7	0.0	0/10	0.0	0/8
Digestive cancer ^d	13	0.4	0.1–1.5	0.4	0.1–2.0	1.5	0.6–3.5	1.5	0.6–3.6	0.8	0.4–1.8	0.8	0.4–1.8
Prostate cancer	19	1.0	0.2–4.1	1.2	0.2–5.6	1.2	0.6–2.6	1.3	0.6–3.1	1.1	0.5–2.9	1.2	0.5–3.4
All cancer	38	0.7	0.3–1.8	0.8	0.3–2.4	1.0	0.6–1.5	1.0	0.6–1.6	0.8	0.5–1.5	0.8	0.4–1.6

^a Among the exclusive ST users.^b Adjusted for race and PIR.^c Adjusted for age, race, and PIR.^d Includes esophagus, stomach, small intestine, colon, rectum, liver, gall bladder, and pancreas.

ST and cigarettes than would have been expected based on the rates for exclusive ST use and for exclusive cigarette smoking. Rates for all cancers and lung cancer were increased among male cigarette smokers when compared with non-tobacco users. Males who used only ST had no increased risk for these outcomes when compared to non-users.

We observed no cases of oral cancer among exclusive ST users. Two cases were observed among white male

ever ST users who were also smokers (one a current smoker, the other a former smoker) (Table 6). The SIR for oral cancer among ever ST users was 30 (95% CI: 3, 95), and the SIR for oral cancer among ever smokers was 153 (95% CI: 100, 217). There were three cases among subjects <45 years of age. Inclusion of these subjects increased the SIR estimate, but the number of observed cases was still less than expected (SIR = 80, 95% CI: 25, 165).

Table 4. HR for exclusive ST users relative to non-tobacco users for selected diseases: females stratified by age

	Observed cases ^a	45–64 years				> 65 years				Overall			
		Crude HR	95% CI	Adjusted HR	95% CI	Crude HR	95% CI	Adjusted HR ^b	95% CI	Crude HR	95% CI	Adjusted HR ^c	95% CI
Lung cancer	4	1.6	0.2–15.4	1.2	0.1–17.2	12.0	2.5–57.2	9.6	1.8–51.2	7.5	2.0–28.2	6.8	1.6–28.5
Digestive cancer ^d	4	2.1	0.6–7.7	1.5	0.1–30.0	0.6	0.2–2.3	0.6	0.1–3.0	1.3	0.6–2.7	0.8	0.3–2.4
Breast cancer	5	0.3	0.0–3.1	1.9	0.2–22.7	0.9	0.3–3.0	1.6	0.4–6.8	0.6	0.2–2.0	1.8	0.5–6.5
All cancer	26	0.8	0.3–1.9	0.9	0.2–4.2	1.3	0.7–2.4	1.3	0.7–2.7	1.1	0.7–1.7	1.2	0.7–2.1

^a Among the exclusive ST users.

^b Adjusted for race and PIR.

^c Adjusted for age, race, and PIR.

^d Includes esophagus, stomach, small intestine, colon, rectum, liver, gall bladder, and pancreas.

Table 5. Adjusted HR^a for combined users for selected diseases: males

	Exclusive ST users		Exclusive smokers		Combined users	
	HR	95% CI	HR	95% CI	HR	95% CI
All cancer ^b	0.8	0.4–1.6	1.4	0.9–1.9	1.3	0.9–2.0
Lung cancer ^c	0.0	0/8	13.2	5.5–31.8	22.3	7.5–66.3

^a Each tobacco group is being compared to non-tobacco users.

^b Adjusted for age, race, PIR, exercise, fruit and vegetable intake, dietary fat intake, alcohol intake, and family history of cancer.

^c Adjusted for age, race, PIR, region of residence, exercise, fruit and vegetable intake, and alcohol intake.

Table 6. Oral cancer cases: description and SIR^a

	Total cases	Exclusive ST use ^b	Ever ST use	SIR for ever ST use	95% CI	Ever smoke ^c	SIR ^a for ever smoke	95% CI
Males	26	0	2	30	3–83	20	123	75–183
Females	11	0	0	0	0–410	6	160	58–315
Overall	37	0	2	30	3–95	26	153	100–217

^a Expected number based on 1982 SEER incidence rates for US adults 45–75 years of age. Indirectly adjusted only for age.

^b Five subjects with missing information on ST use.

^c Four subjects with missing information on smoking.

Discussion

Examining several cancer outcomes, we found no substantial increased risk among ST users compared to non-tobacco users. Male exclusive ST users were similar to non-tobacco users in cancer risk, whereas female exclusive ST users experienced a statistically significant increased risk only for lung cancer, compared to non-tobacco users. Among males, ST users experienced less cancer than cigarette smokers. Combined users experienced an increased risk for lung cancer but not for all cancers.

The overall cancer risk was not significantly greater among ST users than among non-tobacco users for either males or females. Although the number of incident events was small (providing low statistical power), the

results for oral cancer showed no increased risk for exclusive ST users. Several studies have found an increased risk for oral cancer among ST users [4–6, 15]. While the Winn *et al.* study [4] was able to control for cigarette smoking, it was conducted among a very select group of ST users, elderly females in the southern US, who used a particular type of ST product (snuff) that may be more harmful than what is commonly used throughout the US. The results of Blot *et al.* were significant only among female snuff users [6]. The increased risk found by Lewin *et al.* was found only among ever ST users [15]. When their analysis was restricted to never smokers, they found that oral snuff had no increased risk.

Results from studies showing no association [29–33] between ST use and oral cancer also have their

limitations. The study by Bouquot and Meckstroth was an ecologic study and therefore did not allow for the control of confounders [32]. Both the Young *et al.* paper and the Mashberg *et al.* paper suffered from a small sample of ST users [29, 31]. A recent review concluded that ST products increased the risk of oral cancer only minimally [7].

There are several possible explanations for the varying results found in these studies. First, ST products vary by country. Results from our study may not be comparable to results from studies conducted in other countries [15, 33] because the ST products in those countries differ from the products used in the United States. Swedish moist snuff is non-fermented, unlike the fermented product used in the United States. Swedish snuff undergoes a heat treatment that renders it practically free from microorganisms, lowering the risk of nitrate formation and subsequent formation of nitrosamines [33].

Second, oral cancer can be defined in multiple ways. In the present study, oral cancer was broadly defined (ICD-9 code 140–149), but we found no increase in cases for any specific site within the oral cavity. Third, ST is not a uniform product and the effects of different forms of ST may not be identical. A pooled analysis by Rodu *et al.* found a nearly six-fold increase in oral cancer risk associated with dry snuff use, but only a minimal association with chewing tobacco (RR = 1.2, 95% CI: 1.0, 1.4) and no association with moist snuff [7]. We had no information on whether the ST users used dry or moist snuff, and the small sample size prohibited us from analyzing chewing tobacco and snuff separately. Last, oral cancer is a relatively rare disease that is subject to unstable estimates of associations.

The small number of digestive cancer cases among exclusive ST users makes it difficult to derive precise risk estimates, but the absence of an association between ST use and digestive cancer in this study supports results from previous studies that found no association for colon cancer [9], gastric cancer [13, 34], or all digestive cancers [35]. One study reported a positive association between ST use and stomach cancer, but that result was based on only three cases [8]. Though Heineman *et al.* found no association with colon cancer, they found a positive association for rectal cancer [9]. This association did not exist among heavy users (defined as ‘regularly used practically every day’), suggesting some other factor contributed to the association.

We found no association between ST use and prostate cancer, though the power to detect differences was small. Although Hayes *et al.* found no association between prostate cancer and chewing tobacco use or former snuff use, they observed an increased risk among current snuff

users [10]. Again, that study was conducted in Sweden, which makes comparisons to the current study more difficult. We found a positive, but non-significant association between ST use and breast cancer. Spangler *et al.* found a minimal and statistically non-significant increase in a study of Native-American women, though there was no control for any confounders [11]. The original results of the Spangler analysis were retracted [13], so the results of their study must be discounted.

The association between ST use and lung cancer among female ST users 65 years of age and older was unexpected; however, it supports an earlier association we observed between ST use and lung cancer mortality among females [35]. Several factors, alone or in combination, may have contributed to this finding. First, this result is based on only three cases of lung cancer among exclusive ST users. All three subjects were elderly females from the south who used snuff. This finding may indicate some association with lung cancer attributed to a particular brand or type of ST product used by these subjects. This result may also be due to uncontrolled confounding, e.g., exposure to passive smoking. Last, this result could be due to misclassification of tobacco status among these elderly females.

Differences in study design, outcome, study size, and, in particular, nature of ST products may account for the variation in results observed between our study and other studies. The use of different ST products by males compared to females may explain the increased disease risks found in female subjects. Dry snuff was the ST product primarily used by women in the United States [36] particularly in the south where the majority of the female ST users in this study resided. This may have contributed to the increased HR we found. As noted by Rodu *et al.*, dry snuff was the only form of ST associated with an increase in oral cancer risk [7], though we found no increase in oral cancer in this population.

Among males, we found no increased risks when the results were stratified by age. Among females, the statistically significant associations were found among the older age group, suggesting duration of use may be a factor in disease onset. However, neither duration nor amount of ST use was available in the NHANES I data set.

The main limitation of this study is its reliance on self-reported ST use, smoking, and exposure to potential confounders. However, because this information was collected prospectively, the potential for recall bias is less than that found in case-control studies. Also, the positive associations found for smokers and lung cancer suggest validity of the self-reported exposure status.

An additional limitation was that ST use was asked of only a subset of the NHANES I participants at baseline,

requiring the categorization of ST exposure to be based on reported 'ever' use at either the baseline or the first follow-up visit (when the entire NHANES I population was asked about ST use). A potential for misclassification exists among subjects who reported no current use in NHANES I, but were lost to follow-up before the 1982–1984 NHEFS. These subjects were classified as non-ST users, but could have been ever ST users. However, we feel that this misclassification is minimal because the first follow-up was relatively complete (93% of NHANES I subjects were traced in the 1982–1984 NHEFS). The expected effect would be a bias toward the null hypothesis of no association. Similarly, inclusion of the subset of subjects without ST information at baseline may lead to a survival bias. However, we feel that this bias is minimal because the percentage of subjects who died between baseline and first follow-up is small (14%) and there is no reason to believe that ST users died differentially, STs relationship to the major causes of death such as CVD being weak or absent.

The results of this analysis are based on a cohort of 414 exclusive ST users. Even with approximately 20 years of follow-up, we found a small number of outcomes for several of the cancers studied. For example, the increased HR for lung cancer among elderly females was based on nine cases, three of which occurred among exclusive ST users. For this reason, estimation of the magnitude of associations between ST use and infrequent outcomes is not highly precise, and the power to detect associations for infrequent outcomes was relatively low. Future studies, especially among female ST users, are needed to verify these results.

This analysis was limited to incident diseases that required an overnight HCF stay. Medical record abstracts from HCF could be obtained only if subjects or their proxies self-reported any condition requiring an overnight stay. Therefore, this analysis may under-represent the actual number of cancer cases and may be considered a study of hospital-defined incidence, rather than a study of true disease incidence. We believe that this under-representation should be non-differential between ST users and non-ST users. Also, as cancer is likely to require a hospital stay, few cases were likely missed. Cases found incidentally when reviewing HCF abstracts, but not self-reported, were also included in the analysis. These outcomes were included because they were considered confirmed cases. However, because only records of individuals who reported another condition were reviewed, a bias would be introduced if one group of subjects self-reported conditions more frequently than the other did. This bias could explain some results if, for example, female ST users self-reported more conditions than did female non-ST users. However, our

analysis of the self-report data shows that female ST users did not self-report conditions that would require hospitalization (e.g., cancer, cardiovascular disease) at a higher rate than did non-ST users.

In conclusion, ST use was not associated with any increase in risk for oral cancer, the outcome most commonly associated with ST use, in this population. Male ST users experienced disease risks similar to those of non-tobacco users and less than those of smokers. Female ST users experienced some increased cancer risk compared to non-tobacco users, and these disease risks may be a result of a particular type of ST product by these cases who were predominantly from the south, were white, and were snuff users. Most previous studies have focused on male ST users making it difficult to compare our results to other studies. The differences in cancer risks between males and females suggest the use of different ST products by these individuals or different patterns of ST use (e.g., differences in intensity or duration).

It is important to fully understand the cancer risk associated with all forms of tobacco use, alone and in conjunction with each other. The existing literature on ST and cancer has focused mainly on oral cancer. The research on ST and cancers other than oral is very limited and inconclusive. This is the first analysis to follow a representative US cohort forward in time for the development of cancer outcomes. Though the sample of ST users was small, this research demonstrates that ST users may not experience the same cancer risk as users of other tobacco products. Of the five cancers studied, none was found to have a statistically significant positive association with ST use for both males and females.

Larger studies should be conducted in order to verify these results and to determine if ST use leads to the development of less common cancers that we were unable to study. Further studies should be conducted that are specific to particular types of ST products to determine if cancer risk differs by ST type.

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