

Table 2.5 Cross-sectional and case-control studies of smokeless tobacco and precancerous lesions of the oral cavity adjusting for tobacco smoking or among non-smokers

Reference, study location and period	Study population	Prevalence of use, type of tobacco product	Types of lesions	Exposure assessment	Exposure categories	Prevalence of exposure	Relative risk (95% CI)*	Adjustment for potential confounders and comments		
<i>United States</i>										
Ernster et al. (1990); Grady et al. (1990), Countrywide, 1988	1109 professional baseball players; any age, but 77% were 20–29 years of age; participation rate, 85%	Chewing tobacco/snuff: 42% current, 4% occasional, 13% former; among current users, 75% used snuff, 21% chewed tobacco	Oral leukoplakia /erythroplakia, diagnosed by clinical examination by specially trained dentist, graded 1–4 (categories similar to those of Greer & Poulson, 1983)	Participants completed a standardized questionnaire	Non-user	1.4	1.0	Adjustment for age, race, cigarette smoking, alcoholic beverage consumption and dental hygiene did not change results significantly; no chewing tobacco user had a degree 3 or 4 lesion; histology of lesions described in Daniels et al. (1992); 94% of lesions located in the mandibular area, including 42% in the anterior area		
					Former user	1.4	1.0 (0.2–5.0)			
					Occasional	2.5	1.8 (0.2–14.5)			
					Current	46.3	60.0 (27.8–129.5)			
					Chewing	17.2	14.5 (5.7–36.7)			
					Snuff	55.6	86.9 (39.9–189.5)			
					<i>Amount used</i>					
					<i>Snuff (can/week)</i>					
					< 1	36.4	39.8 (17.3–91.7)			
					2–3	69.2	156.2 (66.5–367.1)			
					> 4	83.6	354.1 (129.2–970.2)			
					<i>Chew (pouches/week)</i>					
					< 1	12.5	8.5 (3.0–32.9)			
2–3	16.7	12.3 (3.8–51.3)								
> 3	33.3	30.8 (9.4–128.3)								
<i>Duration of use (years)</i>										
≤ 3	32.4	33.2 (14.2–77.9)								
4–6	52.0	75.1 (33.4–169)								
7–9	52.7	77.4 (32.3–185)								
≤ 10	50.0	69.4 (29.4–164)								

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Ernster et al. (1990) (contd)					<i>Hours in mouth/day</i>				
					0–0.5	24.5			22.6 (9.5–53.7)
					> 0.5–1.0	42.8			52.1 (22.2–122)
					> 1.0–1.5	53.6			80.1 (32.2–199)
					> 1.5–2.0	67.5			144 (53–391)
					> 2.0–4.0	62.5			115 (46.0–291)
					> 4.0	83.8			361 (107–1215)
					<i>Time since last use (hours)</i>				
					> 24	18.6			15.9 (5.9–42.9)
					> 12–24	22.7			20.4 (8.4–49.3)
					> 1–12	55.1			85.2 (37.1–195)
					< = 1	74.3			201 (84.9–475)
					<i>Type of snuff</i>				
					Copenhagen	61.3			111 (50.1–246)
Skoal	54.0	81 (33–199)							
Hawken	5.3	3.9 (0.5–33.0)							
Greene et al. (1992), Countrywide, 1989–90	894 professional baseball players; any age, but 77% were 20–29 years of age; recruited in 1989–90; participation rate, 85%	37% current users (within week of interview)	Oral leukoplakia/erythroplakia, diagnosed by clinical examination by specially trained dentist, graded 1–4 (categories similar to those of Greer & Poulson, 1983)	Participants completed a standardized questionnaire	Non-user Former Current Seasonal use Year-round use Snuff Copenhagen Skoal Hawken Chewing tobacco	2.9 3.5 51.7 32.1 66.7 61.2 72.3 42.6 11.1 14.8	1.0 36.0	Extension of studies by Ernster et al. (1990) and Grady et al. (1990); degree 3–4 lesions found only in current users; prevalence available by seasonality of use for numerous variables. Not smoking adjusted.	

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Tomar et al. (1997), Countrywide excluding Alaska, 1986-87	17 027 children in schools. Sample was nationally representative of schoolchildren aged 12-17 years; response rate, 78%	3.1% smokeless tobacco (2.0% snuff, 1.5% chewing tobacco)	'Smokeless tobacco lesions' diagnosed by clinical examination by trained dental examiners according to Greer & Poulson (1983) criteria	Questionnaire administered by a trained interviewer	All subjects	1.5	<i>Chewing tobacco</i>	Adjusted for age, cigarette smoking (current, former, never) and alcoholic beverage consumption (current, former, never); data on prevalence of lesions of different degrees (1-3) by duration of use, frequency of use and exposure time, for snuff and for chewing tobacco separately; 65% of lesions located in mandibular buccal vestibules, of which 24% in anterior labial vestibule or labial mucosa
					Non-user	1.0		
					Current	18.4 (8.5-39.8)	2.5 (1.3-5.0)	
					Former	2.4 (1.0-6.1)	1.3 (0.7-2.2)	
					<i>Duration (months)</i>			
					< 1	1.0	1.0	
					1-12	8.1 (3.8-17.4)	2.0 (0.6-6.1)	
					13-24	23.3 (10.5-51.4)	6.6 (1.7-25.2)	
					> 24	58.9 (21.3-162)	13.4 (6.1-29.5)	
					<i>Frequency (days/month)</i>			
					0	1.0	1.0	
					1-14	4.2 (1.6-11.4)	2.9 (1.1-7.9)	
					15-29	7.9 (2.9-21.7)	4.8 (1.3-18.2)	
30-31	51.4 (19.7-134)	12.1 (5.5-26.5)						
<i>Min/day in the mouth</i>								
< 1	1.0	1.0						
1-30	9.5 (4.3-20.7)	2.8 (1.1-7.1)						
31-105	14.6 (5.5-39.0)	6.3 (2.7-14.5)						
> 105	26.7 (9.8-72.9)	11.1 (4.3-29.1)						

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Martin et al. (1999), Texas, 1996	3051 male US Air Force trainees; ages 17 and older; participation rate, 99.97%	9.9% current users, of whom 93.4% used snuff, 6.6% chewed	Oral leukoplakia diagnosed by clinical examination by a dentist		<i>Duration of use (months)</i>		11.2 (5.5–22.6) 28.8 (15.1–54.1) 59.9 (34.0–105) 156 (81.0–303) 24.0 (14.6–39.2) 46.0 (25.4–83.6) 108.2 (59.8–196.9) 3.4 (0.08–22.3) 77.7 (43.4–139.6) 40.0 (24.4–65.7) 36.5 (17.8–74.9)	Percentage of severe lesions according to duration of use and amount used per day available; 97% of lesions found in the mandibular buccal or labial sulcus
					1–12	14.8		
					13–24	30.9		
					25–48	48.1		
					> 49	70.8		
					<i>Cans snuff/day</i>			
					< 1/2	29.6		
					1/2–1	44.8		
					> 1	63.0		
					Chewing tobacco			
<i>Type of snuff</i>								
Copenhagen		54.7						
Skoal		38.3						
Kodiak		36.2						
Shulman et al., (2004) US, 1988–1994	17 235 people ages 17 and older from a nationally representative sample survey of the civilian, non-institutionalized population of the US, response rate 33 818/33994	Cannot be determined directly from data	Oral clinical examination by trained dentists in mobile examination centres	Standardized questionnaire administered by trained interviewers	Never smoked or used smokeless tobacco		1.0	Adjusted for age, sex, use of removable dentures, race/ethnicity, smoking
					Former smokeless user		0.53 (0.25–1.13)	
					Current smokeless user		3.90 (2.75–5.55)	
					Smoker and smokeless tobacco user		2.29 (1.44–3.64)	

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Fisher et al. (2005) West Virginia, 1999–2001	90 (54 men, 36 women) cases with oral leukoplakia ages 18 and older; 100% biopsy evidence of hyperkeratosis with or without epithelial atypia or dysplasia. Excluded if clinical diagnosis of keratosis or frictional keratosis. response rate, 55%; compared to 78 (37 men, 41 women) controls with periapical cysts (ICD9–522.8) and no known diagnosis of leukoplakia ages 18 and older from same surgical pathology biopsy service; response rate 50%		Biopsy diagnosis of leukoplakia of oral mucosa including tongue (ICD-9 528.6)	Mailed questionnaire	<i>Smokeless tobacco use</i>		1.0	Adjusted for age (< 50, > = 50), gender, smoked tobacco use (never current, former), current daily alcohol use (yes, no), partial or complete denture (yes, no) (adjusted OR higher than unadjusted)	
					Never		9.21 (1.49–57.00)		
					Current		2.73 (0.69–10.84)		
					Former				
					<i>Snuff use</i>				
					Never		1.0		
					Current		30.08 (2.67–338.48)		
					Former		0.98 (0.17–5.61)		
					<i>Chewing tobacco use</i>				
					Never		1.0		
					Ever		1.62 (0.73–3.57)		
					Current		0.97 (0.19–4.98)		
Former		1.83 (0.76–4.40)							

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<i>Yemen</i>								
Scheifele et al. (2007) Yemen 2004	54 male cases with oral leukoplakia who used shammah from a survey of oral lesions in 48 Yemeni villages, ages 11–74, response rate not stated; compared to 58 male controls without any oral lesions who used shammah from the same survey ages 11–74, response rate not stated		Oral leukoplakia WHO definition	Standardized questionnaires	Among shammah users <i>Type of shammah</i> White Black <i>Frequency of shammah use per day</i> 1–5 > 10 5–10 <i>Duration of shammah use per serving (min.)</i> < 1 1–5 > 5 <i>Mouthrinse after shammah use</i> No Yes		1.0 2.17 (0.95–4.96) 1.0 4.90 (1.99–12.08) 1.93 (0.55–6.74) 1.0 2.71 (0.96–7.68) 6.91 (2.66–17.95) 1.0 0.39 (0.18–0.85)	Age adjusted

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<i>India</i>								
Jacob et al., (2004), Thomas et al., (2003), Kerala, India Years of study not stated	927 cases of oral leukoplakia (516 men, 411 women), 170 submucous fibrosis, and 100 erythroplakia and (516 men, 411 women); compared to 47 773 population-based controls with no oral disease (17 897 men, 29 876 women). Study participants represented 82.1% of the 59 894 persons eligible for a screening trial involving using health workers to screen for oral cancer in 13 agricultural administrative geographic units		Visual oral examination by trained health workers, confirmed by dentists and oncologists	Structured questionnaires administered by health workers	Tobacco chewing Never Ever		1.0 <i>Leukoplakia</i> 30.9 (13.7–69.7) <i>Submucous fibrosis</i> 148.9 (17.9-infinity) <i>Erythroplakia</i> 96.0 (11.3–814.1) <i>Multiple lesions</i> 180.2 (20.7-infinity)	Adjusting for age, sex, education, body mass, pack-years of smoking, and years of drinking alcohol.
					Among non-smokers and non-drinkers		<i>Leukoplakia</i> 236.0 (68.0-infinity)	Adjusting for age, sex, education, body mass.

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<i>Uzbekistan</i>								
Zaridze et al., (1986), Uzbekistan Survey dates not stated	2150 males ages 55–69 invited to attend a medical examination 1 569 male residents in one local authority district. 1 506 participated (790%) as did 63 men 55 and older who came on their own – a total of 1 569.	41% used nass	Oral leukoplakia and preleukoplakia (combined) diagnosed by clinical oral examination using criteria of Pindborg et al., 1980)	Questionnaire	<i>Among non-smokers</i> Never naswar Ex-user Times per day < 6 6–12 > 12		1.0 1.4 (0.2–11.0) 4.9 (2.5–9.5) 5.5 (3.0–10.3) 6.6 (3.5–12.1)	

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Evstifeeva and Zaridze (1992) Uzbekistan Survey dates not stated	Oral leukoplakia 191 male cases with oral leukoplakia compared to 466 male controls free of leukoplakia		Oral leukoplakia and preleukoplakia (combined) diagnosed by clinical oral examination using criteria of Pindborg et al., 1980)	Questionnaire	Naswar		1.0	Adjusting for smoking alcoholic beverage consumption, and age. Lifetime intake is daily frequency times years used
					Never		3.8 (1.2-5.6)	
					Ever		3.9 (2.6-5.5)	
					Current		3.0 (1.1-8.3)	
					Former			
					<i>Age started in years</i>			
					≥ 31		3.03 (1.76-5.20)	
					24-30		2.72 (1.53-4.83)	
					≤ 23		5.79 (3.54-9.48)	
					p for trend		0.027	
					<i>Years used</i>			
					≤ 28		2.93 (1.71-5.02)	
					29-38		2.90 (1.65-5.08)	
					39-60		5.95 (3.58-9.89)	
p for trend		P < 0.001						
<i>Times/day</i>								
≤ 7		2.79 (1.63-4.76)						
8-11		3.96 (2.30-6.83)						
12-20		4.87 (2.92-8.13)						
p for trend		P < 0.001						
<i>Life-intake equivalent</i>								
≤ 154		1.94 (1.07-3.51)						
155-396		4.64 (2.77-7.80)						
397-1160		5.17 (3.10-8.61)						
p for trend		P < 0.001						
<i>Years stopped using</i>								
> 10		3.17 (0.78-12.84)						
10-26		3.98 (0.88-17.92)						
p for trend		0.172						

Relative risk: Prevalence odds ratio or ratio of prevalence rates. CI, confidence interval

a Greer and Poulson (1983) established a classification into three degrees of severity (instead of four degrees used previously) to be applied to persons who have used smokeless tobacco four years or less.