

**Table 2.6 Cohort studies of persistence of oral lesions or progression of oral lesions to cancers of the oral cavity and pharynx among smokeless tobacco users**

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)*	Adjustment for potential confounders	Comments
Roed-Petersen and Pindborg, (1973) 1956–1970 Copenhagen	450 patients with leukoplakia. 87.6% followed for a median of 4.1 years	7.1% used snuff	Dysplasia or malignancy	<i>Snuff</i> Nonuser User	72 2	1.0 [0.32]	None	
Grady et al., (1991) Countrywide, 1988	1031 male professional baseball players, of whom 185 (219 total lesions) had oral lesions similar to those of Greer & Poulson, 1983. 131 players (70.8%) returned 1–21 days later for biopsy. Loss to follow-up unrelated to age, race, education; duration, amount or recent use of smokeless tobacco; original clinical degree of the lesion	Not stated	Lesion healed, or changed in severity	Smokeless tobacco	In 15% of players lesions healed, and 18% had some improvement by at least one clinical degree. More severe lesions less likely to improve		None	Lesions more likely to improve where in players with small lesions, players who stopped or decreased use between examinations, among users of chewing tobacco compared to users of snuff, among users with less hours smokeless tobacco was held in mouth per day, and among seasonal in contract to year round users. Not associated with improvement: days between examinations or duration of use.
Martin et al. (1999), Texas, 1996	119 male US Air Force trainees; ages 17 and older with oral leukoplakia diagnosed by clinical examination by a dentist; trainees not permitted to use tobacco during their 6-week basic training period; 10 dropped out and were not re-examined	9.9% current users, of whom 93.4% used snuff, 6.6% chewed	Presence or absence of oral leukoplakia diagnosed by clinical examination by a dentist	Chewing tobacco	106 (97%) of 109 leukoplakias no longer present at end of follow-up		None	No information on whether the 3 leukoplakias still present after 6 weeks were in tobacco chewers

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Lee et al., (2000) Houston, TX 1988–1991,	70 patients enrolled 1988–1991 with advanced oral leukoplakia)dysplastic, extensive hyperplastic lesion, or hyperplastic lesion in a high risk oral site)(and were disease free for 2 years if had had a previous cancer. Cohort includes the 59 of the 70 who had high dose isotretinoin and had not progressed on the high dose treatment and subsequently received 9 months of low maintenance isotretinoin or B-carotene. All were followed up as of December 31, 1998 through telephone calls and record review for occurrence of aerodigestive tract cancer	Not stated	Aerodigestive tract cancer	<i>Chewing tobacco</i> No Yes	21 1	For chewing tobacco user: 0.57 (0.21, 1.56)	None	
Roosaar et al. (2006), Uppsala County, Central Sweden. 1973–1974	Cohort derived from a population-based oral cavity examination survey of 30 118 persons ages 15 or older in a small town, a small municipality, and 15 surrounding rural parishes of whom 20 333 (67.5%) were	Standardized questionnaires administered	ICD-7 141 (tongue), 143 (floor of mouth), 144 (other parts of oral cavity)	Stopped or not daily snus use	Progression from snus-induced lesion to oral cancer: 3 incident oral cancers and 1 death; Had lesion Had worse	SIR = 2.3 (0.5–6.7)  In 1994–1995: 6.1% 8.8%	None	2 the 3 incident cases smoked daily. Cancers in the 4 cases (incident or mortality) did not match that of lesion site in 1973–1974. Reliability of tobacco use information given in 1973–1974 versus in 1993–1995 in a subset

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	<p>examined and interviewed. Oral lesion identification used Axell (1976) scale; 1 115 men in the follow-up sample had snus-induced lesions at site in mouth where snus placed (only 4 women had lesions and were not included in the follow-up analysis) at baseline in 1973–1974. Mortality follow-up through national death register to January 31, 2002; incidence follow-up followed 27–29 years through national cancer registry to January 31, 2002; cancer registry 98% complete, death registry 100% complete. Oral exams repeated in 1994–1995 in a few zip codes in one area and the entire cohort in the other area (24% of the original cohort) and the response rate was 68%. 16 144 of the original participants (7 890 men and 8 254 women) were eligible for a follow-up study based on area of residence. Of the 267 men with</p>			by 1994–1995 examinations ( <i>n</i> = 66)	lesion grade Had same or less worse lesion	89.7%		<p>of cohort was good as was inter-examiner reliability between initial and follow-up examiner and in follow-up examiner’s intra-examiner reliability. Smoking status in 1994–1995 inversely related to lesion degree in 1994–1995</p>
				Continued snuff use of loose snus ( <i>n</i> = 68)	Had no lesion	1.5%		
				Change to portion-bag snus ( <i>n</i> = 42)	Had worse lesion grade Had same or less worse lesion	9.5% 88.1%		
					Had no lesion	2.4%		
				Hours with snus intraorally daily Less ( <i>n</i> = 9)	Had worse lesion grade Had same or less worse lesion	0% 100%		
					Had no lesion	0%		
				Same ( <i>n</i> = 26)	Had worse lesion grade Had same or less worse lesion	0% 96.2%		
					Had no lesion	3.8%		
				More ( <i>n</i> = 66)	Had worse lesion grade Had same or less worse lesion	12.1% 86.4%		
					Had no lesion	1.5%		

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lesions eligible for the follow-up after excluding loss to follow-up, emigrated, etc. 183 (68.5% of 267) were re-examination in 1994–1995 and of these 182 included in analysis.

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