

**Table 2.1. Cohort studies of smokeless tobacco and cancers of the oral cavity and pharynx**

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
Accortt et al. (2002, 2005) United States	<p>NHANES I Followup Cohort Survey of the non-institutionalized US population who underwent a physical health examination in 1971–75, aged 25–74 years (<math>n = 14\,407</math>); analysis restricted to white and black subjects, aged 45–75 years at baseline (<math>n = 6\,805</math>)</p> <p>Mortality follow-up to 1992; death certificates available for 98% of the decedents; coded according to ICD-9. Incidence of oral cancer determined at 4 follow-up assessments in 1982–1984, 1986, 1987, and 1992. Subjects or their proxies asked about diseases that developed since previous interview. If a cancer case with an overnight health care facility stay was reported, medical records were sought and abstracted. Any additional cancers the subject had that were found in the medical record were abstracted. Cancer listed as a cause of death was considered a confirmed case. 527 participants who could not be traced in any of the four follow-up periods were excluded. Of the 7 787, 6 779 (89%) provided information on both smoking and smokeless tobacco; percent histologically confirmed not stated</p>	Standardized question-naire regarding current use at baseline, or, if not available, inferred from ever use question administered in 1982–1984 questionnaire	Incident oral cancer reported by study participants with confirmation sought in medical records Deaths from oral cancer	Overall	Oral cavity (19)	<b>SMR</b> 107 (10–308)	Mortality: adjusted for age  Incidence: adjusted for age. Both male ever smokeless users also smoked currently or formerly	Mortality: expected based on 1982 US mortality rates Incidence: expected based on 1982 SEER incidence rates for US adults 45–77 years of age. Possibly the same 2 people are the cases in the incidence and the mortality reports
				<i>Smokeless tobacco use</i>	2			
				Ever smokeless tobacco use	2	0 (0–580)		
				Exclusive smokeless tobacco use	0	0.8 expected		
				<i>Smokeless tobacco use</i>		<b>SIR</b>		
				Ever smokeless tobacco use	2	30 (3–95)		
				Exclusive smokeless tobacco use	0			
				<i>Males</i>				
Ever smokeless tobacco use	2	30 (3–83)						
Exclusive smokeless tobacco use	0							
<i>Females</i>								
Ever smokeless tobacco use	0	0 (0–410)						
Exclusive smokeless tobacco use	0							

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Boffetta et al. (2005), Norway	Norwegian cohort Probability sample of general adult population of Norway from 1960 census and relatives of migrants to the USA, alive on 1 January 1966 ( <i>n</i> = 12 431). Response rate to survey > 75%. Mailed questionnaires on lifestyle habits in 1964 and 1967; information on smokeless tobacco available for 10 136 men, 81.5% of eligibles. Follow-up for cancer incidence via cancer registries, 1966–2001 (99.85% complete); percent histologically confirmed not stated	Standardized questionnaire	Incident salivary gland, oral cavity and pharynx cancer (ICD-7 141–148)	Overall	36		Adjusted for age and smoking	In Boffetta et al.(2008) meta-analysis. In Lee and Hamling (2009) meta-analysis
				<i>Smokeless tobacco use</i>				
				Never user	25	1.0		
				Ever used smokeless tobacco	9	1.1 (0.5–2.4)		
				Current use of smokeless tobacco	6	1.1 (0.5–2.8)		
				Former use of smokeless tobacco	3	1.0 (0.3–3.5)		
Henley et al. (2005), United States	CPS-I 456 487 men and 594 544 women (CPS-I), aged > = 30 years, residing in a household in which at least one member was > = 35 years old; analysis restricted to men without prior cancer (except non-melanoma skin cancer) at enrolment and who never used any other tobacco. Questionnaire at enrollment in 1959. Vital status follow-up, 1959–72; 6.7% lost to follow-up and 4.9% with follow-up truncated for logistic reasons in 1965;	Standardized questionnaire	Deaths from lip, salivary gland, oral cavity, and pharynx cancer (ICD-7 140–148) for CPS-I and ICD-9 for 140 – 148 for CPS-II)	<b>Among men who never used any other tobacco product</b>	<i>CPS-I</i>	<b>HR</b>	CPS I: age, race, educational level, body mass index, exercise, alcohol consumption, fat consumption, fruit/vegetable intake and aspirin use. CPS II age, race, educational level, body mass index, exercise, alcohol	In Boffetta et al. (2008) meta-analysis. In Lee and Hamling (2009) meta-analysis
				Overall	13	1.0		
				<i>Smokeless tobacco use</i>				
				Never used smokeless tobacco	9	2.0 (0.5–7.7)		
				Current use of smokeless tobacco	4			
					<i>CPS-II</i>			
				Overall	46	1.0		
<i>Smokeless tobacco use</i>								
Never used smokeless tobacco	45	0.9 (0.1–6.7)						
Current use of smokeless tobacco	1							
Former use of smokeless tobacco	0							

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Henley et al. (2005) contd.	death certificates coded to ICD-7 (97% complete) CPS-II 508 351 men and 676 306 women, aged > = 30 years, residing in a US household in which at least one member was 35 years or older; analysis restricted to men who never used any other tobacco. Questionnaire at enrolment in 1982; only men were asked about smokeless tobacco. Vital status follow-up through 2000; 0.2% lost to follow-up; death certificates coded to ICD-9 (98.9% complete)						consumption, fat consumption, fruit/vegetable intake and aspirin use, employment status and type.	
Luo et al. (2007) Sweden	Cohort of 279 897 male Swedish construction workers who received preventive health check-ups 1978–1992, excluding men with cancer before check-up and 1 392 with incomplete tobacco use data; mortality (essentially complete) and cancer incidence follow-up (98% complete) to December 31, 2004	Personal interviews by nurses at enrolment check-up	Incident lip and oral cavity cancer (ICD 7 140 -lip, 141-tongue, 143-floor of mouth, 144-other mouth)	Overall <i>Among never smokers</i> Never use of any tobacco <i>Ever users of snus</i> Ex-users of snus Current users of snus <i>Snus consumed</i> 1–9 g/day > = 10 g/day p for trend	60 50 10 1 9 2 8	1.0 0.8 (0.4–1.7) 0.7 (0.1–5.0) 0.9 (0.4–1.8) 0.7 (0.2–2.8) 0.9 (0.4–2.0) 0.8	Adjusted for attained age and BMI.	In Boffetta et al. (2008) meta-analysis. In Lee and Hamling (2009) meta-analysis.

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Roosaar et al. (2008) Uppsala County, Central Sweden	Cohort of 20 333 individuals, 68% of all invited to participate in a population-based survey oral lesions in Enköping or Habo ages 15 and older in 1973–1974. Of these, there were 121 with lost data. All of the men with no prior cancer diagnosis were included in this analysis ( $n = 9\ 860$ ). 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 and mortality registries essentially complete.	Face-to-face interview	Incident lip, salivary gland, oral cavity and pharynx cancer (ICD-7 140–148)	Overall <i>Snus use</i> Never daily Ever daily  <i>Among never smokers</i> Never daily Ever daily	Overall  33 23  11 6 5	HR  1.0 3.1 (1.5–6.6)  1.0 2.3 (0.7–8.3)	Calendar period, area of residence, alcohol consumption, smoking, and age X smoking      Calendar period, area of residence, alcohol consumption	

CI, confidence interval; CPS, Cancer Prevention Study; HR, Hazard ratio; NHANES, National Health and Nutrition Examination Survey; SIR, standardized incidence ratio; SMR, standardized mortality ratio