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## The effect on health of switching from cigarettes to snus – A review

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## ABSTRACT

Interest in snus (Swedish type moist snuff) as an alternative to smoking is increasing, but the evidence on the health effects of switching from cigarettes to snus has not previously been reviewed. We identified six epidemiological cohort or case-control studies, all from Sweden, which allowed comparison of cancer or cardiovascular disease risk in current snus users who formerly smoked ("switchers") with that of never snus users who continued to smoke ("continuers") or of never snus users who quit smoking ("quitters"). Based on 13 sets of comparisons, one for oral cancer, one for stomach cancer and 11 for various cardiovascular disease endpoints, switchers were consistently found to have a lower risk than continuers, with relative risks varying from 0.35 to 0.61, and a similar risk to quitters. Based on estimates from four studies for ischaemic/coronary heart disease or acute myocardial infarction, meta-analyses gave combined relative risk estimates of 0.55 (95% confidence interval 0.45–0.68) for switchers vs. continuers and 1.02 (95% confidence interval 0.83–1.26) for switchers vs. quitters. Though based on limited evidence with some weaknesses, these results are consistent with a recent review which found no increased risk of cancer or heart disease from snus use.

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## 1. Introduction

Swedish-type moist snuff ("snus") consists of finely ground air- or sun-cured tobacco, salt (sodium chloride), water, humidifying agents, chemical buffering agents (sodium carbonate), and food-grade flavourings. The tobacco is often heat-treated (pasteurized). In the past, a pinch (or dip) was placed between the gum and upper lip, often for 11–14 h daily (International Agency for Research on Cancer, 2007a), but more recently the commonest application method is by portion-packed tobacco in a small sachet (similar to a tea-bag). Use involves overall nicotine exposure similar to and perhaps somewhat greater than that from smoking (Agewall et al., 2002; Bolinder et al., 1997a,b; Bolinder and de Faire, 1998; Eliasson et al., 1991; Holm et al., 1992; Wennmalm et al., 1991). Although the sale of snus is banned in other EU countries, Sweden has a special derogation due to its long history of use.

In the last decade, there has been increasing interest in snus as a possible safer alternative to smoking. Various reviews (e.g. Boffetta et al., 2008; Broadstock, 2007; Kallischnigg et al., 2008; Lee, 2007; Lee and Hamling, 2009; Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), 2008; Weitkunat et al.,

2007) have considered possible health effects, and oral and pancreatic cancer, oral disease and cardiovascular disease (CVD) have received particular attention.

A recent summary, with meta-analyses, of the epidemiological evidence relating snus to health (Lee, 2011) found no statistically significant association with cancer of any site or with heart disease or stroke, and concluded that any possible risk from snus, if it exists, is much less than that from smoking. It also noted that "snuff dipper's lesion" (Axéll et al., 1976) does not predict oral cancer. Though that summary considered a wide range of possible health effects, and also found no reliable evidence that snus increases initiation of smoking or discourages quitting, it did not evaluate health effects associated specifically with switching from smoking to snus. Such an evaluation is reported here, by comparing switchers with those who continue to smoke or who quit smoking rather than switch.

## 2. Materials and methods

The searches concerned all those health effects considered in sections 3.1 (cancer), 3.2 (non-neoplastic oral disease), 3.3 (circulatory disease) and 3.7–3.14 (diseases of the respiratory and digestive system; psychiatric, neurodegenerative and musculoskeletal disorders; pregnancy and reproductive effects; all-cause mortality; and general health indicators) of the 2011 summary review of snus and health (Lee, 2011). All the publications which were cited in that review on these health effects, as well as additional publications

Abbreviations: AMI, acute myocardial infarction; BMI, body mass index; CHD, coronary heart disease; CI, confidence interval; CVD, cardiovascular disease; IHD, ischaemic heart disease; OR, odds ratio; RR, relative risk; SCD, sudden cardiac death.

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obtained by updating the literature search to September 2012 using the same search criteria as used in the 2011 summary, were considered. All these publications were then examined to assess whether they presented results allowing comparison of risk in current snus users who had formerly smoked (“switchers”) current smokers who had never used snus (“continuers”) and former smokers who had never used snus (“quitters”). We also accepted results where data were given for similar definitions (e.g. current smokers who did not currently use snus may also be considered continuers), though such differences in definition are made clear when presenting the findings.

Studies presenting relevant data generally presented their findings as a set of covariate-adjusted relative risks (RRs) or odds ratios (ORs) with 95% confidence limits (CIs) for a two-way table of smoking by snus use (e.g. never/current/former smoking  $\times$  never/current/former snus), with the RRs and ORs presented relative to those who had never smoked or used snus. As we wished to compare risks between switchers and continuers, and between switchers and quitters, the method of Hamling et al., 2008) was used to derive “pseudo-numbers” of cases and controls (or at risk) corresponding to the adjusted RRs or ORs given, which could then be used to derive the required estimates. Where adjusted RRs were not provided, estimates were based on the given numbers of cases and controls.

Where appropriate, meta-analyses of estimates were derived using standard methods (Fleiss and Gross, 1991).

### 3. Results

The literature searches identified six studies, all cited in the 2011 review. Two were of cancer (Schildt et al., 1998; Ye et al., 1999) and four were of cardiovascular disease (CVD) (Hansson et al., 2009; Hergens et al., 2005; Johansson et al., 2005; Wennberg et al., 2007). All were conducted in Sweden, one based on a random national sample (Johansson et al., 2005), one based on the Swedish twin registry (Hansson et al., 2009), and the rest in defined counties of Sweden.

Table 1 summarizes some features of the studies. Two studies were of prospective cohort design (Hansson et al., 2009; Johansson et al., 2005), three were case-control studies (Hergens et al., 2005;

Schildt et al., 1998; Ye et al., 1999), and one was a nested case-control study, with initial interviews taking place over the period 1980–2002 (Wennberg et al., 2007). The two cancer studies considered both sexes, while the four studies of CVD were restricted to men. All the studies provided RRs or ORs adjusted for age and other covariates, though for one study (Schildt et al., 1998), where the adjusted ORs had been derived by fitting a multiplicative model, unadjusted ORs were used instead. Details of the adjustment factors used are given later, in Tables 2 and 3.

In three of the studies (Hansson et al., 2009; Hergens et al., 2005; Schildt et al., 1998), the relevant results came from tables in which subjects were jointly classified in a  $3 \times 3$  table of never/former/current snus use by never/former/current smoking. The classification in a fourth study (Wennberg et al., 2007) was similar, except that for current smokers snus use was only divided into current/non-current. In the remaining two studies, the results were presented as a  $2 \times 3$  table with the same three-level classification of smoking, but only a two-level classification of snus use, either never/ever (Ye et al., 1999) or non-current/current (Johansson et al., 2005).

The six studies reported results for between one and four endpoints, giving a total of 13 data sets. The results reported essentially relate to men, as the four CVD studies were of men, Ye et al. (1999) only presented results for snus for men, and though Schildt et al. (1998) presented results for the sexes combined, they noted that only one woman reported snus use. The two cancer studies involved between 300 and 400 cases of the cancer studied, either oral or gastric. Three of the studies of CVD were larger, involving over 1000 cases, while the fourth involved 277 cases. Numbers of cases were smaller for the subdivisions of acute myocardial infarction (AMI) or of CVD, but still exceeded 250, except for the cases of fatal AMI in 28 days, and of sudden cardiac death (SCD) in either  $<24$  h or  $<1$  h, in the nested case-control study (Wennberg et al., 2007). Numbers of cases in switchers are not always available, but are substantially lower. They form less than 10% of cases, and are usually defined as current snus users who formerly smoked, except in the study of gastric cancer (Ye et al., 1999), where switchers are defined as ever snus users who formerly smoked. Some of this group may in fact not have switched from smoking to snus, possibly having given up snus before they quit smoking.

**Table 1**  
Studies providing relevant evidence.

Reference	Source table	Study design <sup>a</sup>	Timing <sup>b</sup>	Sex <sup>c</sup>	Age (years)	Data on ST use <sup>d</sup>	Endpoints (cases, cases in switchers) <sup>e</sup>
Schildt et al., 1998	III	CCP	1980–1989	M,F	Mean 69.6 (M), Mean 72.3 (F)	N,X,C	Oral cancer (354,10 <sup>f</sup> )
Ye et al., 1999	VII	CCP	1989–1995	M,F	40–79	N,E	Gastric cancer (375,56)
Hansson et al., 2009	2	PC <sup>g</sup>	1998–2002, 4.9 years	M	40+	N,X,C	All CVD (1119,58), IHD (760,43), Stroke (416,17)
Hergens et al., 2005	3	CCP	1992–1994	M	45–70	N,X,C	AMI (1432,NA), Nonfatal AMI (1173,NA), Fatal AMI (259,NA)
Johansson et al., 2005	3	PC <sup>h</sup>	1988–1989, 12 years	M	30–74	Non-C,C	CHD (277,NA)
Wennberg et al., 2007	2,3	NCC	1985–1999 <sup>i</sup>	M	Mean 53.9	N,X,C <sup>j</sup>	AMI (1668,138), Fatal AMI in 28 days (103,7), SCD,survival $<24$ h (83,6), SCD,survival $<1$ h (49,5)

<sup>a</sup> CCP = case-control study with population controls, PC = prospective cohort study, NCC = nested case-control study.

<sup>b</sup> The timing of the initial interviews is given, and then the length of follow-up for prospective cohort studies.

<sup>c</sup> M = male, F = female.

<sup>d</sup> N = never used, X = former user, C = current user, E = ever user, Non-C = non-current user.

<sup>e</sup> AMI = acute myocardial infarction, CHD = coronary heart disease, CVD = cardiovascular disease, IHD = ischaemic heart disease, NA = not available, SCD = sudden cardiac death.

<sup>f</sup> The source table gives 15 cases and 10 controls for switchers, but these have been taken as 10 cases and 15 controls, so that the total numbers align with the data in other tables.

<sup>g</sup> The study involved 16,642 subjects.

<sup>h</sup> The study involved 3120 subjects.

<sup>i</sup> Initial interviews were carried out in 1985–1999, and all cases occurring after interview in this period were considered in analysis.

<sup>j</sup> For current smokers only, snus users were subdivided by current or non-current use.

**Table 2**

Comparison of health risks in switchers (from smoking to snus) and in continuing smokers.

Reference	Endpoint	Continuing smokers: (current smokers who never used snus) RR/OR (95% CI) (vs never tobacco)	Switchers: (former smokers who currently use snus) RR/OR (95% CI) (vs never tobacco)	Switchers	
				RR/OR (95% CI) (vs continuers)	Adjustment factors
	<b>Cancer</b>				
Schildt et al., 1998	Oral cancer	1.78 (1.22–2.62)	0.77 (0.34–1.79)	0.43 (0.18–1.02)	None
Ye et al., 1999	Gastric cancer	2.00 (1.30–2.90)	1.20 (0.80–1.90) <sup>a</sup>	0.60 (0.38–0.95)	Age,others <sup>b</sup>
	<b>CVD</b>				
Hansson et al., 2009	Total CVD	1.86 (1.56–2.22)	1.04 (0.78–1.39)	0.56 (0.41–0.75)	Age,others <sup>c</sup>
	IHD	1.99 (1.59–2.50)	1.22 (0.82–1.74)	<b>0.61 (0.42–0.90)</b>	Age,others <sup>c</sup>
	Stroke	1.61 (1.22–2.13)	0.77 (0.46–1.29)	0.48 (0.28–0.82)	Age,others <sup>c</sup>
Hergens et al., 2005	Total AMI	2.80 (2.30–3.40)	1.60 (1.10–2.20)	<b>0.57 (0.40–0.81)</b>	Age,area
	Non-fatal AMI	2.70 (2.20–3.30)	1.60 (1.10–2.20)	0.59 (0.42–0.83)	Age,area
	Fatal AMI	3.60 (2.40–5.20)	1.50 (0.69–3.20)	0.42 (0.20–0.86)	Age,area
Johansson et al., 2005	CHD	2.30 (1.66–3.19) <sup>d</sup>	1.18 (0.67–2.06)	<b>0.51 (0.30–0.88)</b>	Age,others <sup>e</sup>
Wennberg et al., 2007	Total AMI	2.60 (1.91–3.54) <sup>d</sup>	1.25 (0.80–1.96)	<b>0.48 (0.30–0.76)</b>	Age,others <sup>f</sup>
	Fatal AMI in 28 days	3.53 (1.83–6.84) <sup>d</sup>	1.24 (0.44–3.53)	0.35 (0.12–1.02)	Age,others <sup>f</sup>
	SCD with survival <24 h	3.12 (1.53–6.33) <sup>d</sup>	1.39 (0.44–4.42)	0.45 (0.14–1.45)	Age,others <sup>f</sup>
	SCD with survival <1 h	4.54 (1.55–13.25) <sup>d</sup>	2.67 (0.52–13.80)	0.59 (0.10–3.53)	Age,others <sup>f</sup>
	Meta-analysis of IHD/CHD/AMI (estimates in bold)				0.55 (0.45–0.68) <sup>g</sup>

Note: estimates used in meta-analysis are shown in bold face.

<sup>a</sup> Former smoking, ever snus.<sup>b</sup> Adjusted for age, area of residence, BMI, socioeconomic status and alcohol consumption.<sup>c</sup> Adjusted for age, diabetes, high blood pressure and cholesterol.<sup>d</sup> Current smoking, non-current snus.<sup>e</sup> Adjusted for age, physical activity, BMI, diabetes and hypertension.<sup>f</sup> Adjusted for age, physical activity, BMI, education and cholesterol level.<sup>g</sup> Chisquared for heterogeneity 0.726 on 3 d.f. ( $p > 0.50$ ).**Table 3**

Comparison of health risks in switchers (from smoking to snus) and in smokers who quit tobacco.

Reference	Endpoint	Quitters: (former smokers who never used snus)	Switchers: (former smokers who currently use snus)	Switchers	
		RR/OR (95% CI) (vs never tobacco)	RR/OR (95% CI) (vs never tobacco)	RR/OR (95% CI) (vs continuers)	Adjustment factors
	<b>Cancer</b>				
Schildt et al., 1998	Oral cancer	0.94 (0.61–1.44)	0.77 (0.34–1.79)	0.83 (0.34–1.99)	None
Ye et al., 1999	Gastric cancer	1.20 (0.90–1.80)	1.20 (0.80–1.90) <sup>a</sup>	1.00 (0.66–1.51)	Age,others <sup>b</sup>
	<b>CVD</b>				
Hansson et al., 2009	Total CVD	1.17 (1.00–1.38)	1.04 (0.78–1.39)	0.89 (0.67–1.19)	Age,others <sup>c</sup>
	IHD	1.34 (1.10–1.64)	1.22 (0.82–1.74)	<b>0.91 (0.63–1.32)</b>	Age,others <sup>c</sup>
	Stroke	1.01 (0.78–1.30)	0.77 (0.46–1.29)	0.76 (0.45–1.28)	Age,others <sup>c</sup>
Hergens et al., 2005	Total AMI	1.30 (1.10–1.60)	1.60 (1.10–2.20)	<b>1.23 (0.87–1.73)</b>	Age,area
	Non-fatal AMI	1.20 (0.98–1.50)	1.60 (1.10–2.20)	1.33 (0.94–1.88)	Age,area
	Fatal AMI	1.70 (0.10–2.60)	1.50 (0.69–3.20)	0.88 (0.42–1.87)	Age,area
Johansson et al., 2005	CHD	1.47 (1.07–2.03) <sup>d</sup>	1.18 (0.67–2.06)	<b>0.80 (0.47–1.38)</b>	Age,others <sup>e</sup>
Wennberg et al., 2007	Total AMI	1.18 (0.82–1.70)	1.25 (0.80–1.96)	<b>1.06 (0.64–1.75)</b>	Age,others <sup>f</sup>
	Fatal AMI in 28 days	1.02 (0.45–2.31)	1.24 (0.44–3.53)	1.22 (0.38–3.90)	Age,others <sup>f</sup>
	SCD with survival <24 h	0.74 (0.28–1.97)	1.39 (0.44–4.42)	1.88 (0.48–7.27)	Age,others <sup>f</sup>
	SCD with survival <1 h	0.35 (0.07–1.78)	2.67 (0.52–13.80)	7.63 (0.42–137.8)	Age,others <sup>f</sup>
	Meta-analysis of IHD/CHD/AMI (estimates in bold)			1.02 (0.83–1.26) <sup>g</sup>	

Note: estimates used in meta-analysis are shown in bold face.

<sup>a</sup> Former smoking, ever snus.<sup>b</sup> Adjusted for age, area of residence, BMI, socioeconomic status and alcohol consumption.<sup>c</sup> Adjusted for age, diabetes, high blood pressure and cholesterol.<sup>d</sup> Former smoking, non-current snus.<sup>e</sup> Adjusted for age, physical activity, BMI, diabetes and hypertension.<sup>f</sup> Adjusted for age, physical activity, BMI, education and cholesterol level.<sup>g</sup> Chisquared for heterogeneity 2.309 on 3 d.f. ( $p > 0.50$ ).

Table 2 gives RR/OR estimates for continuers and switchers, each expressed relative to those who had never used tobacco. In all 13 data sets, the risk of disease in continuing smokers is

significantly ( $p < 0.05$ ) elevated, with relative risk estimates varying between 1.61 and 4.54. In switchers, however, the risk is significantly ( $p < 0.05$ ) elevated in only two data sets. These two

estimates, for AMI and non-fatal AMI from the same study (Hergens et al., 2005), are clearly not independent, as the 1173 non-fatal cases formed 82% of the total of 1432 cases of AMI.

Table 2 also shows that the RRs/ORs for switchers, expressed relative to continuers, are very consistent, varying only from 0.35 to 0.61. Nine of these 13 estimates show a significantly ( $p < 0.05$ ) lower risk in switchers, the only exceptions being where numbers of cases in switchers are low (10 or less). In view of the variety of endpoints and the non-independence of some of the results, meta-analysis of all 13 estimates is not meaningful. However, it is reasonable to combine the single estimates for IHD, coronary heart disease (CHD) or total AMI from the four studies of CVD. These four estimates, shown in bold face in Table 2, are statistically homogenous ( $p > 0.50$ ). Combined, they give an estimate of 0.55 (95% CI 0.45–0.68), consistent with switching to snus being associated with an approximate halving of the relative risk associated with smoking.

Table 3 gives RR and OR estimates for quitters and switchers, each expressed relative to those who had never used tobacco, and also gives estimates for switchers, expressed relative to quitters. There is no significant evidence of a difference between switchers and quitters in any of the data sets. Again, the estimates for IHD, CHD or total AMI are statistically homogenous ( $p > 0.50$ ). Here the combined estimate of 1.02 (95% CI 0.83–1.26) is consistent with switching to snus being associated with essentially the same risk as quitting smoking.

#### 4. Discussion

The results summarized in Tables 2 and 3 consistently show that switching from smoking to snus is associated with a reduction in risk of the endpoints studied, and that switching to snus appears to involve much the same risk as quitting smoking.

A number of limitations of the analyses should be noted. Firstly, the number of studies providing relevant data is low, particularly for cancer where the only evidence available is from one study of oral cancer (Schildt et al., 1998) and one of gastric cancer (Ye et al., 1999). Second, the evidence is essentially restricted to men. Third, none of the studies provide any information on how risk varies by time of switch to snus. While there are plenty of other data on the time course of the decline in risk following quitting smoking (e.g. International Agency for Research on Cancer, 2007b), the studies considered in this review do not allow comparison of duration of switching among the switchers with duration of quitting among the quitters. Fourth, our definition of switching, though the best there is from the available data, does not separate those who switched immediately from smoking to snus, those who took up snus some time after quitting smoking, or those who ended up as snus only users after a period of dual use. Next, the endpoints considered vary from study to study. Only for CVD was it reasonable to carry out any sort of meta-analysis, combining estimates for IHD, CHD and total AMI. Also, the definitions of the groups being compared are not completely consistent from study to study. Finally, it should be noted that while the analyses, with one exception, are adjusted for age and other risk factors, none of the analyses adjust for aspects of smoking which might bias the comparison. Thus, cigarette consumption in switchers at the time they switched may differ from that in continuers, or in quitters at the time they quit, while comparisons may also be biased by lack of control for duration of smoking.

Despite these potential weaknesses, the consistency of the findings is remarkable. All 13 of the RR or OR estimates comparing switchers and continuers are in the range 0.35–0.61, while all of the estimates comparing switchers and quitters are 0.76 or over and did not significantly ( $p < 0.05$ ) differ from 1.0.

The findings are also consistent with those of a recent detailed review of the epidemiological evidence on snus and health

(Lee, 2011). For the endpoints considered here, the meta-analyses in that review showed no evidence of an association with oropharyngeal cancer, with combined RR or OR estimates of 0.97 (95% CI 0.68–1.37) based on 7 studies, or with stomach cancer (0.98, 0.82–1.17,  $n = 5$ ), IHD/AMI (1.01, 0.91–1.12,  $n = 9$ ), stroke (1.05, 0.95–1.15,  $n = 6$ ), or any circulatory disease (1.08, 0.92–1.27,  $n = 5$ ). These meta-analyses are based on results for smokers and non-smokers combined, with adjustment for smoking; estimates based on results for never smokers similarly show no evidence of an increased risk associated with snus use. The earlier review (Lee, 2011) concluded that “Using snus is clearly much safer than smoking. While smoking substantially increases the risk of cancer and CID, any increase from snus use is undemonstrated, and if it exists is probably about 1% of that from smoking”.

#### 5. Conclusion

Though based on a somewhat limited database, the findings consistently demonstrate that switching from cigarettes to snus is associated with a clearly lower risk of CVD and cancer than is continuing to smoke. The risk in switchers is no different from that in smokers who quit smoking. The findings are consistent with other evidence that adverse health effects of snus are at most minimal.

#### Conflict of Interest statement

The author is a long-term consultant to the tobacco industry. However, this is an independent scientific assessment, the views expressed being those of the author alone.

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