

INVESTIGATIVE REPORT

Hand Eczema and Use of Snus (Moist Snuff) – a Population-based Study

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A possible association between use of snus (Swedish moist snuff) and hand eczema was studied. 27,466 individuals responded to questions regarding hand eczema, tobacco use and other life style factors in a Swedish Public Health Survey in 2006, response rate 58%. Of these persons, 12.2% reported daily snus use (men 22.0%, women 4.3%), 15.5% daily smoking (men 14.4%, women 16.5%). Of snus users 7.5% reported hand eczema (men 6.5%, women 11.8%), of smokers 11.7% (men 8.6%, women 13.6%) and of non-tobacco-users 9.7% (men 7.9%, women 11.0%). In multivariate analysis hand eczema was significantly less common in snus users, in total prevalence proportion ratio (PPR) = 0.813, in men PPR = 0.820, but significantly more common in smoking women, PPR = 1.238. Physical exercise was a confounder; sex an effect modifier. No positive association was demonstrated between snus use and hand eczema in contrast to the positive association found between smoking and hand eczema in women. Key words: epidemiology; general population; psoriasis; smoking; snuff; tobacco.

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Tobacco smoking has previously been shown in some population-based studies to be associated with the occurrence of hand eczema (HE) (1–3) and in a Swedish population-based study in 2010 it was observed that snus users had a decreased crude risk of HE (4). Smoking is also associated with other skin diseases, such as psoriasis and palmoplantar pustulosis, and conditions such as skin ageing and impaired wound repair (5–8). An alternative means of self-administering the addictive substance nicotine, is use of smokeless tobacco. Smokeless tobacco exists in several forms: moist snuff, also called Swedish snuff or snus, chewing tobacco for oral use, and dry snuff for sniffing. Observed health hazards of smoking and use of smokeless tobacco differ to some degree. At the behest of the European Commission, a comprehensive report entitled “Health Effects of Smokeless Tobacco

Products” was prepared by the “Scientific committee on emerging and newly identified health risks” (SCENIHR) and adopted in 2008 (9).

In Sweden, moist snuff, here called snus, has been used for centuries. In 2004–2005, the prevalence of daily snus use in Sweden was 23% among men and 3% among women (10). For comparison, 14% of the men and 18% of the women reported daily smoking. Over the past decades, Sweden has seen a trend towards decreased smoking and an increased use of snus.

Sweden has a long tradition of performing public health surveys (11); this offers a unique opportunity to study environmental factors such as different forms of tobacco use that pose risks to the health of the general population. HE is a common disease with a multifactorial background. The present study compiles information on established risk factors for HE and life style factors that have been shown to associate with the occurrence of HE (12).

The aims of the study were to examine a possible association between self-reported daily use of snus and occurrence of HE, and to investigate if the association is similar to that between smoking and HE.

METHODS

Study population

A Public Health Survey of Stockholm County was performed in 2006. A total of 47,931 individuals aged 18–64 years, randomly chosen from the population register in Stockholm, Sweden, were asked to complete a postal questionnaire. The response rate was 58% ($n = 27,994$). Of these, 27,466 individuals (12,359 men and 15,107 women) responded to questions regarding HE and tobacco use and were included in the present study.

Data collection and questionnaire

In 2006, an instruction letter was mailed out, followed shortly by a questionnaire. Three reminders were sent. Data collection was performed by Statistics Sweden. The questionnaire comprised 90 questions regarding physical and mental health, life style factors, social relations, economic status and work. The questions on tobacco use were “Do you use snus daily?” and “Do you smoke daily?”. In the present paper the concepts of “daily use of snus” and “daily smoking” include both exclusive and dual use. A previously validated question on HE was included: “Have you had HE on any occasion during the past 12 months?” (13). “Atopy history” was based on a positive answer to questions about hay fever and/or asthma. A question

about doctor's diagnosis of psoriasis was also included. The concepts of physical exercise and stress have been defined in a previous publication (12). Obesity was defined as BMI > 30.

Data analysis and statistics

For statistical analysis, SPSS version 20.0 was used (IBM Corp., Armonk, NY, USA). One-sample proportion *t*-tests were performed to test possible sex differences in specific groups defined on the basis of responses to the questions on tobacco use habits (non-tobacco-users, exclusive smokers, exclusive snus users and dual users), sex differences in smoking and use of snus, and sex differences in HE.

Cochran's *q*-tests were performed to investigate, in each tobacco use group, i.e. those who exclusively used snus, or exclusively smoked, or who both smoked and used snus, if the distributions of proportions of tobacco use in 5 age-groups were significantly different between men and women. Cochran's *q*-test was also used in order to test if the distributions of proportions of HE in 5 age-groups were significantly different between men and women (14).

The association between tobacco use and HE was assessed by prevalence proportion ratios (PPR). This was done by using a generalised linear model with a logarithmic link function and a binomial distribution function.

A confounder was defined as having an association with HE itself and by significantly changing the association between the tobacco use habits and HE ($\geq 20\%$ change) (15). We also investigated whether any of the factors were effect modifiers rather than confounders. This was done by including an interaction term defined as the specific confounder multiplied by the tobacco use habits: if the interaction was significant (*p*-value < 0.05) the specific confounder was an effect modifier.

Ethical approval

The study was approved by the Regional Ethical Review Board in Stockholm, Sweden (2007/323-31, 2013/140-32).

RESULTS

In total, answers regarding snus use, smoking and HE were obtained from 27,466 individuals. Descriptive data are shown in Table I. Overall, daily snus use was reported by 12.2% (men 22.0%, women 4.3%, *p* < 0.001) and daily smoking by 15.5% (men 14.4%, women 16.5%, *p* < 0.001). Tobacco use habits, exclusive and dual, in relation to sex and age are presented in Fig. 1. Exclusive snus use was significantly more

Table I. Descriptive data on individuals who responded to questions on tobacco use and hand eczema in a public health survey in Stockholm, Sweden. For definitions of variables see Methods

	Total (<i>n</i> = 27,466) <i>n</i> (%)	Men (<i>n</i> = 12,359) <i>n</i> (%)	Women (<i>n</i> = 15,107) <i>n</i> (%)
Age			
18–29 years	5,160 (18.8)	2,167 (17.5)	2,993 (19.8)
30–39 years	6,585 (24.0)	2,858 (23.1)	3,727 (24.7)
40–49 years	6,404 (23.3)	2,914 (23.6)	3,490 (23.1)
50–59 years	5,937 (21.6)	2,733 (22.1)	3,204 (21.2)
60–64 years	3,380 (12.3)	1,687 (13.7)	1,693 (11.2)
Tobacco use			
No tobacco use	20,276 (73.8)	8,208 (66.4)	12,068 (79.9)
Daily exclusive snus use	2,925 (10.7)	2,376 (19.2)	549 (3.6)
Daily exclusive smoking	3,834 (14.0)	1,437 (11.6)	2,397 (15.9)
Daily dual use	431 (1.6)	338 (2.7)	93 (0.6)
Hand eczema ^a	2,681 (9.8)	960 (7.8)	1,721 (11.4)
History of atopy ^b	9,752 (35.6)	4,360 (35.3)	5,392 (36.0)
Physical exercise ^b	12,102 (44.5)	5,686 (46.4)	6,416 (42.9)
Stress ^b	8,320 (30.5)	3,037 (24.7)	5,283 (35.2)
Obesity ^b	2,704 (9.8)	1,304 (10.6)	1,400 (9.3)

^a1-year prevalence. ^bVarying number of responders to the respective questions.

common among men than women, *p* < 0.001. Smoking was more frequent in women of all ages, *p* < 0.001. Cochran's *q*-tests revealed significant *p*-values within each tobacco use group (exclusive snus users (*p* < 0.001), exclusive smokers (*p* = 0.043) and dual users (*p* < 0.001)). The distributions of proportions of tobacco use based on age groups were significantly different between men and women.

The reported one-year prevalence of HE was 9.8%, (men 7.8%, women 11.4%, *p* < 0.001). The one-year prevalence of HE in relation to sex and age is presented in Fig. 2. In all age groups HE was more common in women than in men and the highest prevalence was found in women less than 40 years of age. However, according to Cochran's *q*-test the distributions of proportions of HE based on 5 age groups gave a *p*-value of 0.051 for the difference between men and women.

HE was reported by 7.5% (men 6.5%, women 11.8%) of exclusive snus users, 11.7% (men 8.6%, women 13.6%) of exclusive smokers and 9.7% (men 7.9%, women 11.0%) of non-tobacco users, *p* < 0.001 for these 3 comparisons of HE prevalence between men and women.

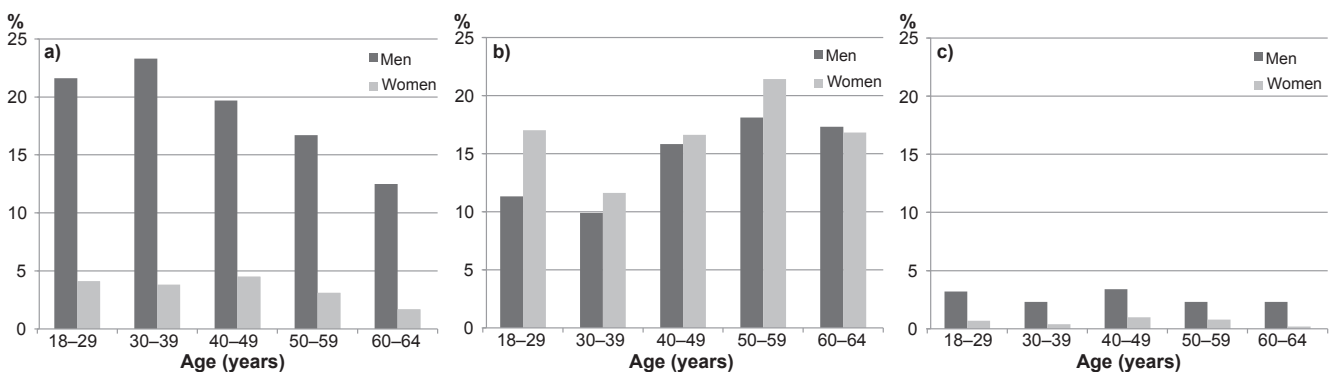


Fig. 1. Tobacco use habits in relation to sex and age: a) exclusive snus use, b) exclusive smoking, c) dual use.

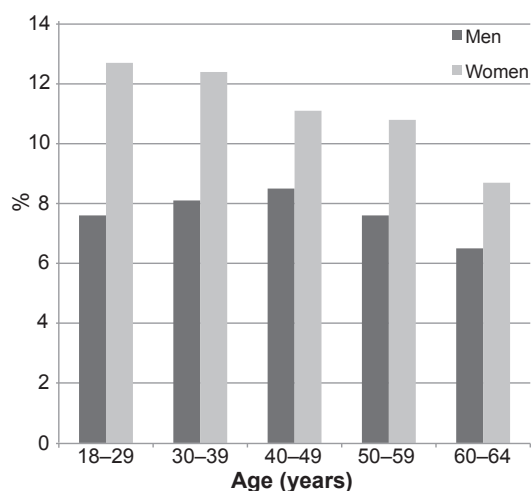


Fig. 2. One-year prevalence of hand eczema in relation to sex and age.

Table II presents univariate analyses of tobacco use habits and the potential confounders of sex, age, history of atopy, physical exercise, stress and obesity in relation to the one-year prevalence of HE. In the group as a whole, there was a negative relation between exclusive snus use and HE (PPR=0.770) and a positive relation between exclusive smoking and HE (PPR=1.205). An increase in PPR was confirmed for history of atopy, stress, female sex, young age and obesity. Physical exercise resulted in a decrease in PPR.

Table III shows results from multivariate analyses regarding the relation between tobacco use habits and one-year prevalence of HE, adjusted for confounders. With non-tobacco-users as reference, HE was significantly less common in exclusive snus users, in total PPR=0.813 and in men PPR=0.820. HE was significantly more common in women reporting exclusive smoking, PPR=1.238. Physical exercise was found to be a confounder in the multivariate analysis of the total study population, and sex was found to be an effect

modifier since the difference in prevalence of HE between men and women was significantly larger among exclusive snus users than among non-tobacco-users, $p=0.046$ (Fig. 3). In the separate multivariate analyses of the sexes no confounders were identified. Additional analyses of the sex distribution of tobacco use habits and of physical exercise in relation to tobacco use habits are presented in Appendix S1¹, Fig. S1¹, Tables SI and SII¹.

Doctor's diagnosis of psoriasis was reported by 3.3% (910/27,338). In a multivariate analysis of tobacco use in relation to psoriasis, exclusive snus use gave PPR=1.064 (95% CI 0.861–1.316), $p=0.566$, and exclusive smoking PPR=1.490 (95% CI 1.264–1.756), $p<0.0001$, with non-tobacco-users as reference. No confounders were identified.

DISCUSSION

Self-reports of tobacco use and HE in data from a large population-based public health survey were analysed. In contrast to smoking, no positive association between snus use and HE was found. HE was found to be significantly more common in smoking than in non-smoking women. As in previous studies HE was found to be significantly more common in women than in men.

In the univariate analysis of the entire study population a negative association was found between HE and snus use. Likewise, in the multivariate analysis when potential confounders and effect modifiers were taken into consideration, snus use gave a PPR=0.813. In the multivariate analyses of the total population, neither sex, nor age nor history of atopy were found to be confounders, but sex was an effect modifier (Fig. 3) reflecting the differences in tobacco use habits between

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Table II. One-year prevalence of hand eczema in relation to tobacco use and potential confounders expressed as prevalence proportion ratio (PPR), univariate analysis. For definition of variables see Methods

	Total		Men		Women	
	PPR	95% CI	PPR	95% CI	PPR	95% CI
Tobacco use						
No tobacco use	1					
Daily exclusive snus use	0.770	0.674–0.881	0.820	0.692–0.971	1.081	0.855–1.366
Daily exclusive smoking	1.205	1.094–1.327	1.091	0.908–1.311	1.238	1.105–1.386
Daily dual use	1.002	0.750–1.340	1.235	0.886–1.722	0.883	0.474–1.647
Potential confounders						
Sex, men vs women	1.467	1.360–1.581				
Age						
18–29 years	1.387	1.203–1.598	1.178	0.933–1.488	1.449	1.209–1.735
30–39 years	1.384	1.207–1.587	1.251	1.004–1.558	1.418	1.189–1.691
40–49 years	1.302	1.133–1.496	1.317	1.060–1.637	1.265	1.056–1.515
50–59 years	1.225	1.063–1.412	1.172	0.937–1.466	1.235	1.028–1.484
60–64 years	1		1		1	
History of atopy, yes vs no	1.909	1.777–2.052	1.852	1.640–2.093	1.937	1.773–2.117
Physical exercise, yes vs no	0.780	0.724–0.840	0.764	0.674–0.866	0.805	0.734–0.883
Stress, yes vs no	1.528	1.420–1.643	1.536	1.352–1.746	1.434	1.312–1.568
Obesity, >30 vs ≤30	1.232	1.104–1.376	1.304	1.093–1.557	1.215	1.056–1.398

Table III. One-year prevalence of hand eczema in relation to tobacco use expressed as prevalence proportion ratio (PPR), multivariate analysis, adjusted for confounders

	Total			Men			Women		
	PPR	95% CI	p-value	PPR	95% CI	p-value	PPR	95% CI	p-value
No tobacco use	1			1			1		
Daily exclusive snus use	0.813	0.686–0.964	0.017	0.820	0.692–0.971	0.022	1.081	0.855–1.366	0.515
Daily exclusive smoking	1.023	0.848–1.234	0.811	1.091	0.908–1.311	0.351	1.238	1.105–1.386	<0.001
Daily dual use	1.187	0.851–1.655	0.313	1.235	0.886–1.722	0.214	0.883	0.474–1.647	0.697

the sexes. From previous experience, the life-style factors stress, obesity and physical exercise were included in the analyses as potential confounders (12). Physical exercise was the only confounder identified in the analysis of the entire study population.

When the sexes were analysed separately, no confounders were identified. The proportions of individuals of young age, who had atopy, high BMI and who experienced stress differed only slightly (and non-significantly) between exclusive smokers, snus users and dual users in comparison with non-tobacco-users.

In the univariate analysis of the entire population, smoking was associated with HE, PPR = 1.205, but in the multivariate analysis the PPR value decreased, PPR = 1.023. Less physical exercise was reported by smokers, and an uneven sex distribution of smokers was shown to be of importance. In the analyses of the sexes separately, a significant positive association between smoking and HE among women was confirmed, PPR = 1.238. Additional analyses are presented in Appendix S1¹.

Previous studies on the association between smoking and the occurrence of HE present ambiguous results (1–3, 16–18). A positive association between heavy smoking and HE as well as a dose-response relation was shown in one population-based study (2), but not indicated in another study with limited response rate (44%) (3). Thus, the level of exposure seems to be of importance. In our study no information was available regarding

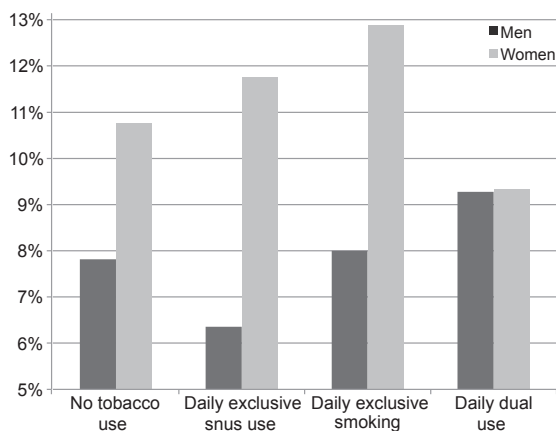


Fig. 3. One-year prevalence of hand eczema in relation to tobacco use habits among men and women. The bars represent estimated proportions calculated from post-hoc analyses which are included in the procedure performing prevalence proportion ratios. The multivariate model includes sex, physical exercise and the interaction term tobacco use*sex.

the intensity of smoking and snus use, which may have contributed to make the results somewhat indistinct. The non-snus-use and non-smoking groups include infrequent snus users and smokers. The influence of this misclassification should be regarded as negligible.

The tobacco use habits differed considerably between the sexes in Sweden at the time of the survey. Our findings correspond to previous reports on Swedish tobacco use habits (10). In 1992, the EU adopted a tobacco directive prohibiting the sale of tobacco for oral use, unless it was to be smoked or chewed (19). Since 1994 Sweden has been exempted from this EU ban on snus. However, the tobacco directive is under revision. The health effects that follow upon use of snus and tobacco smoking differ, though the user attains comparable levels of nicotine through both means of intake (20).

Several studies have compared the health effects of snus use and smoking on inflammatory diseases. A positive association has been demonstrated between smoking and the occurrence of psoriasis (6), rheumatoid arthritis, Chron's disease, ulcerative colitis (21), and multiple sclerosis (21, 22), whereas the same studies found no similar association to use of snus. This is in accordance with the findings in the present study regarding HE and psoriasis.

To the best of our knowledge there is hitherto no comprehensive explanation given for the difference in association between different tobacco exposures and inflammatory diseases. The chemistry of tobacco is complex with more than 3,000 different identified chemicals. *In vitro* studies on the death of blood mononuclear cells exposed to ethanol extracts of cigarette smoke and of snus showed significant differences between the extracts (23). Tobacco plants belong to the botanical family *Solanaceae* which includes around 90 species, including important medical plants. Besides the *Nicotiana* species there are also species with demonstrated anti-inflammatory activity, i.e. the poisonous *Datura stramonium* previously used in anti-asthma cigarettes (24). To what extent such observations can contribute to an explanation/understanding of the lack of positive and even negative association found between regular snus use and HE needs further investigations. It remains to be explored in what way routes of exposure, diverse chemical components, and combustion of tobacco influence the biological effects.

The present study has a cross-sectional design, and thus no conclusions on causality can be drawn. A

strength of the study is the large sample size. Weaknesses include the moderate response rate (58%). This is in line with a downward trend regarding response rates to public health surveys in Stockholm, 72% in 1990 and 57% in 2010. Another weakness is the lack of information on dosage for both snus use and smoking. Since HE is a disease with a multifactorial background it is important to consider possible confounders and effect modifiers. In the present study information on several risk factors and life-style factors was available and was taken into consideration in the analyses. No information on atopic dermatitis was available, which makes the concept of atopy incomplete. The question about HE has previously been validated, and was found to give an underestimation of the true prevalence of HE (13). Trends towards underestimation of the prevalence of smoking were found in a comprehensive survey on the accuracy of self-reported smoking data confirmed by cotinine measurements (25). On the other hand adolescent Swedish smokers and snus users were shown to give valid reports of their tobacco use when examined with cotinine tests (26).

In conclusion, no positive association could be demonstrated between the use of Swedish moist snuff – snus – and the occurrence of HE. This is in contrast to the positive association previously shown between heavy smoking and HE, and now also found in smoking women.

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