Scandinavian Journal of Public Health, 2006; 34: 576–583

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Contribution of Swedish moist snuff to the metabolic syndrome: A wolf in sheep's clothing?

MARGARETA NORBERG[1], HANS STENLUND[1], BERNT LINDAHL[2], KURT BOMAN[3] & LARS WEINEHALL[1,4]

[1]*Epidemiology and Public Health Sciences,* [2]*Behavioral Medicine, Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden,* [3]*Department of Medicine–Geriatric, Skellefteå County Hospital, Skellefteå and Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden, and* [4]*National Public Health Institute, Stockholm, Sweden*

Abstract
Aim: Combined effects of genetic and environmental factors underlie the clustering of cardiovascular risk factors in the metabolic syndrome (MetSy). The aim was to investigate associations between several lifestyle factors and MetSy, with a focus on the possible role of smokeless tobacco in the form of Swedish moist snuff (snus). *Methods:* A population-based longitudinal cohort study within the Västerbotten Intervention Programme in Northern Sweden. All inhabitants at the ages of 30, 40, 50, and 60 are invited to participate in a health survey that includes a questionnaire on psychosocial conditions and lifestyle and measurement of biological variables. Individuals examined in 1990–94 (n=24,230) and who also returned for follow-up after 10 years were included (total of 16,492 individuals: 46.6% men and 53.4% women). Regression analyses were performed. MetSy was the outcome and analyses were adjusted for age, sex, alcohol abuse, and family history of CVD and diabetes. *Results:* Ten-year development of MetSy was associated with high-dose consumption of snus at baseline (OR 1.6 [95% CI 1.26–2.15]), low education (2.2 [1.92–2.63]), physical inactivity (1.5 [1.22–1.73]) and former smoking (1.2 [1.06–1.38]). Snus was associated with separate components of MetSy, including triglycerides (1.6, 1.30–1.95), obesity (1.7 [1.36–2.18]) but not hypertension, dysglycemia and low HDL cholesterol. *Conclusions:* MetSy is independently associated with high consumption of snus, even when controlling for smoking status. The finding is of public health interest in societies with widespread use of snus. More research is needed to better understand the mechanisms underlying this effect.

Key Words: *Lifestyle, metabolic syndrome, smokeless tobacco, risk factors, public health*

Introduction

The metabolic syndrome (MetSy) is a worldwide time bomb, fuelled by increasing obesity [1] and signified clinically and epidemiologically by its association with cardiovascular disease (CVD) [2]. There are several working definitions of MetSy with varying constellations and criteria of the principal components: obesity, impaired glucose regulation, dyslipidemia, and hypertension [3–5]. MetSy is currently debated primarily because an underlying pathophysiologial cause (or causes) has not been clearly elucidated and no specific treatment is available that targets the syndrome beyond the usual treatments of its individual components [6,7]. However, MetSy is thought to facilitate the clinical focus on individuals at high risk of CVD and diabetes [5].

Interacting effects of genetic and environmental factors underlie the clustering of MetSy components [4]. Although genes determine the individual susceptibility to obesity and MetSy, the main reasons for the obesity epidemic are societal changes with increased consumption of energy-dense food and

Correspondence: Margareta Norberg, Epidemiology and Public Health Sciences, Umeå University Hospital Bldg 9B, SE-901 85 Umeå, Sweden. Tel: +46 90 7853343. Fax: +46 90 138977. E-mail: margareta.norberg@epiph.umu.se

(Accepted 2 March 2006)

ISSN 1403-4948 print/ISSN 1651-1905 online/06/060576-8 © 2006 Taylor & Francis
DOI: 10.1080/14034940600665143

decreased physical activity [1]. Psychosocial and sociodemographic factors [8], as well as heavy use of alcohol and cigarette smoking, also contribute to MetSy [9].

In Northern Sweden, rapid shifts in lifestyle habits are occurring with a substantial decrease in smoking, especially among men, paralleled with increased use of Swedish moist snuff (snus) in both men and women [10]. It has been proposed that the use of snus is contributing to the decline in smoking rates [11]. However, snus is not necessary for smoking cessation at the population level [12].

Numerous studies have shown a link between smoking and several components of MetSy [13]. Studies on the effect of smokeless tobacco are fewer and have conflicting results. While acute effects of exposure to smokeless tobacco such as increased heart rate and blood pressure have been reported [14], chronic effects on blood pressure and glucose and insulin levels have not been found [15,16]. However, associations between snus and overweight [17] and triglycerides [15] have been demonstrated. One study also showed ultrasound-measured subclinical atherosclerosis among smokers but not among snus users [15]. Another study demonstrated impaired endothelial function among snus users [18]. A large Swedish study found increased CVD mortality among construction workers using snus [19]. Other studies from Sweden have failed to prove an increased risk of myocardial infarction [20,21] or stroke [22]. Heavy consumers of snus ($\geq$3 cans/week) have been reported to have an increased risk of type 2 diabetes [23]. Another study that did not stratify for different doses of snus failed to find any association with diabetes among snus users [24].

Several overview articles have concluded that although the tobacco-associated risk of disease undoubtedly is greater with smoking, most studies on smokeless tobacco have been too small to be conclusive. More research, with larger and longitudinal panel studies, is therefore needed on the impact of smokeless tobacco on disease outcomes [25–27]. In this study we use a prospective cohort design to investigate associations between lifestyle factors and MetSy, with a focus on the possible role of snus as one piece in the jigsaw puzzle of lifestyle patterns.

Material and methods

This is a prospective cohort study using a subset of the Västerbotten Intervention Programme (VIP), a community programme for prevention of CVD and diabetes. VIP started 1985 in the county of Västerbotten in northern Sweden and has been described in detail previously [28]. Briefly, at the ages of 30, 40, 50, and 60 years, all inhabitants are invited to their primary care centre for a health survey. Participants answer a comprehensive questionnaire on psychosocial conditions and lifestyle. An oral glucose tolerance test (OGTT) is performed. Body mass index (BMI), blood pressure, and blood lipids are measured. Central obesity, as measured by waist circumference, was not recorded until 2003. HDL cholesterol was measured only if the total cholesterol was >6.5 mmol/L or if any of the other criteria of MetSy according to the WHO definition were present. At the end of the health survey information about the examination results and individual lifestyle counselling were given. When the programme was launched, reduction of hypertension, hypercholesterolemia, and smoking was targeted since these were established CVD risk factors. The participation rate has been 60% on average. No significant differences in socioeconomic status have been demonstrated between participants and non-participants [28]. The present study includes individuals aged 30, 40, or 50 years who first were examined in 1990–94 (n=24,230) and returned for follow-up 10 years later. This comprises a total of 16,492 individuals (46.6% men and 53.4% women).

Metabolic syndrome was identified at follow-up according to the new definition from the International Diabetes Federation (IDF). This definition assumes central obesity if the BMI is >30 [5] (Table I). The National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATP III) definition was not applied since waist circumference was not measured in the whole study population. The World Health Organization (WHO) definition was used in an additional analysis.

Subjects were grouped according to lifestyle habits and educational level at baseline. Smoking was stratified into non-smoking, ex-smoking, and daily smoking. The non-smoking group included never smokers, those who smoked occasionally, and former occasional smokers. Ex-smoking included only former daily smokers. Daily smoking included daily smokers of cigarettes (without grading due to number of cigarettes consumed), cigar, and pipe. The questionnaire encoded the use of snus as follows: never use, former use, consumption of <2 cans of snus/week, 2–4 cans/week, 5–6 cans/week, or$\geq$7 cans/week. For simplicity this was categorized into no use (including never and former use), low dose use ($\leq$4 cans/week), and high dose use (>4 cans/week). The Cage questionnaire was used to

Table I. Criteria for the clinical diagnosis of Metabolic Syndrome according to the World Health Organization (WHO), National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATP III) and the International Diabetes Federation (IDF).

WHO criteria	
Impaired glucose regulation identified by one of the following: • Type 2 diabetes • Impaired fasting glucose • Impaired glucose tolerance • Lowest quartile glucose uptake under hyperinsulinemic euglycaemic conditions	Plus any two of the following: • Blood pressure≥140/90 and/or antihypertensive medication • Triglycerides≥1.7 mmol/L and/or HDL cholesterol<0.9 mmol/L in men, <1.0 mmol/L in women • BMI≥30 and/or waist–hip ratio>0.9 in men, >0.85 in women • Urinary albumin≥20 μg/min or albumin:creatinine ratio≥30 mg/g
NCEP/ATP III criteria Any three of the following: • Fasting plasma glucose≥5.6 mmol/L • Blood pressure≥130/85 or antihypertensive medication • Triglycerides≥1.7 mmol/L or specific drug treatment • HDL cholesterol<1.0 mmol/L in men, <1.3 mmol/L in women or specific drug treatment • Waist circumference≥102 cm in men, ≥88 cm in women	
IDF criteria • Waist≥94 cm in men, ≥80 cm in women[1]	Plus any two of the following: • Blood pressure≥130/85 and/or antihypertensive medication • Triglycerides≥1.7 mmol/L or medication • HDL cholesterol<1.03 mmol/L in men, <1.29 mmol/L in women or medication • Fasting plasma glucose≥5.6 mmol/L[2] or previously known diabetes

[1]If BMI is>30, central obesity can be assumed and waist circumference need not be measured. [2]In clinical practice, impaired glucose tolerance (IGT) is also accepted. Prevalences including IGT can be added as supplementary findings.

evaluate for alcohol abuse and graded on the number of positive answers to the four questions (Cut down, Annoyance, Guilt, Eye-opener) [29]. Level of education was grouped into high (≥13 school years or university), medium (10–12 years), and low (9 years or less). Physical activity was assessed from a question on exercise in training clothes in leisure time, and stratified into four groups: at least twice/week, once/week, ''now and then'', and ''never''. Univariate and multivariate logistic regression analyses were performed using SPSS v11, with lifestyle variables at baseline as predictors and the presence of the metabolic syndrome at follow-up as outcome.

The protocol was approved by the Research Ethics Committee of Umeå University and all participants gave informed consent.

Results

Clinical characteristics for participants at baseline and follow-up are given in Table II. The frequency of missing data was 0–5% except for HDL cholesterol, which was missing in 87.9% of women and 86.2% of men at baseline and in 75.2 and 71.4%, respectively, at follow-up. There were 594 subjects with obesity and also one trait out of dysglycemia, hypertension, or hypertriglyceridemia. This could have added at maximum 3.6% to the MetSy prevalence, provided all of them also had low HDL cholesterol. The study subjects were in early middle age at baseline. We did not use the result of 2-h glucose testing in the case definition of MetSy according to IDF as this only added 9 women and 6 men with MetSy at follow-up. There were significant shifts in almost all metabolic variables from baseline to the re-examination at 10-year follow-up. Of note is the large increase in use of lipid-lowering and antihypertensive medications. There was a decrease in smoking rates with only 12.7% of men and 15.6% of women categorized as daily smokers at follow-up. The use of snus, mainly low-grade consumption, increased with a near doubling among women from 3.1% to 6.0%. Almost one out of four men used snus at baseline and there was a small but significant increase to 26.3% at follow-up. Physical activities in leisure time also changed: the number of those who reported never exercising increased, as well as the number reporting exercising at least twice a week. Women reported significantly more, and men significantly fewer alcohol problems at follow-up.

The results of bivariate and multivariate regression analyses are given in Table III. All evaluated lifestyle factors were significantly associated with the

Table II. Clinical characteristics for women and men at baseline and 10-year follow-up. Mean ± SD or numbers of observations and frequency are given.

	Women n=8,800			Men n=7,692		
	Baseline	Follow-up		Baseline	Follow-up	
Age, years	41.6 ± 7.6	51.1 ± 7.6		41.2 ± 7.7	51.2 ± 7.7	
Metabolic syndr IDF *n* (%)	311 (3.5)	940 (10.7)	<0.001	276 (3.6)	864 (11.2)	<0.001
Metabolic syndr WHO *n* (%)	158 (1.8)	768 (8.7)	<0.001	140 (1.8)	836 (10.9)	<0.001
Body mass index (kg/m^2)	24.4 ± 3.9	26.0 ± 4.6	<0.001	25.5 ± 3.1	26.6 ± 3.7	<0.001
Triglycerides (mmol/L)	1.2 ± 0.7	1.3 ± 0.8	<0.001	1.5 ± 1.0	1.5 ± 0.9	0.743
Cholesterol (mmol/L)	5.37 ± 1.12	5.42 ± 1.06	<0.001	5.62 ± 1.21	5.43 ± 1.06	<0.001
HDL cholesterol[1] (mmol/L)	1.5 ± 1.0	1.4 ± 0.6	0.152	1.5 ± 2.4	1.1 ± 0.5	0.001
Lipid-lowering drug *n* (%)	11 (0.1)	261 (3.0)	<0.001	32 (0.4)	374 (4.9)	<0.001
Systolic BP (mmHg)	120.5 ± 15.0	126.5 ± 18.7	<0.001	125.3 ± 13.8	128.9 ± 16.8	<0.001
Diastolic BP (mmHg)	75.6 ± 10.1	76.4 ± 10.5	<0.001	78.5 ± 10.0	79.6 ± 11.4	<0.001
Antihypertensive drug *n* (%)	417 (4.7)	1352 (15.4)	<0.001	261 (3.4)	1015 (13.2)	<0.001
Fasting P-glucose[1] (mmol/L)	5.1 ± 0.7	5.6 ± 0.9	<0.001	5.2 ± 0.8	5.8 ± 1.3	<0.001
2-hour P-glucose[2] (mmol/L)	6.6 ± 1.4	7.0 ± 1.6	<0.001	5.9 ± 1.4	6.6 ± 1.7	<0.001
Ex-smoker *n* (%)	1502 (17.1)	1933 (22.0)	<0.001	1709 (22.2)	1989 (25.9)	<0.001
Daily smoker *n* (%)	1957 (22.2)	1374 (15.6)	<0.001	1418 (18.4)	978 (12.7)	<0.001
Snus ⩽ 4 cans/week *n* (%)	238(2.7)	454 (5.2)	<0.001	1449 (18.9)	1487 (19.3)	<0.001
Snus > 4 cans/week n(%)	32 (0.4)	68 (0.8)	<0.001	438 (5.7)	532 (6.9)	<0.001
Physically inactive[3] *n* (%)	3147 (37.4)	3677 (43.7)	<0.001	2797 (37.9)	3365 (45.6)	<0.001
Physically active[4] *n* (%)	990 (11.8)	1513(18.0)	<0.001	1143 (15.5)	1380 (18.7)	<0.001
Alcohol[5] *n* (%)	180 (2.0)	216 (2.8)	<0.001	727 (9.4)	694 (9.0)	<0.001
Family history[6] *n* (%)	1336 (32.1)	1609 (38.7)	<0.001	1032 (28.8)	1233 (34.4)	<0.001

IDF=International Diabetes Federation. WHO=World Health Organization. [1]Frequency missing data among women and men at baseline 87.9 and 86.2% respectively, at follow-up 75.2 and 71.4% respectively. [2]Measured on capillary plasma at an oral glucose tolerance test. [3]Exercise/training in leisure time: never. [4]Exercise/training: at least twice a week. [5]Cage questionnaire: Answered yes on at least two of the four questions. [6]Family history of cardiovascular disease or/and diabetes in first-degree relatives

MetSy according to the IDF definition. The odds ratio (OR) for family history of CVD and/or diabetes was 1.4 (CI 95% 1.29–1.59). The Cage questionnaire on alcohol habits showed a trend with increasing ORs with number of positive answers to the four questions. Ex-smoking, daily smoking, and consumption of >4 cans of snus/week were significantly associated with MetSy in univariate analysis, but only ex-smoking and high snus consumption contributed to the multivariate model. When the analyses were repeated using the WHO definition of MetSy, results were similar (data not shown). In additional analyses the original variable on snus use was applied with never use of snus as reference. Both in the bivariate and the full model there were significant ORs only for high doses of snus, in the multivariate model 1.5 (1.13–2.10) for consumption of 5–6 cans/week and 2.0 (1.20–3.39) for⩾7cans/week and all other ORs were unchanged.

We also evaluated possible associations of lifestyle factors with the separate components of the metabolic syndrome, i.e. according to the IDF definition, with adjustment for age, sex, educational level, Cage questionnaire, exercise habits, and family history of CVD and/or diabetes (Table IV). In this multivariate analysis daily smoking was not associated with obesity, while there seemed to be a decreased risk of hypertension and increased risk of the other components. We found increased ORs among ex-smokers for all MetSy components except low HDL cholesterol. Any use of snus was associated with hypertriglyceridemia and high snus consumption was associated with obesity. Further adjustment with BMI at baseline and BMI at follow-up in the multivariate analysis with hypertriglyceridemia as outcome showed excess risk for ex-smoking, daily smoking, low-dose and high-dose snus consumption with ORs 1.2 (1.10–1.35), 1.6 (1.48–1.81), 1.2 (1.06–1.37) and 1.4 (1.16–1.78) respectively.

Discussion

To our knowledge, this large-scale longitudinal panel study is the first study to show an independent association between metabolic syndrome and high snus consumption, even when controlling for smoking. However, we could not demonstrate an impact of snus on each of the separate features of metabolic

Table III. Bivariate regression analyses for lifestyle risk factors at baseline with the outcome metabolic syndrome at follow-up.[1]

	MetSy at follow-up *n*		Univariate model		Multivariate model	
Risk factors at baseline	Yes	No	OR	CI (95%)	OR	CI (95%)
Education						
High	248	3,534	1.0			
Medium	922	7,557	**1.8**	1.53–2.05	**1.7**	1.43–1.92
Low	586	3,342	**2.5**	2.10–2.87	**2.2**	1.91–2.63
Alcohol problem[2] (4 questions)						
No	1,563	12,696	1.0			
1 yes	134	1,192	1.0	0.80–1.17	1.0	0.81–1.19
2 yes	73	583	1.1	0.84–1.40	1.1	0.85–1.42
3 yes	24	160	1.3	0.86–2.05	1.2	0.74–1.83
4 yes	12	55	**1.9**	1.00–3.51	1.4	0.68–2.68
Exercise/training						
At least twice a week	182	1977	1.0			
Once/week	276	3136	0.9	0.76–1.13	1.0	0.79–1.17
Now and then	503	3861	**1.4**	1.16–1.65	**1.4**	1.14–1.64
Never	764	5245	**1.5**	1.29–1.82	**1.5**	1.22–1.73
Smoking						
Non-smoking	988	8918	1.0			
Ex-smoker	416	2795	**1.3**	1.18–1.51	**1.2**	1.06–1.38
Daily smoking	402	2973	**1.2**	1.06–1.35	1.0	0.89–1.16
Swedish moist snuff, snus						
No use	1498	12,344	1.0			
$\leqslant$4 cans/week	174	1516	1.1	0.90–1.27	1.0	0.85–1.22
$>$4 cans/week	74	396	**1.8**	1.36–2.30	**1.6**	1.26–2.15

[1]The analyses were adjusted for age, sex, and family history of CVD and/or diabetes in first-degree relatives at follow-up. Statistically significant findings are shown in bold. [2]Cage questionnaire.

syndrome. There was an independent association between high, but not low, snus consumption and obesity development [17]. Second, there was a significant and dose-dependent association between the use of snus at baseline and hypertriglyceridemia after 10 years. Lastly, high-dose snus consumption was associated with hypertension although this did not reach statistical significance. In contrast, we could not demonstrate a link to dysregulation of glucose or HDL cholesterol. Our results are similar to a recent cross-sectional study that showed a dose-dependent association between smoking and MetSy and hypertriglyceridemia, low HDL cholesterol, and abdominal obesity [30]. Our results also support previous findings of associations between family history of CVD and diabetes, educational level, physical inactivity, and smoking with metabolic syndrome.

Table IV. Odds ratios (95% confidence intervals) for smoking and snus consumption in multivariate regression analyses with the components of the metabolic syndrome as outcomes.

	OR of components of Metabolic Syndrome at 10-year follow-up				
Risk factors at baseline[1]	f- P-glucose$\geqslant$5.6 or diabetes[2]	Triglycerides$\geqslant$1.7	Low HDL cholesterol[3]	Hypertension[4]	Body mass index$\geqslant$30
Smoking					
Ex-smoker	**1.2** (1.15–1.35)	**1.3** (1.16–1.41)	1.1 (1.00–1.27)	**1.2** (1.07–1.27)	**1.2** (1.04–1.30)
Daily smoking	**1.3** (1.23–1.45)	**1.6** (1.43–1.73)	**1.2** (1.07–1.35)	**0.8** (0.75–0.89)	1.1 (0.98–1.23)
Use of snus					
$\leqslant$4 cans/week	1.0 (0.86–1.08)	**1.2** (1.05–1.35)	1.0 (0.86–1.18)	0.9 (0.84–1.05)	1.0 (0.88–1.20)
$>$4 cans/week	0.8 (0.69–1.02)	**1.6** (1.30–1.95)	1.1 (0.82–1.42)	1.2 (0.99–1.46)	**1.7** (1.36–2.18)

The metabolic syndrome was defined according to the International Diabetes Federation (IDF). [1]Non-smoking and no use of snus are references with OR 1.0. Multivariate regression analyses were adjusted for age, sex, educational level, alcohol use by Cage questionnaire, physical activity/exercise in leisure time, and family history in first-degree relatives of CVD and/or diabetes. Statistically significant findings are shown in bold. [2]Fasting plasma glucose$\geqslant$5.6 mmol/L or diabetes known before the health survey. [3]HDL cholesterol$\leqslant$1.03 in men and HDL$\leqslant$1.29 mmol/L in women or lipid-lowering medication. [4]Blood pressure$\geqslant$130/85 mmHg or ongoing antihypertensive medication.

Our results agree with several previous studies showing associations between snus and MetSy components of obesity [17,21], hypertriglyceridemia [15] and hypertension [21]. Dose–response relationships between snus and metabolic parameters, as indicated by our results, might explain why previous studies with smaller sample sizes or samples that did not dose-stratify have failed to show associations [16] or have shown non-significant trends [14,31]. A dose-dependent effect from snus is supported by animal studies, which show that high doses of nicotine induce lipolysis in adipose tissue, leading to increased levels of free fatty acids, thereby causing increased levels of triglycerides by the production of very low-density lipoproteins in the liver [25]. Snus may cause impaired endothelial function [18] and thereby further increase cardiovascular risks. This effect and a hypertensive effect have also been suggested as explanations of adverse pregnancy outcomes in snuff users [32]. However, our study can not explain the mechanism of the dysmetabolic effects, particularly at high doses, from snus. In addition to a direct effect from nicotine, or any other chemical substance in snus, the use of snus might also be a marker of other unhealthy behaviours, e.g. food or alcohol habits, as has previously been shown for smoking [33].

Studies on snus and disease outcomes, particularly cardiovascular disease and diabetes, have shown inconsistent results [13,19,20,22,23]. This might be attributed to methodological problems. The large study by Bolinder showed a significant excess risk of cardiovascular disease in snus users compared with non-users of tobacco, but a significantly lower risk than that of smokers [19]. That study has been criticized as it was not adjusted for alcohol consumption and cholesterol. In the studies by Huhtasaari and Asplund [20,22] the snuff-using group was confounded by ex-smokers. In a recent study on myocardial infarction by Hergens the analysis was based on very few cases of former ($n=7$) or current ($n=10$) snuff users not being former or current smokers. Similar concerns can be raised regarding recent studies on diabetes risk and snus [13,23] although the study by Eliasson also had a prospective longitudinal observational design.

In this study we did not stratify smokers by number of cigarettes smoked. However, it is shown that ex-smokers have higher and smokers have lower BMI than non-smokers, and that smokers have a more central fat distribution than non-smokers, with higher waist the more smoked cigarettes (pack years) [34]. Visceral fat has more adverse metabolic effects [5] and this might explain why daily smoking, although not significantly associated with obesity, affected the other components of MetSy in different directions, i.e. increased risk of dysglycemia, hypertriglyceridemia, and low HDL cholesterol and reduced risk of hypertension (see Table IV). These findings support other studies [30], and might explain why we did not find any independent association between daily smoking and MetSy. Ex-smoking, on the other hand, was independently associated with obesity and this might explain the association with MetsSy and its components.

The study should be interpreted with some methodological issues in mind. First it has the strength that it is population-based, large, and longitudinal. Because it is prospective there is no issue of recall bias in the evaluation of the long-term lifestyle habits. One weakness is that we were not able to evaluate alcohol consumption objectively, but were dependent on self-report. The Cage questionnaire is only able to evaluate problems from alcohol abuse. We could not evaluate social conditions in terms of economic situation or occupation but education should be relevant as a socioeconomic measure.

According to the IDF definition we assumed central obesity when BMI was$\geqslant$30 and did not include the waist. Therefore subjects with BMI$<$30 with central obesity and MetSy were missed. VIP has been launched as an intervention programme and therefore subjects who already have established contact with a physician or have a disease might be less prone to participate in the health survey, leading to a possible selection towards a healthy population and contributing to the considerably lower prevalence of MetSy as compared with other studies [2]. However this should not weaken the results with regard to possible effects from snus and other variables, as the effects on less healthy populations probably should be at least as large. The missing values of HDL cholesterol could also to some extent explain the comparatively low prevalences for MetSy in this study.

MetSy includes several single risk factors and this might be especially relevant to snus since it appears to be a product that has the potential to influence several biological metabolic systems. We consider MetSy to be a clinically relevant outcome for research on effects of snus. MetSy is also applicable in the clinical setting because it enables us to focus on individuals at high risk of CVD with multiple possible ways to intervene [4,5]. In our study, the results were essentially the same irrespective of whether the IDF or the WHO definition of MetSy was applied. Therefore it should be possible to generalize our results to cardiovascular morbidity

and mortality as is shown for MetSy by the WHO definition [2]. However, more research is needed to explore the possible role of snus in CVD and diabetes. Both longitudinal studies and experimental mechanistic studies would shed needed light on this subject. The consumption pattern of snus is complicated and highly associated with smoking. People shift from current to former use of either snus or smoking and some use both products concomitantly. Since the CVD risk of smoking is considered to be greater than that of snus, further large studies are needed to separate potential snus effects, at different doses, from effects of smoking and other lifestyle habits. Even if snus carries a smaller individual risk than smoking, from a public health perspective the rapidly increasing use of snus, in both men and women and particularly in the younger subgroups of the population, must be seen as a highly relevant concern.

In summary, in addition to the well-known health risks of cigarette smoking and physical inactivity, high doses of snus increase the risk of metabolic syndrome. Snus has the greatest effect on obesity and hypertriglyceridemia but may also increase risk of hypertension. This is an important public health issue, at least in societies with widespread snus use. At the present time it would be wise to abstain from declaring snus harmless in respect of MetSy with subsequent risk of CVD and diabetes.

Acknowledgement

This study was supported by grants from Västerbotten County Council.

References

[1] WHO. Global strategy on diet, physical activity and health. Geneva: WHO; 2005.

[2] Isomaa B, Almgren P, Tuomi T, Forsen B, Lahti K, Nissen M, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care 2001;24:683–9.

[3] Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications, Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med 1998;15:539–53.

[4] Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome. An American Heart Association/ National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005.

[5] Alberti KG, Zimmet P, Shaw J. The metabolic syndrome: A new worldwide definition. Lancet 2005;366:1059–62.

[6] Kahn R, Buse J, Ferrannini E, Stern M. The metabolic syndrome: Time for a critical appraisal. Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetologia 2005;48:1684–99.

[7] Gale EA. The myth of the metabolic syndrome. Diabetologia 2005;48:1679–83.

[8] Lidfeldt J, Nyberg P, Nerbrand C, Samsioe G, Schersten B, Agardh CD. Socio-demographic and psychosocial factors are associated with features of the metabolic syndrome. The Women's Health in the Lund Area (WHILA) study. Diabetes Obes Metab 2003;5:106–12.

[9] Zhu S, St-Onge MP, Heshka S, Heymsfield SB. Lifestyle behaviors associated with lower risk of having the metabolic syndrome. Metabolism 2004;53:1503–11.

[10] Lindahl B, Stegmayr B, Johansson I, Weinehall L, Hallmans G. Trends in lifestyle 1986–99 in a 25- to 64-year-old population of the Northern Sweden MONICA project. Scand J Public Health 2003;61(Suppl):31–7.

[11] Rodu B, Stegmayr B, Nasic S, Cole P, Asplund K. Evolving patterns of tobacco use in northern Sweden. J Intern Med 2003;253:660–5.

[12] Gilljam H, Galanti MR. Role of snus (oral moist snuff) in smoking cessation and smoking reduction in Sweden. Addiction 2003;98:1183–9.

[13] Eliasson B. Cigarette smoking and diabetes. Prog Cardiovasc Dis 2003;45:405–13.

[14] Westman EC. Does smokeless tobacco cause hypertension? South Med J 1995;88:716–20.

[15] Wallenfeldt K, Hulthe J, Bokemark L, Wikstrand J, Fagerberg B. Carotid and femoral atherosclerosis, cardiovascular risk factors and C-reactive protein in relation to smokeless tobacco use or smoking in 58-year-old men. J Intern Med 2001;250:492–501.

[16] Eliasson M, Asplund K, Evrin PE, Lundblad D. Relationship of cigarette smoking and snuff dipping to plasma fibrinogen, fibrinolytic variables and serum insulin. The Northern Sweden MONICA Study. Atherosclerosis 1995;113:41–53.

[17] Rodu B, Stegmayr B, Nasic S, Cole P, Asplund K. The influence of smoking and smokeless tobacco use on weight amongst men. J Intern Med 2004;255:102–7.

[18] Rohani M, Agewall S. Oral snuff impairs endothelial function in healthy snuff users. J Intern Med 2004;255:379–83.

[19] Bolinder G, Alfredsson L, Englund A, de Faire U. Smokeless tobacco use and increased cardiovascular mortality among Swedish construction workers. Am J Public Health 1994;84:399–404.

[20] Huhtasaari F, Lundberg V, Eliasson M, Janlert U, Asplund K. Smokeless tobacco as a possible risk factor for myocardial infarction: A population-based study in middle-aged men. J Am Coll Cardiol 1999;34:1784–90.

[21] Hergens MP, Ahlbom A, Andersson T, Pershagen G. Swedish moist snuff and myocardial infarction among men. Epidemiology 2005;16:12–16.

[22] Asplund K, Nasic S, Janlert U, Stegmayr B. Smokeless tobacco as a possible risk factor for stroke in men: A nested case-control study. Stroke 2003;34:1754–9.

[23] Persson PG, Carlsson S, Svanstrom L, Ostenson CG, Efendic S, Grill V. Cigarette smoking, oral moist snuff use and glucose intolerance. J Intern Med 2000;248: 103–10.

[24] Eliasson M, Asplund K, Nasic S, Rodu B. Influence of smoking and snus on the prevalence and incidence of type 2 diabetes amongst men: Rhe northern Sweden MONICA study. J Intern Med 2004;256:101–10.

[25] Kilaru S, Frangos SG, Chen AH, Gortler D, Dhadwal AK, Araim O, et al. Nicotine: A review of its role in atherosclerosis. J Am Coll Surg 2001;193:538–46.
[26] Asplund K. Smokeless tobacco and cardiovascular disease. Prog Cardiovasc Dis 2003;45:383–94.
[27] Hatsukami DK, Lemmonds C, Tomar SL. Smokeless tobacco use: Harm reduction or induction approach? Prev Med 2004;38:309–17.
[28] Weinehall L, Hallgren CG, Westman G, Janlert U, Wall S. Reduction of selection bias in primary prevention of cardiovascular disease through involvement of primary health care. Scand J Prim Health Care 1998;16:171–6.
[29] Aertgeerts B, Buntinx F, Kester A. The value of the CAGE in screening for alcohol abuse and alcohol dependence in general clinical populations: A diagnostic meta-analysis. J Clin Epidemiol 2004;57:30–9.
[30] Oh SW, Yoon YS, Lee ES, Kim WK, Park C, Lee S, et al. Association between cigarette smoking and metabolic syndrome: The Korea National Health and Nutrition Examination Survey. Diabetes Care 2005;28:2064–6.
[31] Bolinder G, Noren A, de Faire U, Wahren J. Smokeless tobacco use and atherosclerosis: An ultrasonographic investigation of carotid intima media thickness in healthy middle-aged men. Atherosclerosis 1997;132:95–103.
[32] England LJ, Levine RJ, Mills JL, Klebanoff MA, Yu KF, Cnattingius S. Adverse pregnancy outcomes in snuff users. Am J Obstet Gynecol 2003;189:939–43.
[33] Schroder H, Marrugat J, Elosua R, Covas MI. Tobacco and alcohol consumption: Impact on other cardiovascular and cancer risk factors in a southern European Mediterranean population. Br J Nutr 2002;88:273–81.
[34] Canoy D, Wareham N, Luben R, Welch A, Bingham S, Day N, et al. Cigarette smoking and fat distribution in 21,828 British men and women: A population-based study. Obes Res 2005;13:1466–75.