Snus use and cardiovascular risk factors in the general population: The HUNT3 study

Article *in* Addiction · July 2013

DOI: 10.1111/add.12313 · Source: PubMed

5 authors, including:

Simon Øverland
Norwegian Institute of Public Health
113 PUBLICATIONS **2,902** CITATIONS
SEE PROFILE

Jens Christoffer Skogen
Norwegian Institute of Public Health, Bergen…
60 PUBLICATIONS **783** CITATIONS
SEE PROFILE

Ottar Bjerkeset
Nord University
63 PUBLICATIONS **1,208** CITATIONS
SEE PROFILE

Tore Tjora
Uni Research AS
5 PUBLICATIONS **77** CITATIONS
SEE PROFILE

Addiction
RESEARCH REPORT
doi:10.1111/add.12313

Snus use and cardiovascular risk factors in the general population: the HUNT3 study

Simon Øverland[1,2,3], Jens Christoffer Skogen[1,3,8], Lauren Lissner[2], Ottar Bjerkeset[4,5], Tore Tjora[1,3,6] & Robert Stewart[7]

Department of Health Promotion and Development, Faculty of Psychology, University of Bergen, Bergen, Norway,[1] Department of Public Health and Community Medicine, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden,[2] Division of Mental Health, National Institute of Public Health, Bergen, Norway,[3] Department of Research and Development (R&D), Levanger Hospital, Levanger, Norway,[4] Department of Neuroscience, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway,[5] Uni Health, University of Bergen, Bergen, Norway,[6] Institute of Psychiatry, King's College London, London, UK[7] and Alcohol And Drug Research Western Norway, Stavanger University Hospital, Stavanger, Norway[8]

ABSTRACT

Background and aims Snus, a form of smokeless tobacco, is increasingly popular in its traditional Nordic markets, and was recently launched commercially in the United States. We examined the cross-sectional associations between snus use and cardiovascular risk factors, and compared them with the corresponding associations of smoking. **Design** Cross-sectional study. **Setting** The HUNT3 general population survey, Nord-Trøndelag, Norway (2006–08). **Participants** A general population sample of $n = 25\,163$. **Measurements** Measured triglyceride,- glucose- and high-density lipoprotein (HDL)-cholesterol levels, blood pressure and waist circumference, registry information on gender, age and education level, self-reported snus use, smoking, physical exercise and alcohol use. **Findings** In age- and gender-adjusted linear regression analyses, extensive snus use was associated with larger waist circumference ($b = 1.65$, 95% CI = 0.86, 2.43) and higher systolic blood pressure ($b = 2.58$, 95% CI = 1.48, 3.68), but with higher rather than lower levels of HDL-cholesterol ($b = 1.66$, 95% CI = 0.79, 2.53). These three differences remained significant after additional adjustment for smoking, education level, physical exercise and alcohol use. Smokers had higher triglyceride and lower HDL-cholesterol than snus users, but lower systolic blood pressure. **Conclusions** After adjusting statistically for major confounding variables, Norwegians who use snus extensively have a mixed profile in terms of cardiovascular risk: slightly higher waist circumference and systolic blood pressure but also higher high-density lipoprotein-cholesterol.

Keywords Cardiovascular risk, smokeless tobacco, smoking, snus.

Correspondence to: Simon Øverland, Department of Health Promotion and Development, Faculty of Psychology, University of Bergen, Christiesgate 13, 5015 Bergen, Norway. E-mail: Simon.overland@uib.no
Submitted 1 October 2012; initial review completed 27 November 2012; final version accepted 22 July 2013

INTRODUCTION

Snus, a Swedish-made smokeless tobacco product, has been launched recently onto the US market [1]. Test market surveys indicate that the product has substantial potential for attracting users [2], and early figures suggest that 29% of young male adults have tried snus during the last year [3]. Snus has been widely available for decades in Sweden and Norway, but its use has increased further in later years, particularly among young adults [4,5], so that in both these countries snus use is now about as common as smoking among men. In young women, prevalence of snus use has increased from negligible levels to near 5% in a few years [4,5]. In light of the increasing prevalence of snus use where it is available, and its introduction to new markets, research on snus use and health becomes increasingly relevant. Potential health effects from snus are often inferred from the smoking literature, but few studies have compared health risks associated directly with these two tobacco products [6].

Several reviews have concluded that snus use has acute cardiovascular effects, but that long-term contributions to cardiovascular disease are less clear [1,7–9]. A Swedish study found an association between high-dose snus consumption and the metabolic syndrome, but

not to all its individual components [10]. Others have reported elevated waist–hip ratio and triglyceride levels among people with long-standing snus use [11]. A Swedish population-based study suggested an association between snus use and type 2 diabetes, but not with reduced glucose tolerance [12]. Several studies have reported associations between snus and higher body weight [10,11,13], and one study reported weight gain and incident obesity among long-term snus users [14]. Several cross-sectional studies have failed to find any association between snus use and increased blood pressure [7], although two studies have reported this [15,16].

Snus use has been limited historically to males in only a few countries, and previous research has been based mainly on non-representative study samples, with possible selection effects [7]. Cardiovascular diseases and risks are influenced by many factors and not all studies have been able to account for relevant health behaviours, such as physical exercise, alcohol use and smoking, that may also correlate with snus use [4,17].

In the present study, conducted in a large, general population sample, we examined if snus use was associated cross-sectionally with risk factors for cardiovascular disease, while accounting for other health-related variables. We also directly compared these associations with those of smoking.

METHODS

Data

HUNT3, the third wave of the Nord-Trøndelag Health Surveys [18], was carried out from 2006 to 2008 in the county of Nord-Trøndelag, Norway. The county is considered representative for Norway in terms of geography, economy, industry and sources of income for the inhabitants, age distribution and morbidity [19], although it is relatively rural and with a level of education that is lower than the national average [20]. A total of 93 010 individuals aged 20–89 years were invited using the same procedure as in previous waves, and 50 797 (54%) attended. Those who participated completed questionnaires, and trained nurses/research assistants collected clinical data such as physical measurements (height, weight, hip and waist circumference, blood pressure and pulse) and blood serum samples. Triglycerides, glucose and cholesterol levels were analysed for a random total of 38 919 participants. Education levels (a possible confounder) from the national education registry were linked to the health survey data. We excluded 1583 who did not answer the questions on snus use, 640 who could not be traced back to the education registry and 3029 who either failed to answer other included self-report items or where measurements were incomplete. People with manifest cardiovascular disease (CVD) or high CVD risk conditions (such as diabetes and clinical hypertension) are likely to receive risk management, including advice to refrain from smoking, and probably tobacco use in general [21]. Therefore, we excluded all people with any self-reported CVD (angina, myocardial infarction, stroke, heart failure or other CVD), diabetes or current antihypertensive treatment ($n = 8504$) which left a final sample of $n = 25\,163$. Those excluded because of previous CVD reported less current or previous snus use than the remaining sample (overall $\chi^2 = 189.19$, d.f. = 4, $P < 0.001$). They were, however, more likely to be previous smokers, and less likely to be current smokers (overall $\chi^2 = 389.27$, d.f. = 4, $P < 0.001$).

The Norwegian regional committee for medical research ethics and the HUNT administration board approved the study.

Exposure: use of snus

Practically all snus products commercially available in Norway are produced in Sweden and conform to the Gothiatek standard [22]. The questionnaire included three items on snus use. The first was: 'Do you use, or have you previously used snus?', with four response alternatives: 'No, never', 'Yes, but I have quit', 'Yes, sometimes' and 'Yes, every day'. Those who at some stage had used snus, were asked at what age they started and consumption per month. We used the first item to identify four different groups in terms of snus use. To capture those with an extensive use of snus, we combined all three items and identified those who reported: (i) current daily snus use, (ii) a monthly consumption above the mean and (iii) having used snus for more than 5 years, leaving a variable on snus use over five levels: (i) never (reference), (ii) previous, (iii) sometimes, (iv) daily, and (v) extensive.

Outcome: cardiovascular risk factors

Information on cardiovascular risk factors was obtained from the physical examinations where specially trained nurses measured hip and waist circumference (with a band, to the nearest centimetre [18]), drew non-fasting blood samples and measured blood pressure. The latter was measured three times, and the mean of the two last measurements was used. Triglycerides, high-density lipoprotein (HDL) cholesterol and glucose levels from blood serum samples were analysed by use of Architect *c*Systems™. Due to the size of the study, keeping all participants fasting at time of blood sampling was impossible.

Covariates

From registry information (Statistics Norway) on achieved education, we constructed an ordinal variable

classifying the following three groups: 'primary education only', 'upper secondary schooling' and 'university or college degree'.

Engagement in physical exercise was reported using a five-point ordinal scale, recoded into three groups: those seldom engaging in physical activity (combined categories 'never' and '<once a week'), those engaging in physical activity every week (combined 'about once a week' and '2–3 times a week') and those engaging in physical activity 'nearly every day'.

Frequency of alcohol consumption during the last 12 months was self-reported and grouped as follows: 'abstainer or consumption about once a month', 'consumption 2–3 times a month to about once a week' and 'consumption 2 to 7 days a week'.

Participants were asked about current or past smoking, with the same response categories as for snus use: 'No, never', 'Yes, but I have quit', 'Yes, sometimes' and 'Yes, every day'. For the main analyses, we compared 'daily smoking' with the remaining categories as a binary variable.

Variable for comparing associations between snus use and smoking

For the analysis comparing associations between snus use and smoking, we generated a categorical variable with four groups: never-smoker and never snus user (reference), occasional or daily snus user and non-smoker (i), occasional or daily smoker not using snus (ii) and occasional or daily smoking and snus use (iii). Those reporting previous snus use or previous smoking and no current tobacco use were excluded from this set of analyses to obtain a more 'tobacco-free' comparison group. Because individuals who quit smoking may start to use snus, or use snus as help in smoking cessation [23], it is important that this study does not mix potential effects of smoking and snus, e.g. on body weight, in subjects who have switched their form of tobacco use.

Statistical analyses

Sample characteristics by snus use categories were described. We modelled the associations between snus use and the cardiovascular risk factors in linear regressions. As snus use is much more common in men and in younger participants, and levels of cardiovascular risk factors are higher in men but increase with age, primary analyses were adjusted for gender and age. In the second and third models we added adjustment for smoking status and education, before physical exercise and frequency of alcohol use was added in a final model to examine if associations were related to clustering of health compromising behaviours. We tested for snus × gender interactions, and present gender-stratified results for the outcomes where a significant multiplicative interaction was observed in the initial age-adjusted analysis.

In the second set of analyses, we used the variable identifying snus users, smokers and both as a categorical exposure variable, and examined associations with levels of CVD risk using the 'snus only' group as reference.

RESULTS

The total prevalence of current snus use (sometimes, daily or extensive) was 11.9% [95% confidence interval (CI) = 11.5–12.3], 21.9% (95% CI = 21.1, 22.7) for men and 3.8% (95% CI = 3.5, 4.1) for women. Participants with no current snus use were on average older than current snus users (Table 1). There were overall univariate associations between snus use and education, alcohol consumption, physical activity and all the CVD risk factors. Those who reported using snus 'sometimes' had higher smoking rates, than both previous and never users. Smoking rates were lower among daily snus users, and lowest among extensive users (Table 1).

Main effects were studied in age- and gender-adjusted regression analyses using those reporting never having used snus as reference, and results are presented in Table 2. Extensive snus use was associated with a higher waist circumference. This association was explained partly by education level, but remained after further adjustment for physical exercise and alcohol use. There was also a borderline significant association among previous snus users for this outcome, across all levels of adjustment. Both daily and extensive snus use was associated with an increased HDL-cholesterol level and, having accounted for smoking, there was also a statistically significant increase in HDL-cholesterol for 'sometimes' snus users. Adjustment for physical exercise and alcohol use reduced the strength of associations with HDL-cholesterol, but it remained statistically significant in the final model. Previous and 'sometimes' snus users had increased triglyceride levels, but smoking explained much of this association for the latter group. Extensive snus users had higher systolic blood pressure, and adjusting for confounders and covariates did little to reduce the association. We found no evidence of associations between snus use and diastolic blood pressure or non-fasting glucose levels (Table 2).

There were significant snus × gender interactions for triglyceride levels and systolic blood pressure (Table 3). For triglycerides, there was an increase in levels among male sometime users, while females with a daily snus use had a lower level of triglycerides, both compared to their respective group of never snus users. These statistical differences were attenuated after adjustment for smoking. The association between extensive snus use and

Table 1 Sample characteristics and key variables described as *n* (%) for categorical variables and means (standard deviations) for continuous measurements, and tests for differences using χ^2 tests and *F*-tests, respectively.

	Never snus use (n = 20 894)		*Previous snus use (n = 1265)*		*Sometimes snus use (n = 941)*		*Daily snus use (n = 1214)*		*Extensive snus use (n = 849)*		*Difference*
Categorical variables (*n*, % and χ^2 tests)											
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	
Gender											$\chi^2 = 3.2e^3$, d.f. = 4, $P < 0.001$
Female	13 123	62.81	177	13.99	303	32.20	171	14.09	47	5.54	
Male	7 771	37.19	1088	86.01	638	67.80	1043	85.91	802	94.46	
Education											$\chi^2 = 73.82$, d.f. = 8, $P < 0.001$
Primary	3 692	17.67	201	15.89	165	17.53	168	13.84	123	14.49	
Upper secondary	10 708	51.25	722	57.08	473	50.27	703	57.91	528	62.19	
College/university	6 494	31.08	342	27.04	303	32.20	343	28.25	198	23.32	
Physical exercise											$\chi^2 = 193.65$, d.f. = 8, $P < 0.001$
<Once a week	4 197	20.09	339	26.80	243	25.82	352	29.00	279	32.86	
Weekly	12 991	62.18	743	58.74	567	60.26	725	59.72	478	56.30	
Almost every day	3 706	17.74	183	14.47	131	13.92	137	11.29	92	10.84	
Frequency of alcohol consumption											$\chi^2 = 413.27$, d.f. = 8, $P < 0.001$
Abstainer or a few times a year	8 414	40.27	330	26.09	237	25.19	279	22.98	184	21.67	
About once a month	9 437	45.17	681	53.83	547	58.13	693	57.08	476	56.07	
2–3 times a month	3 043	14.56	254	20.08	157	16.68	242	19.93	189	22.26	
Daily smoking											$\chi^2 = 329.00$, d.f. = 4, $P < 0.001$
No	16 319	79.88	1014	82.91	603	66.19	1077	90.58	792	95.77	
Yes	4 110	20.12	209	17.09	308	33.81	112	9.42	35	4.23	
Continuous variables (mean, SD and *F*-tests)											
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age	49.83	14.49	46.09	12.83	39.23	14.85	42.92	12.85	41.20	12.65	$F = 256.69$, d.f. = 4, $P < 0.001$
HDL-cholesterol (mg/dl)	53.03	13.44	48.22	12.17	49.31	12.41	48.69	11.68	47.78	11.14	$F = 105.72$, d.f. = 4, $P < 0.001$
Systolic blood pressure (mmHg)	128.03	17.68	128.76	15.07	125.76	15.07	128.41	15.23	130.05	13.82	$F = 7.44$, d.f. = 4, $P < 0.001$
Diastolic blood pressure (mmHg)	72.58	10.91	74.62	10.55	70.96	11.00	73.45	11.56	74.39	10.49	$F = 22.87$, d.f. = 4, $P < 0.001$
Triglyceride (mg/dl)	134.48	82.17	157.83	103.56	151.34	126.96	147.34	90.21	155.84	91.33	$F = 43.69$, d.f. = 4, $P < 0.001$
Non-fasting glucose (mg/dl)	95.99	20.07	97.80	21.30	95.35	17.92	95.60	16.91	94.71	15.90	$F = 3.91$, d.f. = 4, $P < 0.01$
Waist circumference (cm)	91.41	11.90	95.06	10.38	91.74	12.01	93.72	11.12	96.00	10.65	$F = 64.93$, d.f. = 4, $P < 0.001$

HDL = high-density lipoprotein; SD = standard deviation.

Table 2 Associations (*b*, parameter estimates and 95% CI) between snus use and cardiovascular risk factors in a linear regression analysis.

		Waist circumference	*HDL-cholesterol*	*Triglycerides*	*Systolic blood pressure*	*Diastolic blood pressure*	*Non-fasting glucose*
Adjusted for age and gender	Never snus use	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
	Previous snus use	0.69 (0.05, 1.34)	0.59 (–0.13, 1.30)	5.74 (0.86, 10.62)	–0.70 (–1.61, 0.20)	0.32 (–0.27, 0.91)	0.87 (–0.26, 2.00)
	Sometimes snus use	–0.49 (–1.23, 0.25)	0.80 (–0.01, 1.62)	10.27 (4.71, 15.84)	0.85 (–0.18, 1.88)	–0.89 (–1.56, 0.21)	1.00 (–0.28, 2.29)
	Daily snus use	–0.24 (–0.91, 0.42)	1.48 (0.75, 2.21)	–3.00 (–7.99, 2.00)	0.65 (–0.28, 1.58)	–0.15 (–0.75, 0.46)	–0.46 (–1.61, 0.69)
	Extensive snus use	1.65 (0.86, 2.43)	1.66 (0.79, 2.53)	2.98 (–2.94, 8.90)	2.58 (1.48, 3.68)	0.71 (–0.00, 1.43)	–1.24 (–2.61, 0.12)
Adjusted for age, gender and smoking	Never snus use	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
	Previous snus use	0.70 (0.05, 1.36)	0.55 (–0.17, 1.27)	5.83 (0.91, 10.75)	–0.83 (–1.75, 0.09)	0.22 (–0.38, 0.82)	0.79 (–0.36, 1.93)
	Sometimes snus use	–0.48 (–1.23, 0.28)	1.43 (0.60, 2.25)	6.41 (0.78, 12.04)	0.98 (–0.08, 2.03)	–0.94 (–1.62, 0.25)	1.07 (–0.24, 2.38)
	Daily snus use	–0.24 (–0.91, 0.43)	1.24 (0.51, 1.98)	–2.04 (–7.05, 2.97)	0.59 (–0.34, 1.53)	–0.15 (–0.76, 0.46)	–0.36 (–1.53, 0.81)
	Extensive snus use	1.62 (0.82, 2.42)	1.32 (0.45, 2.20)	4.96 (–1.00, 10.93)	2.31 (1.20, 3.43)	0.64 (–0.09, 1.37)	–1.08 (–2.47, 0.31)
Adjusted for age, gender, smoking and education	Never snus use	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
	Previous snus use	0.66 (0.00, 1.31)	0.58 (–0.14, 1.31)	5.57 (0.66, 10.48)	–0.88 (–1.80, 0.03)	0.21 (–0.39, 0.81)	0.77 (–0.37, 1.92)
	Sometimes snus use	–0.52 (–1.27, 0.23)	1.45 (0.63, 2.28)	6.19 (0.58, 11.81)	0.93 (–0.12, 1.98)	–0.95 (–1.63, 0.26)	1.06 (–0.24, 2.37)
	Daily snus use	–0.34 (–1.01, 0.33)	1.32 (0.58, 2.05)	–2.61 (–7.60, 2.39)	0.47 (–0.46, 1.41)	–0.18 (–0.79, 0.43)	–0.39 (–1.55, 0.78)
	Extensive snus use	1.38 (0.59, 2.18)	1.49 (0.62, 2.37)	3.60 (–2.35, 9.56)	2.03 (0.92, 3.14)	0.57 (–0.16, 1.30)	–1.14 (–2.53, 0.25)
Adjusted for age, smoking, gender, education, physical exercise and frequency of alcohol use	Never snus use	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
	Previous snus use	0.78 (0.13, 1.43)	0.19 (–0.52, 0.90)	5.86 (0.96, 10.76)	–0.89 (–1.80, 0.03)	0.10 (–0.50, 0.69)	0.70 (–0.44, 1.85)
	Sometimes snus use	–0.29 (–1.04, 0.45)	0.95 (0.14, 1.76)	6.87 (1.26, 12.47)	0.94 (–0.10, 1.99)	–1.05 (–1.73, 0.36)	1.01 (–0.30, 2.32)
	Daily snus use	–0.32 (–0.98, 0.35)	0.92 (0.20, 1.64)	–2.78 (–7.77, 2.21)	0.44 (–0.49, 1.37)	–0.37 (–0.98, 0.24)	–0.51 (–1.68, 0.66)
	Extensive snus use	1.38 (0.59, 2.17)	1.03 (0.17, 1.89)	3.24 (–2.70, 9.19)	1.98 (0.87, 3.10)	0.32 (–0.40, 1.05)	–1.31 (–2.70, 0.08)

HDL = high-density lipoprotein; CI = confidence interval.

Table 3 Gender-stratified associations[a] (*b*, parameter estimates and 95% CI) between snus use and triglycerides and systolic blood pressure in linear regression analyses.

		Triglycerides			*Systolic blood pressure*		
		Males	*Interaction*	*Females*	*Males*	*Interaction*	*Females*
Adjusted for age	Never snus use	Ref.	d.f. = 4, $F = 4.22$, $P < 0.01$	Ref.	Ref.	d.f. = 4, $F = 6.96$, $P < 0.001$	Ref.
	Previous snus use	5.92 (–0.40, 12.25)		2.21 (–7.79, 12.22)	–0.60 (–1.55, 0.34)		–2.03 (–4.39, 0.33)
	Sometimes snus use	11.49 (3.37, 19.62)		4.06 (–3.68, 11.80)	0.60 (–0.62, 1.81)		0.42 (–1.40, 2.25)
	Daily snus use	–4.36 (–10.86, 2.14)		–10.27 (–20.45, –0.10)	0.31 (–0.66, 1.28)		–1.38 (–3.78, 1.02)
	Extensive snus use	–1.15 (–8.50, 6.19)		–0.24 (–19.50, 19.03)	1.66 (0.56, 2.75)		–1.02 (–5.57, 3.52)
Adjusted for age and smoking	Never snus use	Ref.	d.f. = 4, $F = 2.95$, $P < 0.05$	Ref.	Ref.	d.f. = 4, $F = 7.74$, $P < 0.001$	Ref.
	Previous snus use	5.99 (–0.42, 12.41)		1.62 (–8.35, 11.59)	–0.72 (–1.68, 0.25)		–2.12 (–4.49, 0.26)
	Sometimes snus use	7.33 (–0.98, 15.63)		3.09 (–4.67, 10.86)	0.84 (–0.41, 2.08)		0.35 (–1.50, 2.19)
	Daily snus use	–4.07 (–10.63, 2.48)		–7.54 (–17.66, 2.57)	0.31 (–0.68, 1.29)		–1.65 (–4.06, 0.75)
	Extensive snus use	–0.16 (–7.58, 7.26)		5.03 (–14.64, 24.70)	1.43 (0.32, 2.54)		–1.90 (–6.58, 2.78)
Adjusted for age, smoking and education	Never snus use	Ref.	d.f. = 4, $F = 2.28$, $P = 0.06$	Ref.	Ref.	d.f. = 4, $F = 6.46$, $P < 0.001$	Ref.
	Previous snus use	5.68 (–0.72, 12.01)		2.07 (–7.86, 12.01)	–0.76 (–1.72, 0.20)		–2.01 (–4.37, 0.36)
	Sometimes snus use	7.08 (–1.21, 15.37)		3.21 (–4.53, 10.95)	0.80 (–0.44, 2.04)		0.37 (–1.47, 2.21)
	Daily snus use	–4.57 (–11.12, 1.98)		–6.77 (–16.85, 3.31)	0.24 (–0.74, 1.22)		–1.47 (–3.86, 0.93)
	Extensive snus use	–1.05 (–8.48, 6.37)		5.19 (–14.41, 24.79)	1.31 (0.19, 2.42)		–1.86 (–6.52, 2.80)
Adjusted for age, smoking, education, physical exercise, frequency of alcohol use	Never snus use	Ref.	d.f. = 4, $F = 2.40$, $P < 0.05$	Ref.	Ref.	d.f. = 4, $F = 6.50$, $P < 0.001$	Ref.
	Previous snus use	5.59 (–0.80, 12.00)		2.28 (–7.62, 12.17)	–0.85 (–1.81, 0.11)		–1.98 (–4.34, 0.38)
	Sometimes snus use	7.67 (–0.61, 15.95)		4.32 (–3.39, 12.03)	0.74 (–0.50, 1.99)		0.49 (–1.35, 2.33)
	Daily snus use	–5.34 (–11.89, 1.21)		–6.15 (–16.19, 3.90)	0.12 (–0.86, 1.10)		–1.39 (–3.78, 1.01)
	Extensive snus use	–2.27 (–9.70, 5.15)		5.68 (–13.84, 25.20)	1.15 (0.03, 2.26)		–1.79 (–6.45, 2.86)

[a]For cardiovascular risk factors where the multiplicative interaction term (snus × gender) was significant in the age-adjusted regression model. CI = confidence interval.

increased systolic blood pressure was confined to males only (Table 3).

In Table 4, associations with CVD risk factors are displayed for those never having used snus or smoked, current smokers and dual users of snus and cigarettes—all compared to those using snus only. Compared to snus users, all other groups had lower levels of HDL-cholesterol, irrespective of adjustments. Triglyceride levels were associated positively with both smoking only and dual use, remaining so after all adjustments. Smoking was associated with lower systolic blood pressure across adjustments (Table 3).

Finally, we ran a *post-hoc* analysis to examine the role of previous smoking on the waist circumference–excessive snus use association with all daily smokers excluded. With those never having used snus as reference ($n = 16\ 784$) and adjusted for age and gender, current extensive snus users with previous smoking ($n = 246$) had a larger waist circumference ($b = 1.83$, $P = 0.01$), while the corresponding increase among current snus users with no previous smoking ($n = 390$) was not statistically significant ($b = 1.09$, $P = 0.06$).

DISCUSSION

Main findings

In this large general population sample, extensive snus users had a larger waist circumference and higher systolic blood pressure than those who did not use snus. Snus users also had an increased level of HDL-cholesterol, both compared to smokers and those with no previous use of tobacco. Levels of triglyceride, glucose levels or diastolic blood pressure were essentially the same in snus users and those who reported never having used snus.

Strengths and limitations

This study was based on objective data on recognized cardiovascular risk factors and also included information on relevant confounding factors. In contrast to many previous studies of snus and health, it was based on a large and broadly representative general population sample. The general participation rate was 53%, but lower among the younger [18]. As snus use was associated with age, we may have under-represented snus users in the entire sample, but beyond reducing snus use prevalence estimates there should be less risk of distorted associations from non-participation [24]. Misclassification would bias results towards the null. Although previous studies support the validity of self-reported tobacco use [25], both snus use and smoking was based entirely on self-report, and misclassification cannot be ruled out. This problem might be greater for smoking than snus, as the

Table 4 Associations (b, parameter estimates and 95% CI) to CVD risk factors from snus (daily or weekly, $n = 1934$), smoking (daily or weekly, $n = 6052$) or both ($n = 1070$) compared to those not using snus or smoking.[a]

		Waist circumference	*HDL-cholesterol*	*Triglycerides*	*Systolic blood pressure*	*Diastolic blood pressure*	*Non-fasting glucose*
Adjusted for age and gender	No previous/current tobacco use	−0.40 (−0.97, 0.16)	−1.31 (−1.92, −0.70)	−3.27 (−7.50, 0.96)	−0.96 (−1.73, −0.19)	−0.73 (−1.24, −0.22)	−0.03 (−0.99, 0.93)
	Current snus only	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
	Current smoking only	−0.22 (−0.83, 0.38)	−3.31 (−3.96, −2.66)	10.92 (6.42, 15.41)	−2.01 (−2.83, −1.19)	−0.38 (−0.92, 0.16)	0.94 (−0.08, 1.96)
	Current smoking and snus use	0.59 (−0.25, 1.43)	−1.78 (−2.68, −0.88)	12.30 (6.04, 18.56)	−0.23 (−1.37, 0.91)	−1.47 (−2.23, −0.72)	0.64 (−0.78, 2.06)
Adjusted for age, gender and education	No previous/current tobacco use	−0.26 (−0.82, 0.30)	−1.41 (−2.02, −0.81)	−2.46 (−6.68, 1.76)	−0.79 (−1.56, −0.02)	−0.70 (−1.21, −0.19)	−0.00 (−0.96, 0.96)
	Current snus only	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
	Current smoking only	−0.56 (−1.16, 0.04)	−3.07 (−3.72, −2.42)	9.02 (4.52, 16.53)	−2.41 (−3.23, −1.59)	−0.45 (−0.99, 0.10)	0.87 (−0.16, 1.90)
	Current smoking and snus use	0.25 (−0.58, 1.09)	−1.54 (−2.45, −0.64)	10.43 (4.18, 16.69	−0.62 (−1.76, 0.52)	−1.54 (−2.30, −0.79)	0.57 (−0.86, 2.00)
Adjusted for age, gender, education, physical exercise, frequency of alcohol use	No previous current tobacco use	−0.41 (−0.97, 0.15)	−0.81 (−1.41, −0.21)	−2.82 (−7.05, 1.41)	−0.77 (−1.55, 0.00)	−0.50 (−1.01, 0.01)	0.13 (−0.83, 1.10)
	Current snus only	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
	Current smoking only	−0.83 (−1.43, −0.24)	−2.77 (−3.40, −2.13)	8.00 (3.50, 12.49)	−2.45 (−3.27, −1.63)	−0.49 (−1.03, 0.06)	0.84 (−0.19, 1.87)
	Current smoking and snus use	0.10 (−0.73, 0.93)	−1.57 (−2.46, −0.69)	9.75 (3.50, 15.99)	−0.66 (−1.81, 0.48)	−1.67 (−2.42, −0.91)	0.48 (−0.95, 1.91)

[a] All who reported previous smoking and previous snus use, and no current use of any tobacco product were excluded ($n = 5742$), leaving $n = 19\ 421$ for this analysis. HDL = high-density lipoprotein; CI = confidence interval; CVD = cardiovascular disease.

former is seen as less attractive [26]. Also, 'previous' smokers and snus users could comprise various lengths of exposure and time since cessation.

Also, the strong increase in snus use in the years leading up to this health survey could potentially dilute true associations that might depend on long-term use. This limitation would, however, not be relevant for the group 'extensive snus user', which by definition had used snus for more than 5 years.

Blood serum samples were drawn from non-fasting participants. No attempt was made to prompt potential participants to be fasting, as that seemed futile given the design of the study, and could have introduced bias. Although fasting may not be the most important factor to obtain fully reliable glucose levels [27], we acknowledge this as a weakness, and have abstained from converting scores into the metabolic syndrome for this reason [28]. Triglyceride levels may also be affected by fasting state, but recent studies suggest that non-fasting measurements are superior in prediction of CVD [29,30]. However, fasting state should not affect the results of our analyses unless there is a bias whereby users and non-users are more or less likely to participate while in a fasted state.

We are uncertain if those with a truly high CVD risk profile would receive advice on snus use in clinical settings, as would be expected for smokers [21]. Some smokers with manifest CVD or high risk may have been advised to switch to snus if previous cessation attempts have been unsuccessful [23]. By excluding all with reported CVD, diabetes and those receiving medication for hypertension, we wanted to remove those most likely to be encouraged to reduce their tobacco use to lower their CVD risk. As a sensitivity analysis, we also ran all analyses without exclusion of participants with diabetes and on hypertensive medication, and this did not alter any of the main findings.

Interpretation

The significant associations between snus use and the cardiovascular risk factors we found were generally quite weak, and not particularly consistent. Some of the results were, however, in line with findings from previous studies. The association between extensive snus use and larger waist circumference is consistent with several previous reports of elevated body mass index (BMI) and overweight among snus users [10,11,13,31]. Our study design precludes causal inferences and limits discussions of causality to informed speculation and whether the observations are in line with a proposed causal model. On that note, it remains uncertain if the association between snus use and waist circumference is due to direct physiological mechanisms where snus can alter metabolic processes, or if the increased waist circumference reflects snus use being clustered with weight-increasing life-style factors [4,17]. Adjusting for physical activity and alcohol use had little impact on the results, but residual confounding cannot be ruled out. Smoking cessation is associated with weight gain [32], and snus is sometimes used as a replacement product to help smoking cessation [23]. Our *post-hoc* analysis suggested that the increased waist circumference among extensive snus users could be due to weight gain among previous smokers switching to snus use. The transition from smoking to snus use, and how this affects health, should be attended to carefully in future longitudinal studies.

At least three previous studies have also linked snus to increased blood pressure and hypertension [15,16,33], although more studies have failed to find such associations [7]. We found this association for extensive snus users only, which aligns with previous reports of increased systolic blood pressure among men with high snus consumption in a Swedish sample [33]. Snus use acutely increases blood pressure [8], and this increase can persist for about an hour after the product is removed [34]. We therefore cannot exclude that at least some of the observed increase in blood pressure is a residual of acute snus use before entering the health examination. This temporality effect should, however, also be relevant for smokers (although shorter [34]), but we found no increase in systolic blood pressure among smokers. While Table 1 suggests lower levels of HDL-cholesterol among snus users, this was strongly gender-confounded; snus use was much more common among men, and men have lower levels of HDL-cholesterol than women [35]. Having adjusted for age and gender, HDL-cholesterol was higher among both daily and extensive snus users compared to those who reported never having used snus. These associations remained robust to further adjustments for possible confounders and covariates. The few previous studies on this relationship have not found similar associations [1,10,11]. Smoking is associated to lower HDL-cholesterol [36]. In our data, snus users were less likely to smoke than non-snus users. Snus use could therefore be a marker for 'non-smoking', and thus appear beneficial for HDL-cholesterol levels. The fact that a significant association emerged among the 'sometimes' snus users when smoking was adjusted for would support this interpretation. However, snus users had higher HDL-cholesterol than both smokers and those with no previous tobacco use, which is contrary to this interpretation. As before, we cannot say if this association is a result of biological mechanisms or other differences coinciding with snus use. Either way, this result needs replication, and also prospective studies, before inferences can be drawn.

Our results regarding snus and triglycerides levels align with two previous reports of no association [37,38], while two other studies have found increased levels of triglycerides among users [10,11]. The absence of significant associations between snus use and diastolic blood pressure or glucose levels is in line with previous findings [1,7].

A second aspect of our study was the direct comparison with the corresponding associations to CVD risk factors for smoking. A recent study examined a wide range of biomarkers in relation to smoking, and found smokers had higher triglyceride levels and lower HDL-cholesterol, but no different blood pressure compared to non-smokers [36]. In our study, smokers had significantly lower levels of HDL-cholesterol and higher triglyceride levels than snus users. We also found elevated systolic blood pressure among snus users compared to a group with no previous tobacco use. Nicotine absorption is similar between snus and cigarettes [39]. The weak associations and the differences between snus and smoking would support the notion that nicotine itself plays a minor role in any relationship between use of tobacco and CVD risk [40]. An alternative explanation could, however, be that smokers and snus users represent subsets of the population with an overall different CVD risk profile.

Cross-sectional associations between snus use and CVD risk factors remain controversial. We found few strong associations and, in fact, snus use was associated with more favourable HDL-cholesterol levels. The most consistent finding seems to be increased body weight among snus users, in our study reflected through increased waist circumference. The results regarding blood pressure diverge, and we cannot exclude that the increase observed in this study was a residual acute effect. Overall, our results do not indicate any strong associations between snus use and at least the CVD risk factors included here. This should serve as one piece in the puzzle where most prospective studies fail to find any excess risk of myocardial infarction incidence among snus users [1,7–9,41,42], including a recent pooled analysis of eight prospective observational studies [43]. However, as some studies have indicated an increased risk for fatal myocardial infarction [44–46], stroke [46,47] and heart failure [48] for snus users, the need for further studies on snus and health remains.

Our results would comply with a hypothesis of few, or only weak biomedical mechanisms between snus use and CVD risk. They could also be explained by health selection we are unable to identify, or residual confounding. The latter points to the importance of monitoring user profiles in emerging markets such as the United States [17], and prospective observational studies on how snus use affects health parameters and manifest disease.

Declaration of interests

None.

Acknowledgements

The Nord-Trøndelag Health Study (The HUNT Study) is a collaboration between the HUNT Research Centre (Faculty of Medicine, Norwegian University of Science and Technology NTNU), Nord-Trøndelag County Council, Central Norway Health Authority and the Norwegian Institute of Public Health.

References

1. Piano M. R., Benowitz N. L., Fitzgerald G. A., Corbridge S., Heath J., Hahn E. *et al*. Impact of smokeless tobacco products on cardiovascular disease: implications for policy, prevention, and treatment: a policy statement from the American Heart Association. *Circulation* 2010; **122**: 1520–44.
2. Biener L., Bogen K. Receptivity to taboka and camel snus in a U.S. test market. *Nicotine Tob Res* 2009; **11**: 1154–9.
3. Biener L., McCausland K., Curry L., Cullen J. Prevalence of trial of snus products among adult smokers. *Am J Public Health* 2011; **11**: 1154–9. AJPH.2010.200097.
4. Norberg M., Malmberg G., Ng N., Brostrom G. Who is using snus?—Time trends, socioeconomic and geographic characteristics of snus users in the ageing Swedish population. *BMC Public Health* 2011; **11**: 929.
5. Øverland S., Tjora T., Hetland J., Aarø L. E. Associations between adolescent socioeducational status and use of snus and smoking. *Tob Control* 2010; **19**: 291–6.
6. Roth H. D., Roth A. B., Liu X. Health risks of smoking compared to Swedish snus. *Inhal Toxicol* 2005; **17**: 741–8.
7. Lee P. N. Summary of the epidemiological evidence relating snus to health. *Regul Toxicol Pharmacol* 2011; **59**: 197–214.
8. Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). Health Effects of Smokeless Tobacco Products. Brussels: SCENIHR; 2008.
9. Royal College of Physicians (RCP). *Harm Reduction in Nicotine Addiction: Helping People Who Can't Quit*. London: Royal College of Physicians; 2007.
10. Norberg M., Stenlund H., Lindahl B., Boman K., Weinehall L. Contribution of Swedish moist snuff to the metabolic syndrome: a wolf in sheep's clothing? *Scand J Public Health* 2006; **34**: 576–83.
11. 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.
12. Persson P. G., Carlsson S., Svanstrom L., Ostenson C. G., Efendic S., Grill V. Cigarette smoking, oral moist snuff use and glucose intolerance. *J Intern Med* 2000; **248**: 103–10.
13. Hergens M. P., Ahlbom A., Andersson T., Pershagen G. Swedish moist snuff and myocardial infarction among men. *Epidemiology* 2005; **16**: 12–6.
14. Hansson J., Galanti M. R., Magnusson C., Hergens M. P. Weight gain and incident obesity among male snus users. *BMC Public Health* 2011; **11**: 371.
15. Bolinder G. M., Ahlborg B. O., Lindell J. H. Use of smokeless tobacco: blood pressure elevation and other health hazards

found in a large-scale population survey. *J Intern Med* 1992; **232**: 327–34.
16. Hergens M. P., Lambe M., Pershagen G., Ye W. Risk of hypertension amongst Swedish male snuff users: a prospective study. *J Intern Med* 2008; **264**: 187–94.
17. Loukas A., Batanova M., Cayley E. *et al*. Who uses snus? A study of Texas Adolescents. *Nicotine Tob Res* 2012; **14**: 626–30.
18. Krokstad S., Langhammer A., Hveem K., Holmen T., Midthjell K., Stene T. *et al*. Cohort profile: the HUNT study, Norway. *Int J Epidemiol* 2012; doi: 10.1093/ije/dys095
19. Helvik A. S., Engedal K., Krokstad S., Selbaek G. A comparison of life satisfaction in elderly medical inpatients and the elderly in a population-based study: Nord-Trondelag Health Study 3. *Scand J Public Health* 2011; **39**: 337–44.
20. Krokstad S., Westin S. Health inequalities by socioeconomic status among men in the Nord-Trondelag Health Study, Norway. *Scand J Public Health* 2002; **30**: 113–24.
21. Graham I., Atar D., Borch-Johnsen K., Boysen G., Burell G., Cifkova R. *et al*. European guidelines on cardiovascular disease prevention in clinical practice: executive summary. *Eur Heart J* 2007; **28**: 2375–414.
22. Rutqvist L., Curvall M., Hassler T., Ringberger T., Wahlberg I. Swedish snus and the GothiaTek(R) standard. *Harm Reduct J* 2011; **8**: 11.
23. Lund K. E., McNeill A., Scheffels J. The use of snus for quitting smoking compared with medicinal products. *Nicotine Tob Res* 2010; **12**: 817–22.
24. Knudsen A. K., Hotopf M., Skogen J. C., Øverland S., Mykletun A. The health status of nonparticipants in a population-based health study. *Am J Epidemiol* 2010; **172**: 1306–14.
25. Post A., Giljam H., Rosendahl I., Meurling L., Bremberg S., Galanti M. R. Validity of self reports in a cohort of Swedish adolescent smokers and smokeless tobacco (snus) users. *Tob Control* 2005; **14**: 114–7.
26. Wiium N., Aaro L. E., Hetland J. Subjective attractiveness and perceived trendiness in smoking and snus use: a study among young Norwegians. *Health Educ Res* 2009; **24**: 162–72.
27. Moebus S., Gores L., Losch C., Jockel K. H. Impact of time since last caloric intake on blood glucose levels. *Eur J Epidemiol* 2011; **26**: 719–28.
28. Alberti K. G., Eckel R. H., Grundy S. M., Zimmet P. Z., Cleeman J. I., Donato K. A. *et al*. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009; **120**: 1640–5.
29. Bansal S., Buring J. E., Rifai N., Mora S., Sacks F. M., Ridker P. M. Fasting compared with nonfasting triglycerides and risk of cardiovascular events in women. *JAMA* 2007; **298**: 309–16.
30. Mora S., Rifai N., Buring J. E., Ridker P. M. Fasting compared with nonfasting lipids and apolipoproteins for predicting incident cardiovascular events. *Circulation* 2008; **118**: 993–1001.
31. Engstrom K., Magnusson C., Galanti M. Socio-demographic, lifestyle and health characteristics among snus users and dual tobacco users in Stockholm County, Sweden. *BMC Public Health* 2010; **10**: 619.
32. Filozof C., Fernandez Pinilla M. C., Fernandez-Cruz A. Smoking cessation and weight gain. *Obes Rev* 2004; **5**: 95–103.
33. Ångman M., Eliasson M. Snuff and blood pressure. Cross-sectional study of blood pressure in rest among men in the MONICA study in Northern Sweden. *Läkartidningen* 2008; **105**: 3530–5.
34. Benowitz N. L., Porchet H., Sheiner L., Jacob, P., 3rd. Nicotine absorption and cardiovascular effects with smokeless tobacco use: comparison with cigarettes and nicotine gum. *Clin Pharmacol Ther* 1988; **44**: 23–8.
35. Davis C. E., Williams D. H., Oganov R. G., Tao S. C., Rywik S. L., Stein Y. *et al*. Sex difference in high density lipoprotein cholesterol in six countries. *Am J Epidemiol* 1996; **143**: 1100–6.
36. Frost-Pineda K., Liang Q., Liu J. *et al*. Biomarkers of potential harm among adult smokers and nonsmokers in the total exposure study. *Nicotine Tob Res* 2011; **13**: 182–93.
37. 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.
38. Eliasson M., Lundblad D., Hägg E. Cardiovascular risk factors in young snuff-users and cigarette smokers. *J Intern Med* 1991; **230**: 17–22.
39. Digard H., Proctor C., Kulasekaran A., Malmqvist U., Richter A. Determination of nicotine absorption from multiple tobacco products and nicotine gum. *Nicotine Tob Res* 2012; **15**: 255–61.
40. Benowitz N. Snuff, nicotine and cardiovascular disease: implications for tobacco control. *J Am Coll Cardiol* 1999; **34**: 1791–3.
41. Janzon E., Hedblad B. Swedish snuff and incidence of cardiovascular disease. A population-based cohort study. *BMC Cardiovsc Disord* 2009; **9**: 21.
42. Hansson J., Pedersen N. L., Galanti M. R., Andersson T., Ahlbom A., Hallquist J. *et al*. Use of snus and risk for cardiovascular disease: results from the Swedish Twin Registry. *J Intern Med* 2009; **265**: 717–24.
43. Hansson J., Galanti M. R., Hergens M. P., Fredlund P., Ahlbom A., Alfredsson L. *et al*. Use of snus and acute myocardial infarction: pooled analysis of eight prospective observational studies. *Eur J Epidemiol* 2012; **27**: 771–9.
44. Hergens M. P., Alfredsson L., Bolinder G., Lambe M., Pershagen G., Ye W. Long-term use of Swedish moist snuff and the risk of myocardial infarction amongst men. *J Intern Med* 2007; **262**: 351–9.
45. Bolinder G., Alfredsson L., Englund A., Defaire U. Smokeless tobacco use and increased cardiovascular mortality among Swedish construction workers. *Am J Public Health* 1994; **84**: 399–404.
46. Boffetta P., Straif K. Use of smokeless tobacco and risk of myocardial infarction and stroke: systematic review with meta-analysis. *BMJ* 2009; **339**: b3060.
47. Hergens M. P., Lambe M., Pershagen G., Terent A., Ye W. Smokeless tobacco and the risk of stroke. *Epidemiology* 2008; **19**: 794–9.
48. Arefalk G., Hergens M. P., Ingelsson E., Arnlov J., Michaelsson K., Lind L. *et al*. Smokeless tobacco (snus) and risk of heart failure: results from two Swedish cohorts. *Eur J Prev Cardiol* 2012; **19**: 1120–7.

