

Risk of hypertension amongst Swedish male snuff users: a prospective study

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Background. The scientific evidence on whether long-term use of snuff is associated with high blood pressure is limited, inconsistent and based only on cross-sectional data.

Objective. We aimed at studying the risk of hypertension in relation to long-term use of snuff based on longitudinal data.

Design. Repeated health check-ups were offered to all employees in the Swedish construction industry between 1978 and 1993. Blood pressure was measured at the health check-up and information on tobacco use and other risk factors was collected through questionnaires.

Setting. In total, 120 930 never smoking men with information on blood pressure and snuff use at base-

line were included. The association of high blood pressure and snuff use at baseline was estimated by logistic regression. Further, 42 055 men were identified as normotensive at baseline and had at least one subsequent health check-up. Through repeated blood pressure measurements and linkage to the Swedish National Inpatient Register, information on hypertension was obtained. Relative risk estimates were derived from Cox proportional hazards regression model.

Results. Almost 30% of all men had used snuff. The adjusted odds ratio of high blood pressure amongst snuff users at baseline was 1.23 (95% CI 1.15–1.33) compared to never snuff users. The relative risk of high blood pressure during follow-up was 1.39 (95% CI 1.08–1.79) amongst snuff users and 1.36 (95% CI 1.07–1.72) for hypertension as recorded in the Inpatient Register.

Conclusion. Use of Swedish moist snuff appears to be associated with a moderately increased risk of hypertension.

Keywords: cohort, hypertension, snuff.

Background

Moist snuff (snus) is a type of smokeless tobacco widely used by men in Sweden; approximately 20% of adult men are daily snuff users [1]. The adverse cardiovascular health effects from cigarette smoke are well known; however, the evidence on snuff use and cardiovascular outcomes is limited. Results from some

studies show an elevated risk of cardiovascular mortality and morbidity amongst snuff users and other smokeless tobacco products, but the evidence appears inconsistent [2–8].

The acute effects, probably mainly due to nicotine exposure, from smokeless tobacco use on blood pressure and pulse rate, have been documented both in

animal and human experiments. Several studies reported increases in cardiac output as well as vascular constriction [9–14]. One Swedish study observed that pulse rate and blood pressure were approximately 5–10% higher amongst those who used snuff within 2 h before measurements compared to those who were not exposed [15]. Another study found that snuff users had higher pulse rate and blood pressure at rest compared to those who were not exposed, but no differences were observed during exercise [16].

Hypertension is a major risk factor for the development of cardiovascular disease; however, evidence on the possible long-term effects of snuff use on blood pressure is limited. A large Swedish cross-sectional study reported a higher prevalence of high blood pressure amongst snuff users compared to subjects who never used tobacco [17], and in a case-control study an increased risk of hypertension amongst snuff users was observed in the control group [6]. A third Swedish study showed a higher mean systolic blood pressure during a 24-h period amongst snuff users compared to nontobacco users [18]. On the other hand, several cross-sectional studies from both Sweden and the United States did not find an association between long-term use of snuff and the risk of hypertension [12, 15, 19–22]. There are no longitudinal studies on snuff use and risk of hypertension.

In this prospective study, our aim was to assess the risk of high blood pressure and hypertension amongst male long-term users of snuff, particularly based on longitudinal data.

Material and methods

Setting

Between 1969 and 1993, the Swedish Construction Industry's Organization offered free health check-up to both blue-collar and white-collar employees. These health check-ups were voluntary and with no limits as to how many times an individual could attend. The mean number of visits was 3 but some employees had up to 13 visits. Approximately 25% of the workers did not attend at any time. There is no information

on whether the nonattendants did not get an invitation or whether they were unwilling to participate. At each visit resting blood pressure was measured in a supine position, in addition to heart rate, height and weight. The workers also completed a questionnaire regarding medical history, working environment and detailed history of smoking and snuff use.

The cohort

Approximately 390 000 individuals were registered in the cohort between 1971 and 1993. No information was available on tobacco use between the years 1975 and 1977, therefore we chose to use exposure information (snuff use) from the first visits after 1 January 1978. To avoid confounding from smoking we excluded all persons who had ever smoked, using information from all visits available from 1971 to 1993. The Swedish personal registration number, an individually unique identifier, enabled follow-up through record linkage to several national registers, i.e. the Inpatient Register, the Causes of Death Register, the Migration Register and the Total Population Register. Subjects were further excluded because of other inconsistencies or missing information on area of domicile, weight, height or snuff use. In all, approximately 1.4% of the men were lost to follow-up because of inconsistent personal registration numbers. The final population consisted of 120 930 men. The exclusion criteria and the number of subjects included in the different analyses are outlined in detail in Fig. 1.

Outcome

Cases of hypertension were identified in the Inpatient Register using discharge diagnoses in which hypertension was coded as the underlying cause or as co-morbid condition. The definition included malignant and benign hypertension with or without heart and kidney failure (ICD-7: 440–447, ICD-8: 400–404, ICD-9: 401–405 and ICD-10: I10–I15). A systolic blood pressure >160 mmHg or diastolic blood pressure >100 mmHg at the health visit was classified as high. Only subjects with repeated measurements of blood pressure were included when calculating the

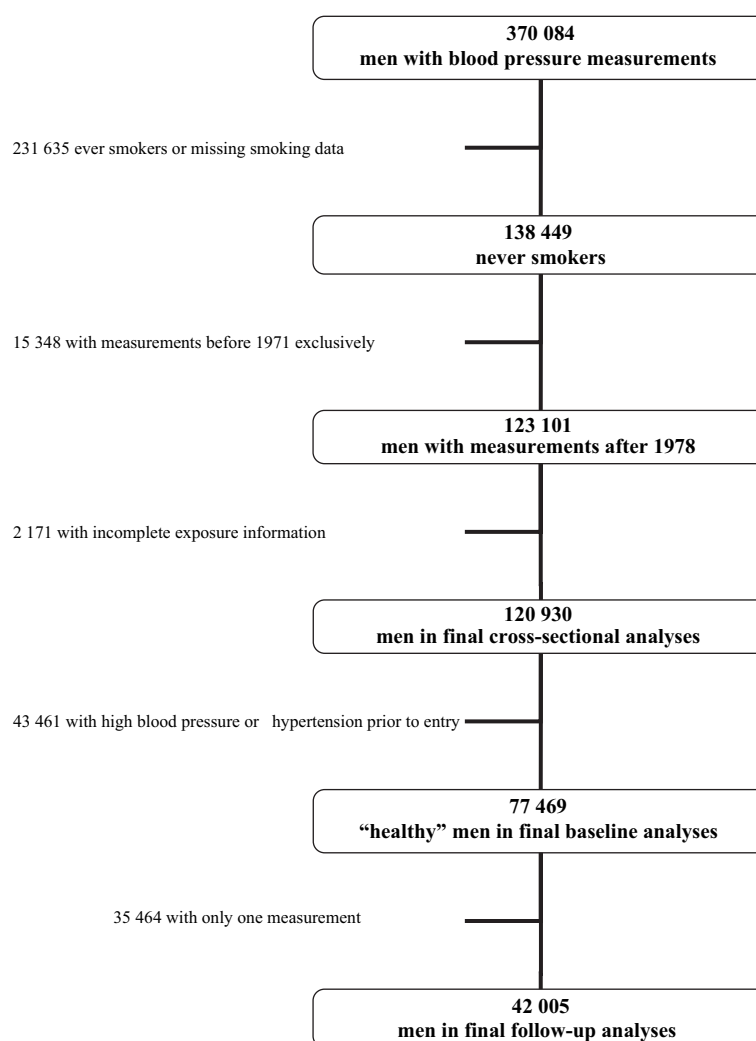


Fig. 1 Flowchart of the Construction Workers Cohort.

mean systolic and diastolic blood pressure over time. For those with two measurements at one health visit the mean was used. A 'healthy' cohort was created for the follow-up analyses including only those with systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg at the first visit along with those never registered with hypertension in the Inpatient Register prior to baseline (see Fig. 1).

Information on snuff dipping and other risk factors

From 1978 information on the amount of snuff use (g week^{-1}), duration of snuff dipping, and time since cessation of snuff dipping (years) was obtained.

Regular snuff use was defined as consumption of at least 1 g day^{-1} for at least 1 year. Former snuff users were those subjects who had stopped using snuff more than 1 year before enrolment. The mean consumption reported amongst current snuff users was 22.5 g day^{-1} . We only used snuff information from the first visit registered as the repeat visits varied in number and timing because of self-selection. For this reason and the fact that duration was age dependent we did not use this information in the analyses. Current users were divided into four groups according to the amount of daily snuff intake (g week^{-1}): $<12.5 \text{ g day}^{-1}$, $12.5\text{--}24.9 \text{ g day}^{-1}$, $25\text{--}49.9 \text{ g day}^{-1}$ and 50 or more g day^{-1} .

Body mass index [BMI, weight (kg)/height (m²)] was calculated using information from the health check-up. Area of domicile at baseline was established by linkage to the Total Population Register and the Register of Domestic Migration. We grouped the residence areas of participants into northern, middle and southern Sweden. No information on alcohol, diet or physical activity was available.

Statistical analysis

At baseline the relationship between snuff use and high blood pressure was measured as odds ratios through logistic regression models with adjustment for age, BMI and region of residence. The cohort members contributed person-years from the entry date until the date of first diagnosis (hypertension in the Inpatient Register or high blood pressure at subsequent health visit), death, emigration out of Sweden or the end of year 2004 (1993 for analyses of high blood pressure), whichever occurred first. If an individual was living in a county with incomplete coverage of the Inpatient Register, the entry date was reset to the date of complete coverage to ensure complete follow-up for hypertension. The association between snuff use and risk of hypertension was estimated by relative risks derived from Cox proportional hazards models with adjustment for attained age (as time

scale) [23], BMI and region of residence. Repeated blood pressure measurements on individuals allowed us to study the effect of snuff on change in high blood pressure (binary outcome variable) over time. Repeated measurements on individuals are usually correlated and the Generalized Estimation Equation was used to adjust for this within-individual correlation [22]. Age at entry was considered as a potential confounder and was included in the analyses. All analyses were conducted using SAS, version 9.1 (Cary, NC, USA). This study was approved by the Regional Ethics Committee at Umeå University.

Results

In all, 120 930 never smoking men with information on blood pressure and snuff use at baseline were included, and 42 005 of those had more than one measurement on blood pressure and were normotensive at baseline (Fig. 1). Approximately 30% of the men were ever snuff users. More than 5900 men had high blood pressure (systolic ≥ 160 mmHg or diastolic ≥ 100 mmHg) at baseline. Amongst the normotensive men with repeated measurements 949 cases with high blood pressure or hypertension were observed. The prevalence of snuff use and number of men with high blood pressure/hypertension is presented in Table 1.

Table 1 Use of snuff and high blood pressure or hypertension amongst nonsmoking men in the Swedish Construction Workers Cohort

	Baseline cohort (<i>N</i> = 120 930)		Healthy baseline (<i>N</i> = 77 469)		Healthy baseline with repeated measurements (<i>N</i> = 42 005)		
	<i>n</i> (%)	High blood pressure ^a	<i>n</i> (%)	Hypertension ^b	<i>n</i> (%)	High blood pressure ^a	Hypertension ^a
Never snuff use	85 413 (71)	4815	52 456 (68)	581	29 892 (71)	337	397
Ever snuff use	35 517 (29)	1100	25 013 (32)	158	12 093 (29)	124	91
Former snuff use	2487 (2)	90	1631 (2)	12	858 (2)	10	7
Current snuff use	32 973 (27)	1010	23 382 (30)	146	11 235 (27)	114	84
<12.5 g day ⁻¹	7175 (6)	280	4828 (6)	37	2641 (6)	34	22
12.5–24.9 g day ⁻¹	14 832 (12)	435	10 637 (14)	66	5252 (13)	51	36
25–49.9 g day ⁻¹	7529 (6)	183	5479 (7)	30	2366 (5)	18	17
>50 g day ⁻¹	3437 (3)	112	2438 (3)	13	976 (3)	11	9

^aCases identified at health check-up for those with more than one health check-up. End of follow-up 1993.

^bCases identified in the Inpatient Register.

The odds ratios for high blood pressure (SBP >160 mmHg or DBP >100 mmHg) amongst ever snuff users was 1.23 (95% CI 1.15–1.33) compared with nontobacco users following adjustment for age, BMI and region of residence (Table 2). Following stratification for age, slightly higher odds ratios for high blood pressure were observed amongst ever snuff users in the older age groups.

Amongst subjects with normal blood pressure at baseline no clear risk of hypertension was observed in snuff users compared with nonsnuff users (Table 4). However, amongst the normotensive with repeated measurements, the relative risk of high blood pressure at a subsequent health visit was 1.39 (95% CI 1.08–

1.79) amongst ever snuff users (Table 4). In this group the relative risk of hypertension was 1.36 (95% CI 1.07–1.72). The risk estimates were generally higher amongst current users, although no clear dose–response effect was detected (Tables 3 and 4). The effect of snuff on the risk of high blood pressure increased with time ($P = 0.02$).

Discussion

Our findings indicate that the prevalence of high blood pressure is increased amongst ever snuff users. We also observed an increased risk of high blood pressure and hypertension during follow-up amongst snuff users with normal blood pressure at baseline.

Table 2 Prevalence of high blood pressure (systolic blood pressure >160 mmHg or diastolic blood pressure >100 mmHg) at baseline ($N = 120\,930$) in different age groups according to snuff use amongst Swedish male construction workers

Age at baseline (years)		Ever used snuff		Former snuff users		Current snuff users	
	Never used snuff n (%)	n (%)	OR ^a (95% CI)	n (%)	OR ^a (95% CI)	n (%)	OR ^a (95% CI)
All	4815 (5.63)	1106 (3.11)	1.23 (1.15–1.33)	90 (3.69)	1.04 (0.83–1.31)	1010 (3.07)	1.25 (1.16–1.35)
<45	1174 (1.83)	529 (1.61)	1.18 (1.06–1.32)	41 (1.85)	0.98 (0.72–1.35)	487 (1.59)	1.20 (1.08–1.34)
45–49	505 (8.28)	110 (12.00)	1.37 (1.10–1.72)	14 (11.63)	1.42 (0.80–2.51)	95 (12.06)	1.35 (1.07–1.72)
50–54	763 (13.97)	116 (19.02)	1.37 (1.10–1.71)	8 (15.52)	1.12 (0.52–2.39)	107 (19.38)	1.39 (1.10–1.75)
55–59	1157 (20.90)	168 (28.19)	1.35 (1.11–1.63)	11 (17.46)	0.73 (0.38–1.43)	156 (29.46)	1.43 (1.17–1.75)
60–64	1114 (27.27)	176 (32.06)	1.20 (0.98–1.45)	16 (32.69)	1.30 (0.70–2.40)	158 (31.99)	1.19 (0.97–1.46)
≥65	102 (34.58)	7 (53.85)	2.20 (0.70–6.95)	0	–	7 (53.85)	2.20 (0.70–6.95)

^aOR, odds ratio derived from logistic regression model; CI, confidence interval; adjusted for age at entry, body mass index [weight (kg)/height (m²), categorized into <20, 20–24.9, 25–29.9 and ≥30] and region of residence (northern, middle and southern Sweden).

Table 3 Prevalence of high blood pressure (systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 100 mmHg) at baseline in different age groups according to snuff use amongst Swedish male construction workers

Age at baseline (years)	OR ^a (95% CI)			
	<12.5 g day ⁻¹	12.5–24.9 g day ⁻¹	25–49.9 g day ⁻¹	≥50 g day ⁻¹
All	1.12 (0.98–1.28)	1.31 (1.17–1.46)	1.25 (1.07–1.47)	1.45 (1.18–1.78)
<45	1.18 (0.96–1.44)	1.12 (0.96–1.31)	1.30 (1.07–1.58)	1.36 (1.06–1.75)
45–49	1.24 (0.80–1.90)	1.62 (1.17–2.26)	1.01 (0.57–1.83)	1.22 (0.62–2.42)
50–54	1.11 (0.74–1.65)	1.37 (0.97–1.96)	1.68 (1.01–2.8)	2.18 (1.11–4.3)
55–59	1.15 (0.83–1.6)	1.73 (1.29–2.31)	1.31 (0.76–2.25)	1.61 (0.75–3.46)
60–64	0.96 (0.72–1.29)	1.65 (1.22–2.23)	0.61 (0.29–1.29)	1.83 (0.70–4.80)
≥65	1.78 (0.38–8.36)	4.57 (0.44–47.6)	1.36 (0.08–24.0)	–

^aOR, odds ratio derived from logistic regression model; CI, confidence interval; adjusted for age at entry, body mass index [weight (kg)/height (m²), categorized into <20, 20–24.9, 25–29.9 and ≥30] and region of residence (northern, middle and southern Sweden).

	Healthy baseline (<i>N</i> = 77 469)		Healthy baseline with repeated measurements (<i>N</i> = 42 005)	
	Hypertension ^b		High blood pressure ^a	
	RR ^c (95% CI)		RR ^c (95% CI)	
Never snuff use	Ref.		Ref.	
Ever snuff use	1.08 (0.89–1.29)		1.39 (1.08–1.79)	
Former snuff use	0.78 (0.43–1.41)		1.49 (0.76–2.90)	
Current snuff use	1.10 (0.91–1.33)		1.34 (1.03–1.74)	
<12.5 g day ⁻¹	1.03 (0.74–1.43)		1.49 (0.97–2.27)	
12.5–24.9 g day ⁻¹	1.15 (0.88–1.49)		1.24 (0.86–1.80)	
25–49.9 g day ⁻¹	1.15 (0.79–1.69)		1.19 (0.69–2.05)	
>50 g day ⁻¹	1.03 (0.59–1.79)		1.67 (0.86–3.28)	

^aCases identified at health check-up for those with more than one health check-up. End of follow-up 1993.

^bCases identified in the Inpatient Register.

^cRR, relative risk derived from Cox proportional hazard regression model; CI, confidence interval; adjusted for age (age at follow-up was used as time scale), body mass index [weight (kg)/height (m²), categorized into <20, 20–24.9, 25–29.9 and ≥30) and region of residence (northern, middle and southern Sweden).

Table 4 Relative risk of high blood pressure or hypertension amongst Swedish male construction workers using snuff

Our findings are in line with two previous studies on snuff use and hypertension, of which one was based on an earlier subset of the present cohort [17] whilst the other was a case-control study showing an increased prevalence of hypertension amongst controls using snuff [6]. However, several studies have failed to find such an association [12, 15, 19–23]. These apparent discrepancies could have several explanations: the age distribution in the study populations is different, three of them (including ours), have an older/middle aged study population [6, 17, 22] whilst others have restricted the study population to young and healthy athletes [12, 15, 19, 20, 23]. In some studies adjustment was made for potential confounding factors, such as smoking, BMI and physical activity [6, 12, 17, 19, 21], whilst others did not [20, 23]. All previous studies on snuff use and hypertension were cross-sectional studies, which limits the possibility of evaluating causality. Our study is the first study using a prospective design for assessing the long-term effect of snuff use on blood pressure and hypertension. We were able to restrict the cohort to a normotensive study population for follow-up both by blood pressure measurements at health check-ups and inpatient care for hypertension.

Smokeless tobacco and snuff have a documented acute hypertensive effect lasting up to 90 min after intake [13]. This effect is presumably the result of nicotine exposure. Studies have shown that snuff users have serum nicotine concentrations comparable to those of cigarette smokers [9, 10, 24]. Nicotine infusion can increase systolic blood pressure by activating the sympathetic nervous system [25, 26], an effect which is observed at relatively low blood levels of nicotine, and the effect reaches a maximum even if the nicotine level in the blood is further increased; and persists as long as the nicotine levels are moderate, including overnight. This means that a snuff user can have a sympathetic activation 24 h per day [26]. The results of the present study may thus partly be due to a short-term effect from snuff use. However, subjects were not allowed to use tobacco during the health check-up and the blood pressure was measured after 5 min of rest in supine position. Another way of limiting any bias from short-term effect is to use a high cut-off for the definition of high blood pressure. A review article indicates that the maximal elevation in blood pressure after snuff intake ranges from 4 to 15 mmHg for systolic blood pressure and 6–11 mmHg for diastolic blood pressure [13]. For the

purpose of the present study, we defined high blood pressure as systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 100 mmHg. These cut-off points for high blood pressure exceed those which are currently recommended. The increase in blood pressure from the direct effect of snuff is unlikely to rise above this cut-off value in a normotensive person. It should also be noted that the effect of former snuff use on high blood pressure in the present study was not as consistent, or statistically significant as for current snuff users, which may imply that the effect of snuff use decreases after cessation.

Strengths of the present study include the prospective design, the large sample size and a homogeneous study population. During prolonged follow-up, misclassification of exposure might happen because of subsequent changes in tobacco use. The data on snuff exposure have not been validated in the present study. However, a previous study on the Construction Workers Cohort showed that the inconsistency over time was only 2.6% regarding tobacco smoking [27]. Another Swedish study found that once snus use was initiated, more men continued using snus rather than quit tobacco completely [28]. Although we lacked individual level information by which to control for education, diet and physical activity, the variability of these factors is expected to be less amongst construction workers than in the general population. We were able to adjust directly for BMI. This is an important risk factor for hypertension, and to some extent helps control caloric intake and physical inactivity. As we did not have any information on the nonattendants, we do not know whether there would be a potential selection bias and how this would influence the results.

It is important to point out that the identification of cases of hypertension in this study is not optimal. One report indicates that only 17% of all patients with hypertension can be identified in the Inpatient Register [29]. Such misclassification of outcome is probably nondifferential, i.e. both snuff users and nonsnuff users have the same probability of presence in the register. If anything, this bias would primarily contribute to a dilution of the effect from snuff use on hypertension

but the magnitude may be unimportant if mainly the sensitivity (underdiagnoses) is affected [30].

In conclusion, we found an increased risk of elevated blood pressure and hypertension amongst snuff users. These results are of potential public health importance as the prevalence of snuff use is high in Sweden and that hypertension is one of the major risk factors for cardiovascular disease.

Conflict of interest statement

No conflict of interest was declared.

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