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Are the health risks of moist oral snuff (snus) underestimated?

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The use of moist oral snuff (snus) has increased significantly, particularly among young adults who have not previously smoked. Snus increases the risk of cancer, cardiovascular disease, type-2 diabetes and birth defects.

In recent decades, there has been a worrying increase in the use of moist oral snuff (snus) in Norway, particularly amongst young people and adults under the age of 40. Many who use snus have not previously smoked. The nicotine content of some of the new types of snus is several times higher than that of smoking tobacco and earlier types of snus.

Commissioned by the Ministry of Health and Care Services, in autumn 2019 the Norwegian Institute of Public Health updated the evidence base for assessing the health risks associated with using Swedish snus, which dominates the Norwegian snuff market (1, 2). The update and our conclusions are based on systematic literature reviews. We have included studies that compare risk amongst users of snus with that of non-users, evidence from in vivo and in vitro studies on nicotine effects and mechanisms, knowledge about tobacco-specific nitrosamines and snus, as well as evidence of adverse health effects from using other tobacco products. Compared to earlier reports, there is now stronger evidence to suggest that the risk of contracting several serious diseases is higher among those who use snus. The results give cause for concern.

Using snus versus non-smoking

Our emphasis was on studies that compare the risk of disease and death amongst non-smoking users of snus with that of non-tobacco users. The reason for this emphasis was that any adjustment made for smoking habits without data about smoking volume or duration, will be inaccurate and incomplete. If smokers who also use snus smoke less than those who only smoke cigarettes, this may lead to an over-adjustment of the smoking component and a consequential underestimation of the effect of snus.

In some studies, the risk estimates for snus-exposed groups were not significantly different from the control groups, and the estimates had broad and asymmetrical confidence intervals. Although such results do not provide a basis for unambiguous conclusions, they are often incorrectly interpreted as an absence of risk.

Risk of disease

We found that the use of snus increases the risk of cancer of the oesophagus, stomach, pancreas and rectum. Using snus also increases the risk of high blood pressure, increases the mortality rate after cancer, myocardial infarction and cerebral stroke, and increases the risk of non-affective psychosis, type-2 diabetes, metabolic syndrome, weight gain and obesity. We also found evidence to suggest that the use of snus may reduce the risk of Parkinson's disease (table 1).

Table 1

Estimated risk per 100,000 users of snus, based on the control groups (non-users of tobacco products) in studies included in the evidence report on health risks of snus from the Norwegian Institute of Public Health (1). The study populations are not directly comparable because of dissimilar follow-up periods and age distribution. RR = relative risk, HR = hazard ratio, OR = odds ratio, MD = mean difference

Condition	Number per 100,000 users of snus	Time since tobacco habits were recorded (as per the last year of observation)	Risk estimate (95 % confidence interval)
Oesophageal cancer	39 more	34	RR 3.5 (1.6–7.6)
Gastric cancer	95 more	34	RR 1.4 (1.1–1.9)
Pancreatic cancer	79 more	27	RR 2.1 (1.2–3.6)
Rectal cancer	8 more	5–36	HR 1.38 (1.07–1.77)

Condition	Number per 100,000 users of snus	Time since tobacco habits were recorded (as per the last year of observation)	Risk estimate (95 % confidence interval)
High blood pressure	440 more	-	RR 1.39 (1.08–1.79)
Non-affective psychosis	72 more	8	HR 1.38 (1.09–1.75)
Type 2-diabetes	70 more (c. 4 tins of snus per week)	5–16	HR 1.15 (1.00–1.32)
Metabolic syndrome	5,963 more (> 4 tins of snus per week)	10	OR 1.6 (1.26–2.15)
Weight gain	4,731 more	5	OR 1.31 (1.04–1. 65)
Obesity	2,559 more	5	OR 1.93 (1.13–1.30)
Parkinson's disease	199 fewer	20	HR 0.38 (0.23–0.63)
Stillbirths	108 more	-	OR 1.43 (1.02–1.99)
Extreme preterm delivery, < 28 weeks	101 more	-	OR 1.69 (1.17–2.45)
Moderately preterm delivery, 32–36 weeks	841 more	-	OR 1.26 (1.15–1.38)
Small for gestational age	543 more	-	OR 1.38 (1.01–1.88)
Birth weight	39 g lower[1]	-	MD −39 (−79–−6)
Ceasarean section	2,405 more	-	OR 1.19 (1.02–1.40)
Neonatal arrhythmia	1.16 more [1]	-	MD 1.16 (0.55–1.77)
Oral cleft malformation	85 more	-	OR 1.48 (1.00–2.21)
Neonatal apnoea	147 more	-	OR 1.96 (1.30–2.96)

[1]Mean difference

Insufficient information about exposure

Insufficient data about possible changes in the participants' tobacco habits during the follow-up period was a common weakness of population studies with a long follow-up period. Good information about exposure and health outcomes is essential for population studies to reveal the true effects of exposure. Several of the population studies that we examined, were not originally designed to study the effects of using snus. In the cohort with the largest number of participants, use of snus was recorded as one of several life style factors, and the analyses were most often based exclusively on the first registration (3). Many participants may have discontinued using snus in the course of the follow-up period, as suggested by studies that repeatedly recorded the participants' snus habits. Any change in this habit will lead to misclassification of exposure, which in turn may weaken the association between using snus and health outcomes, potentially making it impossible to prove such a link.

Impact of snus on women and fetuses

Among women who used snus throughout pregnancy, we found an increased risk of stillbirth, premature delivery, small-for-gestational age fetus, low birth weight, caesarean section, neonatal arrhythmia, oral cleft malformations and neonatal apnoea. A higher level of the nicotine metabolite cotinine detected in the urine of neonates confirmed nicotine exposure from maternal snus use. Long-term effects of using snus while pregnant have also been found: at 5–6 years of age, children of mothers using snus during pregnancy had higher blood pressure, more frequent arrhythmias and stiffer artery walls than children of mothers not using any tobacco products.

Using snus also increases the risk of high blood pressure, increases the mortality rate after cancer, myocardial infarction and cerebral stroke, and increases the risk of non-affective psychosis, type-2 diabetes, metabolic syndrome, weight gain and obesity

More than 600,000 people in Norway are estimated to regularly use Swedish snus, mainly in the younger age groups (1). Women who use snus are generally under 35 years of age. This is unique to Norway and is of particular concern in view of the health risks during pregnancy.

The disease progression, symptoms and prognoses associated with several diseases, amongst them cardiovascular disease, affect women and men differently. With the exception of pregnancy outcomes, there tended to be too few women included in the studies for the results to be reliable. Consequently, we have very little knowledge about the impact of snus on women's health.

Interpretation of results

The literature often reports the risk of health outcomes as relative risk estimates, which says little about the impact on public health, i.e. the numbers affected. We therefore chose to calculate the absolute risk increase for 100,000 users of snus based on the absolute risk found in the control group (Table 1). Where the use of snus could worsen the disease prognosis, we calculated the absolute increase in risk per 1,000 patients who used snus.

In the pooled analyses of risk of myocardial infarction and cerebral stroke, we found that the 95 % confidence interval for myocardial infarction ranged from 214 fewer to 518 more myocardial infarctions per 100,000 users of Swedish snus, and that the confidence interval (CI) for cerebral stroke ranged from 212 fewer to 449 more strokes per 100,000 users of Swedish snus. We concluded that these are imprecise results because the confidence intervals include much more than what we would refer to as little or no difference. In a relatively recent review, Rostron et al. summarised the use of snus in the Nordic countries and the USA based on the same studies that we used (4). The authors conclude that Americans who use smokeless tobacco have an increased risk of stroke and myocardial infarction, whereas a similar increase in risk was not identified for users of Swedish snus in the Nordic countries.

Poorer prognosis

Our calculations show that using snus results in 44 more fatalities per 1,000 patients after a cancer diagnosis, 51 more fatalities after myocardial infarction, 35 more fatalities after cerebral stroke, and 73 more fatalities during a long follow-up period (17 years) after cerebral stroke. Patients who quit using snus after a myocardial infarction halve the risk of dying in the next two years (5).

The estimated risk of dying within 28 days of both myocardial infarction and cerebral stroke had broad confidence intervals that only just included 1. The results are thus borderline statistically significant, but indicate that the risk of dying in the first four weeks after myocardial infarction and cerebral stroke increased by 28 and 42 per cent respectively. These results are supported by a considerably reduced risk of dying after a myocardial infarction when quitting the snus habit and a statistically significant increased mortality rate associated with the use of snus in a study that involved a long follow-up period after cerebral stroke. Evidence of the vasoconstrictive effect of nicotine and the ability of snus to increase blood pressure and adversely affect the endothelial cells of blood vessels also supports our conclusion that snus increases the mortality rate after myocardial infarction and cerebral stroke.

Different conclusions for pancreatic cancer and cardiovascular diseases

In some cases, our assessment differs from that of the authors of the original study. One

example concerns pancreatic cancer. In a study from 2007, Luo et al. investigated a cohort of Swedish construction workers who had been followed up for a period of up to 27 years (3). With close to 280,000 participating men, this is the largest available Swedish cohort with registered snus habits. Luo et al. found that the use of snus doubled the risk of pancreatic cancer. Nine years later, the same construction workers were included in a pooled analysis with men from eight other Swedish cohorts. Araghi et al., who conducted the pooled analysis, found a hazard ratio (HR) of 1.07 (95 % CI 0.77–1.50) for pancreatic cancer among men who used snus only, compared with men who did not use snus and did not smoke (6). The confidence interval suggested a potential risk reduction of up to 23 per cent as well as a potential risk increase of up to 50 per cent.

Users of snus who quit after myocardial infarction halve the risk of dying in the aftermath

We consider this result of the pooled analysis to be inaccurate. In their article, Araghi et al. put particular emphasis on an analysis conducted amongst men who used snus, irrespective of their smoking habits, compared to men who did not use snus, also irrespective of smoking habits (6). The authors adjusted (in the pooled analysis) for smoking, but had no data for volume or duration, and found a hazard ratio of 0.96 (95 % CI 0.83–1.11). They interpreted this to indicate that snus does not cause pancreatic cancer in men. As already discussed above, this methodology may lead to overadjustment for smoking and underestimation of the effect of using snus. Furthermore, the long follow-up period may carry an increased risk of misclassification, because many may have quit their snus habit in the course of the follow-up period. Consequently, several factors may render it impossible to reveal an association.

We therefore have most confidence in the study conducted by Luo et al. (3), which shows a doubling of the risk, i.e. an effect that is sufficiently strong to qualify for an upgrade according to the GRADE method (7). We also know that the tobacco-specific nitrosamine NNK (nicotine-derived nitrosamine ketone) causes pancreatic cancer in animal studies and that exposure to other tobacco products such as cigarette smoking leads to a similar increase in the risk of pancreatic cancer. It has been proven that the risk of this form of cancer decreases to the background level after smoking cessation. It is reasonable to assume that the same is the case on snus cessation.

The conclusions drawn in the studies on cardiovascular disease and cancer have incorrectly been cited in support of the claim that using snus does not carry a health risk (4, 6). However, the absence of a statistically significant difference is not synonymous with an absence of effect in the exposure group.

Main message to healthcare personnel

The use of Swedish moist oral snuff (snus) is associated with an increased risk of cancer, high blood pressure, increased mortality after cancer, cardiovascular diseases, increased risk of psychosis, obesity, metabolic syndrome – and (in cases of high consumption) increased risk of type-2 diabetes. Users of snus who quit after myocardial infarction halve the risk of dying in the aftermath. Using snus during pregnancy is harmful to the child. The high rate of snus use is therefore worrying.

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