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## **Snus and Health: A Review of the Literature on the Impact of Swedish Smokeless Tobacco on the Human Body**

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**Abstract**

**Introduction:** Snus is a tobacco-containing product particularly popular in Scandinavian countries. It comes in the form of a pouch filled with tobacco, which is typically placed under the upper lip, allowing nicotine to be absorbed through the mucous membrane. Due to the absence of combustion during snus use—and consequently the lack of substances produced by this process—many manufacturers claim that snus is a healthier alternative to cigarettes. The aim of this article is to review scientific studies examining the effects of snus on the human body and to objectively summarize its impact on human health.

**Materials and Methods:** This study was conducted by collecting scientific articles from the PubMed database and other online scientific databases. The articles were identified using keywords such as "snus," "smokeless tobacco," and "snus health impact."

**Results:** Snus cannot be considered a healthier alternative to tobacco use. While it does not cause many of the diseases associated with smoking and the toxic compounds produced during combustion, it is still addictive and contributes to other health issues caused by the substances it contains and the way it is consumed. This product requires more detailed scientific research.

**Key words:** snus, nicotine, health impact, smokeless tobacco

## **Introduction**

Snus is a tobacco-containing product, particularly popular in Sweden, where it is estimated that up to 12% of the population uses it. The product consists of a mixture of dried tobacco leaves and salt, which is then moistened with hot steam. Snus may also include flavoring additives. The resulting moist powder is shaped by hand or with a special device, and the mass is placed under the upper lip (known as *lössnus*).

The second available form of snus is the so-called "portion snus," which is sold in small cellulose pouches approximately 3 cm x 1 cm in size. These pouches come in two types: dry ("white") or moist ("original" or "black"). Each pouch contains between 2 and up to 50 mg of nicotine. Portion snus is more common than *lössnus*. In Norway, this form is preferred by nearly 70% of men and almost all women.

## **Snus – How is it made?**

The process of preparing the mixture required to produce snus consists of three stages.

1. **Grinding:** In this stage, tobacco leaves are crushed, dried, and placed in a grinder, which breaks them into small pieces. This results in a fine powder.
2. **Blending and Pasteurization:** The powder is weighed, and appropriate amounts are placed in blenders, where water and salt are added. The mixture is heated in a process known as pasteurization. After cooling, additional ingredients, such as flavor additives, are introduced. These flavors are often inspired by popular chewing gum (e.g., mint, fruit) or beverages (e.g., cola). During this stage, quality control is also performed. Samples are checked, and once approved, the process moves to the third stage.
3. **Packaging:** The tobacco mixture, after weighing, is placed in paraffin-coated cardboard cans (*lössnus*) or sealed in small cellulose pouches, which are then packaged into larger containers (portion snus). [1]

## **Snus – Why is it harmful, and can it cause cancer?**

Snus contains N-nitrosornicotine (NNN) and 4-(N-methyl-N-nitrosamino)-1-(3-pyridyl) butanone (NNK), which are potent tobacco-specific nitrosamines (TSNAs) known to be carcinogenic. These compounds are created during the drying and processing of tobacco. These nitrosamines can be metabolically activated by enzymes in various cell types, such as those in the liver, lungs, and oral cavity, converting them into reactive forms. These reactive metabolites can bind to DNA, leading to permanent damage, which may mark an initial step in the development of cancer. Both animal and human cells have the ability to produce such

DNA-binding metabolites, indicating that the cancer-causing process in humans likely mirrors what occurs in lab animals. The International Agency for Research on Cancer (IARC) classifies NNK and NNN as human carcinogens based on robust evidence from studies on cells, animals, and populations, which show a clear link between exposure levels to these nitrosamines and cancer risk, particularly in smokers.

Research on cells has revealed that nicotine triggers various signaling pathways that are important for understanding its potential role in enhancing cancer progression once it has been initiated by established carcinogens. Experimental studies in animals suggest that nicotine may act as a promoter, meaning it could accelerate the progression of cancer after its initial development.

### **Snus Use and the Risk of Developing Lung Cancer**

The relationship between snus use and the risk of lung cancer is a topic of much research and debate. Unlike cigarettes, snus is not burned, which significantly reduces exposure to toxic substances present in tobacco smoke, such as polycyclic aromatic hydrocarbons and benzo[a]pyrene. However, snus contains other compounds, such as tobacco-specific nitrosamines (TSNAs), which may increase the risk of cancer development.

It is well-known that traditional cigarettes are a risk factor for lung cancer. Because of this, companies producing snus often market it as a healthier alternative to smoking. As a result, one of the first questions asked by snus users is whether it truly does not increase the likelihood of developing this disease. A cohort study conducted on nearly 280,000 Swedish construction workers found a similar relative risk of lung cancer incidence between snus users and individuals who had never used tobacco. [2] Similarly, a study conducted in Norway by Boffetta et al. (2005) did not find an increased relative risk of lung cancer (considering all histological types of this cancer). [3]

### **The Impact of Snus on the Pancreas**

While cigarette smoking is a well-documented risk factor for pancreatic cancer, the impact of snus is less well-established. This concept arises from the fact that snus contains tobacco-specific nitrosamines, which are carcinogenic, and the pancreas, as a metabolically active organ, may be particularly susceptible to their effects. Additionally, nicotine-induced inflammation can alter pancreatic cell metabolism, promoting cancer development. Nicotine

products also impair local immune responses, creating a favorable environment for carcinogenesis.

Araghi et al. (2017) collected data from nine cohort studies to assess the association between snus use and the risk of pancreatic cancer. In total, they analyzed data from over 424,000 Swedish men. Compared to never-snus use, current snus use was not associated with risk of pancreatic cancer (HR 0.96, 95% CI 0.83–1.11). This indicates that the use of snus is not associated with the development of pancreatic cancer. The authors of the study suggested that this might be linked to the lower levels of nitrosamines in snus compared to their presence in tobacco smoke. [4] However, in 2019, the Norwegian Institute of Public Health updated its report on the health effects of snus. The organization stated in the report that a connection with pancreatic cancer is possible. [5]

### **Oral Cavity Changes**

Due to the method of snus usage, various changes can occur in the oral cavity. Repeated placement of a nicotine pouch under the upper lip causes localized irritation of the oral mucosa, which may manifest as redness, stinging, itching, or a burning sensation. These changes can extend to the entire oral cavity and throat, leading to coughing. The ability to perceive tastes can also be affected.

More disturbing changes include ulcers (affecting up to 30% of users [6]), canker sores, or disturbances in saliva secretion. These changes are caused by impaired blood flow in the oral mucosa, a reduction in the number of white blood cells, and prolonged exposure to the causative factor.

A study conducted on young adults in Norway between 2015 and 2016 revealed that as many as 79.2% of daily snus users experienced snus-induced changes. [7] In the same study, the authors mentioned gum recession, observed in 18.4% of participants.

This condition is caused by the loss of connective tissue, which diminishes at the site where snus is applied. [8][9]

Another potential change caused by snus is leukoplakia, a precancerous condition characterized by the presence of white patches on the surface of the mucosa. [10] Leukoplakia is particularly dangerous and serves as a warning sign because it can transform into squamous cell carcinoma. While some studies have confirmed the carcinogenic effects of snus on the oral cavity [11][12], others have not found such a connection or deemed it statistically insignificant. [13][14] These discrepancies could appear from variations in the methodologies

used in different studies. This aspect should be explored further and requires additional research. Ann Roosaar et al. arrived at a similar conclusion, stating that the risk associated with snus is biologically possible and that it cannot be categorically claimed that snus does not contribute to the development of oral cancers. [15] Interestingly, one study found that snus use was associated with less dental calculus in the front teeth, where the cellulose pouch is placed, compared to the back teeth. [16] This is attributed to increased local salivation and more frequent mechanical manipulation with the tongue in these areas.

### **Other Gastrointestinal Cancers**

Several studies have examined the impact of snus on the development of gastrointestinal cancers, including stomach, colon, and rectal cancer. These studies do not provide a definitive conclusion that would allow for the formulation of a clear position on this matter. In its latest report from 2019, the Norwegian Institute of Public Health stated that the link between snus and stomach cancer is likely. [5]

The NIPH's stance is partly based on studies by Zendehdel et al., which reported a relative risk of 1.4 (95% CI 1.1 to 1.9, 68 exposed cases) for developing non-cardia stomach cancer. [17] The situation is similar concerning colorectal and rectal cancer. Research indicates that snus users, compared to non-tobacco users, are at a higher risk of developing colon cancer. For individuals who exclusively use snus and have never used tobacco, the study reported the following hazard ratios (HR): for colon and rectal cancer combined, an HR of 1.16 (95% CI: 0.97–1.37, based on 153 cases); for colon cancer alone, an HR of 1.02 (95% CI: 0.81–1.29, based on 80 cases); and for rectal cancer, an HR of 1.38 (95% CI: 1.07–1.77, based on 73 cases). [18] Valen et al. undertook a summary of the available studies in 2022. The authors' findings do not indicate a strong link between snus use and the aforementioned diseases. [19]

### **The Impact of Snus on the Cardiovascular System**

Nicotine exposure leads to an increase in heart rate (nicotine stimulates nicotinic receptors in the autonomic nervous system, particularly in sympathetic ganglia. This results in the release of adrenaline and noradrenaline, which accelerate heart rate and increase its contractility) and blood pressure (caused by the vasoconstrictive effect of nicotine on blood vessels). This effect is temporary, but prolonged and regular nicotine consumption can lead to heart failure due to increased oxygen demand. Consequently, heart function may be impaired, which can lead to arrhythmias. Also, inflammation triggered by nicotine can contribute to the buildup of plaques in the arteries, which raises the likelihood of developing atherosclerosis, a condition

characterized by the hardening and narrowing of the arteries. As a result, nicotine potentially elevates the risk of cardiovascular disease in both smokers and snus users.

Interesting results were obtained in the study by Antoniewicz et al., in which healthy young daily snus users participated in two sessions spaced at least one week apart. During these sessions, they were exposed to either conventional snus (containing 8mg/g of nicotine) or a flavored, plant-based, nicotine- and tobacco-free snus pouch, which is often used as a cessation aid for snus users. Participants were required to abstain from alcohol for 24 hours and avoid food, tobacco, and caffeine-containing drinks for at least 12 hours before each session. After resting for 20 minutes, a pouch of either snus or the nicotine/tobacco-free control was placed under their upper lip. Measurements of systolic and diastolic blood pressure (SBP and DBP), heart rate (HR), and arterial stiffness (evaluated using pulse wave analysis [PWA] and pulse wave velocity [PWV]) were taken every five minutes over a 45-minute exposure period and for an additional 30 minutes post-exposure. Men initially had higher baseline blood pressure values. All participants in the study were of a similar age, had been using snus for approximately the same duration, and in similar quantities.

Upon analyzing the results, it was found that snus use caused an increase in blood pressure; however, this increase was significant only in women.

The study authors also measured arterial stiffness using the AIx75 index, which is a cardiovascular measurement used to evaluate arterial stiffness and wave reflection. It offers valuable information about arterial health and serves as an indicator of cardiovascular risk. The term "AIx75" refers to the Augmentation Index adjusted to a heart rate of 75 beats per minute (bpm), ensuring consistent comparisons between people with varying resting heart rates. Analiza wyników nie udowodniła, że snusy zwiększają sztywności naczyń. [20]

Even in individuals who had never used nicotine, the use of snus leads to an increase in blood pressure. This was confirmed in a pilot study conducted in 2016 by Ozga et al. [21]. In this study, 11 participants who had never used nicotine were exposed to 6 snus sachets, each containing an increasing dose of nicotine. The interval between the use of each sachet was 45 minutes. The study also observed that the higher the nicotine dose administered to participants (the maximum used in the study was 8 mg), the more significant the changes in blood pressure.

Another aspect worth considering is whether the use of snus contributes to more frequent episodes of heart attacks and strokes. The effects of nicotine, such as raising blood pressure, increasing heart rate, causing vasoconstriction (which leads to reduced blood flow through

coronary vessels), triggering inflammatory processes in vessels (which result in the formation of atherosclerotic plaques), and enhancing the tendency for platelet aggregation, suggest that snus use may influence the occurrence of cardiovascular events.

In one study conducted in Sweden, a group of researchers utilized data from a population cohort of over 41,000 Swedish adults aged 56–94 years. Participants completed questionnaires about their lifestyle, health, and snus use. The cohort also included individuals who had never used nicotine. They were subsequently monitored for 8 years for cardiovascular incidents. In this Swedish cohort of middle-aged and older adults, current use of snus showed no correlation with the risk of significant heart or valvular diseases, abdominal aortic aneurysm, or cardiovascular disease (CVD) mortality across the entire study group. [22] Researchers studying another cohort consisting of 585 snus users and smokers, along with a control group of 589 participants, reached a similar conclusion. The study found no association between snus use and heart attacks, but an increased incidence of cardiovascular events among smokers. The researchers concluded that nicotine itself is not the primary substance contributing to heart disease. [23]

However, other studies have indicated an increased relative risk of death due to cardiovascular diseases. The risk was higher for smokers—1.9 (95% CI 1.7–2.2)—than for smokeless tobacco users—1.4 (95% CI 1.2–1.6)—compared to individuals who reported never using tobacco. [24]

Another study differentiated between participants who had ever used snus and those who were heavy users (daily) compared to individuals who had never used nicotine. The results showed a relative risk (RR) of 1.28 (95% CI 1.06–1.55) for fatal heart attack cases in the first group and 1.96 (95% CI 1.08–3.58) for the second group. [25] It is important to highlight that these studies did not account for the smoking history of snus users, which represents a significant confounding variable. In addition, the studies did not consider alcohol consumption, medical history or any changes regarding tobacco product use. Additionally, all data were self-reported, and the research included only male participants. This aspect certainly requires further scientific studies and observations.

Researchers have also examined the issue of strokes among snus users. Meta-analysis doesn't show link between current snus use and stroke. The combined relative risk (RR) estimate was 1.05 (95% CI 0.95–1.15) for the entire population and 1.06 (95% CI 0.96–1.17) among individuals who had never smoked. [26] W publikacji z 2014r. badano częstość występowania udarów i przeżywalność po udarze. Nie zaobserwowano żadnych powiązań między



stosowaniem snusów a ogólnym ryzykiem udaru. [27] Based on the findings related to snus use, several researchers have proposed that nicotine is unlikely to play a significant role in the development or progression of stroke. [28][29]

### **The Role of Snus in the Development of Diabetes**

Nicotine affects insulin and glucose metabolism. It reduces tissue sensitivity to insulin, leading to insulin resistance, which is a key factor in the development of type 2 diabetes. Additionally, by stimulating the release of adrenaline, which triggers glycogenolysis in the liver, it increases blood sugar levels. Furthermore, nicotine products can exacerbate oxidative stress, which promotes metabolic disorders. Inflammation in the body caused by nicotine is also significant, as it is associated with the development of insulin resistance.

The earliest study suggested a link between snus use and the development of type 2 diabetes. More than 3,000 men were studied, with over half reporting a family history of type 2 diabetes. The results showed that snus users had nearly a fourfold higher chance of developing type 2 diabetes compared to those who had never used tobacco. These results were adjusted for age, family history of type 2 diabetes, alcohol consumption, and BMI of the participants, but the history of smoking was not taken into account. [30] Next studies no longer demonstrated such a significant risk of developing type 2 diabetes. [31][32][33]

Another study investigating the risk of type II diabetes among a large cohort of middle-aged male snus users who had never smoked found no significant impact on the overall group. However, it was observed that the risk of developing diabetes increased with higher levels of snus consumption per week. For example, among men using 4 or more cans of snus per week, the odds ratio was 2.1, and with consumption of 5 cans per week, this parameter increased to 3.3. [34]

The study authors acknowledge, however, that existing research has its limitations and that further studies are needed to confirm the link between snus use and the occurrence of type 2 diabetes.

### **The Impact of Snus on the Fetus**

Due to the fact that snus contains nicotine, it has negative effects on the developing fetus. Nicotine can lead to miscarriage, preterm birth, or low birth weight. This is primarily caused by nicotine-induced vasoconstriction, which restricts blood flow through the placenta, thereby reducing oxygen and nutrient delivery to the fetus. Additionally, compounds in snus may

cause structural damage to the placenta. Nicotine also disrupts the development of the central nervous system (CNS), which may result in cognitive and behavioral disorders in the child.

In a study summarizing previous research, Brinchmann et al. concluded that the use of snus during pregnancy increases the risk of stillbirth and preterm delivery. It also reduces the average birth weight of the fetus and raises the likelihood of congenital defects such as cleft lip and palate. The association between snus use and the occurrence of preeclampsia or antepartum hemorrhage remains uncertain. Mothers who used snus during pregnancy were also more likely to undergo cesarean deliveries. [35]

Even after the child is born, the effects of nicotine use during pregnancy can be severe. One study concluded that such behavior is associated with an increased risk of postnatal mortality and Sudden Infant Death Syndrome (SIDS). [36]

### **Summary:**

The impact of snus on health is a broad topic that certainly warrants further investigation in future studies. Many studies suggest that snus is less harmful to the human body than smoking cigarettes, which is attributed to the lower concentration of harmful substances generated during combustion. However, the health effects of snus use in comparison to individuals who have never used nicotine remain inconclusive and require additional research and analysis.

It is important to remember that snus is a mixture of several substances, including nicotine, whose effects are well-documented. Therefore, it cannot be considered neutral in its impact on the human body.

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