

### KEY MESSAGES

- The available evidence suggests that use of Swedish snus is not associated with an increased risk of oral cancer. Three high-quality epidemiology studies specifically examined the possibility that use of snus causes oral cancer, and found no relationship. Of three additional studies that looked at the development of multiple cancer types and an association with snus use, only one study found a significant association with oral cancer.
- Two public health agency reports have concluded that there is “sufficient evidence” that *smokeless tobacco* use causes oral cancer in humans; however, both reviews combine data from studies of different types of smokeless tobacco from around the world which have known composition differences.
- Three meta-analyses (a study that combines results of several studies that address a similar hypothesis) restricted to Swedish snus did not find a significantly increased risk of oral cancer.

### QUESTIONS AND ANSWERS

#### **Why have researchers studied the relationship between snus use and oral cancer?**

Cigarette smoking and use of some types of smokeless tobacco are known to cause oral cancer. It is logical that researchers would be interested in the relationship between snus use and oral cancer.

#### **Is there evidence that snus use is associated with oral cancer?**

The available evidence suggests that use of Swedish snus does not increase the risk of oral cancer. Three high-quality epidemiology studies specifically examined the possibility that use of snus causes oral cancer, and found no relationship. Of three additional studies that looked at the development of multiple cancer types, only one study found an association between use of snus and increased risk of oral cancer.

Three epidemiology studies (Lewin et al. 1998; Schildt et al. 1998; Rosenquist et al. 2005) were performed specifically to understand the role of snus use and other habits (such as alcohol drinking and current or prior smoking) in the development of oral cancer. These studies used widely accepted methods (the case-control design), involved a significant number of subjects (more than 2,300 Swedish people), and none found evidence of a statistically significant increased risk of oral cancer. In addition, these studies were careful to rule out the influence of a number of "confounding factors" (such as smoking, age, and alcohol consumption) that might obscure the true relationship between snus use and oral cancer.

Three additional cohort studies examined the relationship between use of *smokeless tobacco* and the development of several types of cancer. Boffetta et al. (2005) followed more than 10,000 Norwegian men for more than 30 years and found that men who used smokeless

tobacco were not at significantly increased risk of oral cancer, compared to men who had never used smokeless tobacco. Luo and colleagues (2007) confirmed the lack of a significant association between snus use and risk of oral cancer in more than 125,000 men from a cohort of Swedish construction workers who had never smoked tobacco. This analysis allowed them to distinguish the possible effects of snus from those of smoking. Most recently, Roosaar et al. (2008) reported the findings of a study suggesting a significant association of snus use with oral cancer, adjusted for the effect of smoking, in a cohort of 9,860 men in central Sweden. However, because the analysis included men who could have smoked in addition to using snus, a separate analysis was conducted that compared *smokeless tobacco* users to never smokers. The association was no longer statistically significant, which suggests that the statistical method for control of smoking was incomplete. A limitation of this study is that there were only a small number of cases who were exclusive snus users, making this risk estimate unstable.

Several review studies (meta-analyses) developed overall risk estimates for oral cancer associated with snus, adjusted for cigarette smoking, based on individual epidemiology studies (Boffetta et al. 2008; Weitkunat et al. 2007; Lee and Hamling 2009). None of the meta-analyses (in which results from individual studies are combined to provide a single estimate of risk) observed an overall increased risk of oral cancer associated with use of snus. Lee and Hamling (2009) and Lee (2010) concluded that no real evidence of a relationship with snuff use is seen in studies conducted in Scandinavia.

### **What conclusions have been reached by public health agencies about the association between snus use and oral cancer?**

The International Agency for Research on Cancer (IARC) concluded that there is “sufficient evidence” that *smokeless tobacco* causes oral cancer in humans (Cogliano et al. 2004; IARC 2007) based on a 2004 re-evaluation that did not alter their original conclusions in the 1985 IARC Monograph. IARC relied heavily on a U.S. case-control study (Winn et al. 1981) and four studies in India and Pakistan. Many scientists believe studies from South Asia are not relevant to assessing the health effects of snus. In addition, the U.S. studies that they considered for additional support (Blot et al. 1988; Kabat et al. 1994; Stockwell and Lyman 1986; Williams and Horn 1977) almost certainly included exposures that are likely not relevant to snus.

The Scientific Committee on Emerging and Newly Identified Health Risks evaluated the health effects of *smokeless tobacco* with particular attention to snus, but also relied upon studies of *smokeless tobacco* from other countries (SCENIHR 2008). They also concluded that there is “sufficient evidence” that *smokeless tobacco* causes oral cancer in humans based on the same studies as IARC with the addition of the Roosaar et al. (2008) study. The Roosaar study has several methodological limitations (noted previously).

### **Snus users sometimes get lesions in their mouths. Are they cancerous?**

No. These lesions, known as “snus-induced lesion,” are considered non cancerous, does not progress to become cancerous, and is reversible if snus use is stopped. Studies have shown that these lesions do not worsen over time, do not progress, and that oral cancers rarely occur at the site of use (Roosaar et al. 2006; Kallischnigg et al. 2008).

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