# Systematic review of the relation between smokeless tobacco and cancer of the pancreas in Europe and North America

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## BACKGROUND

Recent reviews claiming smokeless tobacco increases pancreatic cancer risk appear not to have considered all available epidemiological evidence, nor were meta-analyses included.
We present a systematic review of studies from North America and Europe, as data are lacking from other continents. Risk is also difficult to quantify elsewhere due to the various products, compositions, and usage practices involved.

## METHODS

### Study identification and selection

Relevant studies were identified by literature searches through December 2007 using EMBASE, MEDLINE, and references listed in the identified publications. The search was not limited by period or language. The main searches were based on combinations of the terms “smokeless tobacco”, “chewing tobacco”, “snuff”, and “snus” for exposure and “pancreatic cancer” for outcome. Study selection was restricted to epidemiological reports which presented data on pancreatic cancer mortality or morbidity associated with use of snuff, chewing tobacco, or unspecified smokeless tobacco.

### Meta-analyses

Fixed-effect and random-effects meta-analyses were conducted. For selected meta-analyses, a forest plot is shown.

## RESULTS

Nine North American and two Scandinavian studies were identified. Reporting was limited in four studies, so only seven studies were included in meta-analyses, some providing results for never (or non-current) smokers, some for the overall population of smokers and non-smokers, and some for both. Giving preference to study-specific estimates for the overall population, if available, and for never (or non-current) smokers otherwise, the random-effects estimate for ever smokeless tobacco use was 1.10 (95% confidence interval 0.73-1.65), based on heterogeneous estimates from seven studies (Figure 1). The estimate varied little by continent, study type, or type of smokeless tobacco.
Giving preference to estimates for never (or non-current) smokers, if available, and overall population estimates otherwise, the estimate was 1.15 (0.67-1.98), again based on heterogeneous estimates (Figure 2). Estimates varied (Chi-square p=0.014) between cohort studies (1.75, 1.20-2.54) and case-control studies (0.87, 0.35-2.16). The value for cohort studies was derived mainly from one study, which reported an increase for never smokers (2.0, 1.2-3.3), but not overall (0.9, 0.7-1.2). This study contributed to increases seen for snuff use and for European studies as well. In both cases, the significant increases were observed only in fixed-effect analyses.

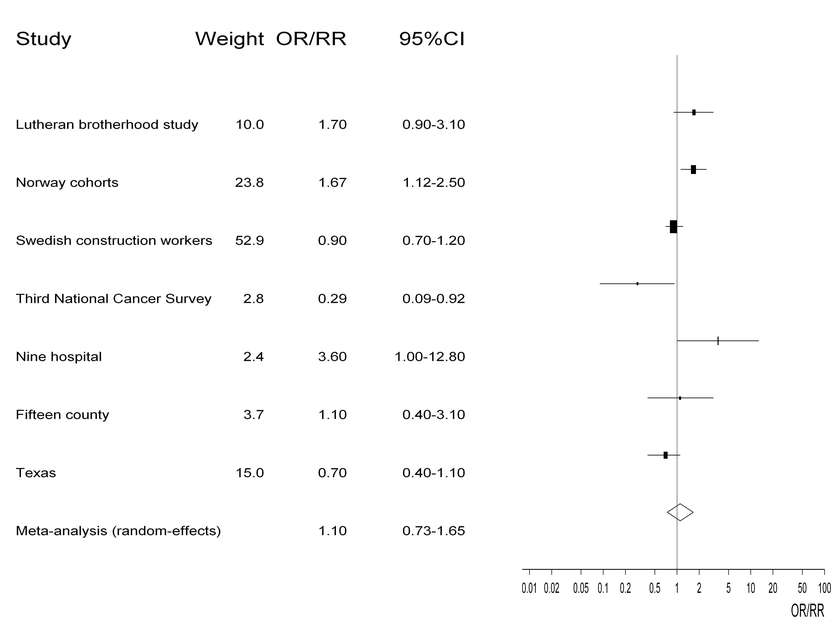


Figure 1. Forest plot of study-specific effect estimates and 95% CIs, using overall population estimates where available.

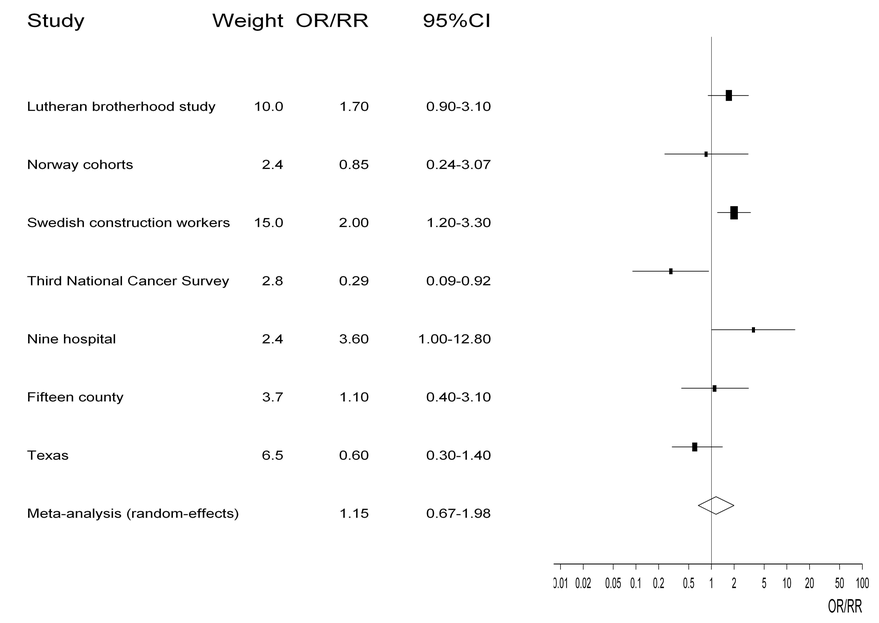


Figure 2. Forest plot of study-specific effect-estimates and 95% CIs, using estimates for never (or non-current) smokers where available.

## CONCLUSIONS

The available data relating pancreatic cancer to smokeless tobacco use are limited and relatively weak. Random-effects meta-analyses based on evidence from seven studies do not show a significant relationship of smokeless tobacco use with pancreatic risk, whether (a) attention is restricted specifically to estimates for never (or non-current) smokers, (b) estimates for never (or non-current smokers) are used where available and overall population estimates used otherwise, or (c) overall population estimates are used where there is a choice. While some subgroup analyses based on the second set of estimates seem to suggest a possible association, all of these are heavily dependent on the contribution of one specific relative risk estimate from one study with known weaknesses. The data, taken as a whole, are no more than suggestive of a possible effect. More evidence is needed to determine if a true relationship exists. Any risk that may exist is highly likely to be less than that associated with active smoking.

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