

**Epidemiological evidence on “snus”
(Swedish moist snuff) and health in adults**

By Peter Lee

Relevant publications specifically on snus

- Lee, P.N., 2011. Summary of the epidemiological evidence relating snus to health. Regul. Toxicol. Pharmacol. 59, 197-214.
- Lee, P.N., 2013a. The effect on health of switching from cigarettes to snus - a review. Regul. Toxicol. Pharmacol. 66, 1, 1-5.
- Lee, P.N., 2013b. Epidemiological evidence relating snus to health - an updated review based on recent publications. Harm Reduct. J. 10, 1, 36.
- Rutqvist, L.E., Fry, J.S., Lee, P.N., 2013. Systematic review of Swedish snus for smoking cessation based on primary subject data from randomised clinical trials. J. Smok. Cessat. 8, 1, 33-44.
- Lee, P.N., 2014. Health risks related to dual use of cigarettes and snus - A systematic review. Regul. Toxicol. Pharmacol. 69, 125-134.
- Lee, P.N., 2015. Appropriate and inappropriate methods for investigating the "gateway" hypothesis, with a review of the evidence linking prior snus use to later cigarette smoking. Harm Reduct. J. 12:8.

Relevant publications on smokeless tobacco (ST) more generally

- Weitkunat, R., Sanders, E., Lee, P.N., 2007. Meta-analysis of the relation between European and American smokeless tobacco and oral cancer. *BMC Public Health*. 7, 334.
- Kallischnigg, G., Weitkunat, R., Lee, P.N., 2008. Systematic review of the relation between smokeless tobacco and non-neoplastic oral diseases in Europe and the United States. *BMC Oral Health*. 8, 13.
- Sponsiello-Wang, Z., Weitkunat, R., Lee, P.N., 2008. Systematic review of the relation between smokeless tobacco and cancer of the pancreas in Europe and North America. *BMC Cancer*. 8, 356.
- Lee, P.N., Hamling, J.S., 2009a. The relation between smokeless tobacco and cancer in Northern Europe and North America. A commentary on differences between the conclusions reached by two recent reviews. *BMC Cancer*. 9, 256.
- Lee, P.N., Hamling, J.S., 2009b. Systematic review of the relation between smokeless tobacco and cancer in Europe and North America. *BMC Med*. 7, 36.

Also – Comments on the recent rule proposal by FDA on a standard for NNN in smokeless tobacco products.

Some background

- Selling snus is banned in the EU except in Sweden.
- Sweden has a long history of snus use. Around 20% of men and 3% of women use snus regularly.
- Sweden has the lowest percent smokers in Western Europe.
- Snus users get a nicotine “dose” similar to that in cigarette smokers.
- Nitrosamine levels in snus have markedly decreased in Sweden over time. Levels in ST products are higher in the USA, and much higher in South Asia.
- There are numerous good epidemiological studies on snus.
- Some present results in never smokers, some in the whole population.

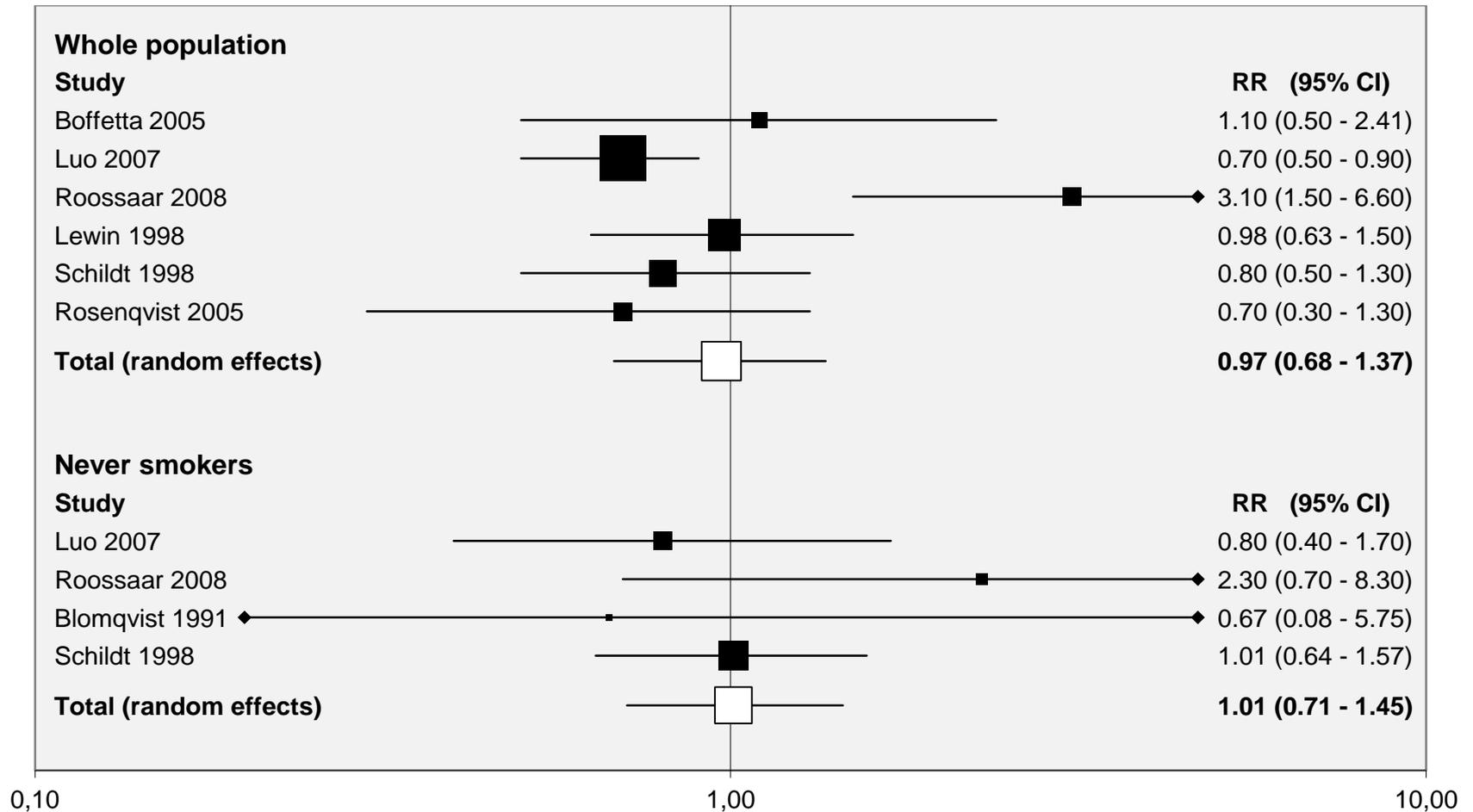
Cancer and snus

Oral and pharyngeal cancer

Overall evidence from 7 studies shows no relationship. Combined relative risk estimates are 0.97 (95%CI 0.68-1.37) for the whole population and 1.01 (0.71-1.45) in never smokers.

This contrasts with a 5-fold increased risk for oral cancer and a 3-fold increased risk for pharyngeal cancer for Indian studies of ST.

Figure 1. Oral/pharyngeal cancer and snus



Cancer and snus

Oesophageal cancer

Four studies show no association for smokers and non-smokers combined, with an overall estimate of 1.10 (95% CI 0.92-1.33).

The construction workers study reported an estimate of 1.92 (1.06-3.68) in never smokers. This study has limitations and tends to report associations not seen in other studies.

In contrast to the clear evidence of about a 3-fold increase in Indian ST users, the evidence for snus is at most suggestive.

Cancer and snus

Pancreatic cancer – 1

The claim that snus (and ST generally) causes pancreatic cancer came from a 2008 report on ST which used an inconsistent approach when selecting multiple estimates from the same study.

In one of the two studies on snus then available, they included in their meta-analyses a whole population estimate which showed an association, ignoring the lack of association in never smokers. In the other they did the reverse, including only the result in never smokers which showed an association.

Pancreatic cancer – 2

Since then, the evidence has increased. Reviews by Bertuccio *et al* in 2011 and Burkey *et al* in 2014 found no evidence of a relationship of ST with pancreatic cancer.

More relevantly, a very recent report by Araghi *et al*, based on a pooled analysis of nine cohort studies in Sweden, found no association whatsoever between snus use and pancreatic cancer.

The original claim was unscientific and is clearly incorrect.

Cancer and snus

Other evidence

Snus use is not associated with an increased risk of other cancers, including lung and stomach cancer, though the evidence for some cancers is quite sparse.

Nor is there any relationship with overall cancer risk, whether in never smokers or the whole population.

In 2009, Jan Hamling and I estimated that tobacco-attributable deaths would reduce by about 99% were all smokers to switch to ST and had the excess risks of ST users in Western populations. It is clear that snus-related cancer deaths, if they exist, are substantially lower than smoking-related cancer deaths.

Stroke and snus

- In 2011, I reviewed evidence from six studies. All reported results in never smokers with a combined RR estimate of 1.06 (95% CI 0.96-1.17). Three reported results in the whole population with a combined estimate of 1.05 (0.95-1.15).
- In 2014, Hansson *et al* pooled data from eight prospective studies, three in my review. They reported no association in never smokers, with a combined estimate of 1.04 (0.92-1.17).

Ischaemic heart disease (IHD) or acute myocardial infarction (AMI) and snus (1)

- In 2011, I reviewed evidence from nine studies. All reported results in never smokers with a combined RR estimate of 0.99 (95% CI 0.85-1.14). Seven reported results in the whole population with a combined estimate of 1.01 (0.91-1.12).
- In 2012, Hansson *et al* pooled data from eight prospective studies, three in my review. They reported no association in never smokers, with a combined estimate of 1.04 (0.93-1.17).
- There was marginal evidence of increased case fatality in snus users, attributed by the author to confounding by socioeconomic or lifestyle factors.

IHD or AMI and snus (2)

- In 2014, Arefalk *et al* reported that stopping snus use post-AMI reduced mortality risk, but the reduction was not statistically significant – 0.57 (95% CI 0.32-1.02).
- Recent studies have reported no association of snus with atrial fibrillation (Hergens *et al*, 2014) or left ventricular function (Sundström *et al*, 2013), but possibly an increase in heart failure (Arefalk *et al*, 2012).
- My 2011 review noted that snus users have increased weight, but chronic hypertension and diabetes seemed unaffected.

IHD or AMI and snus (3)

- More recently, Carlsson *et al* concluded that “high consumption of snus is a risk factor for type 2 diabetes” based on pooled results from five studies.
- I will shortly submit for publication a review paper on snus and diabetes, based on 18 studies. As shown in the following slides, there was no clear evidence of an increased risk in current users, for never smokers or for the whole population.
- The highest level of snus exposure was associated with an increased risk in never smokers, but more data are needed.

Figure 2. Diabetes and current snus use in never smokers

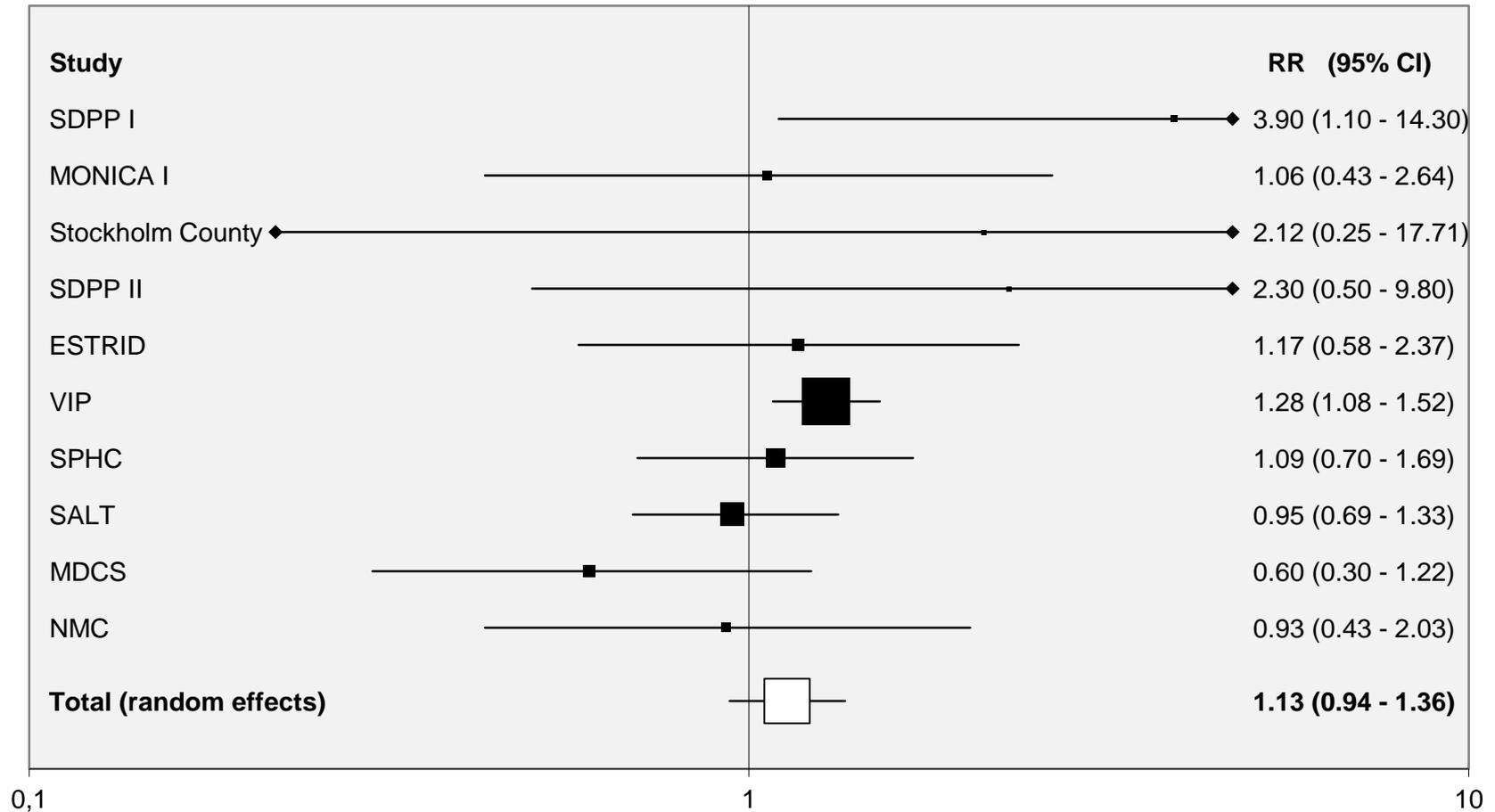


Figure 3. Diabetes and current snus use in the whole population

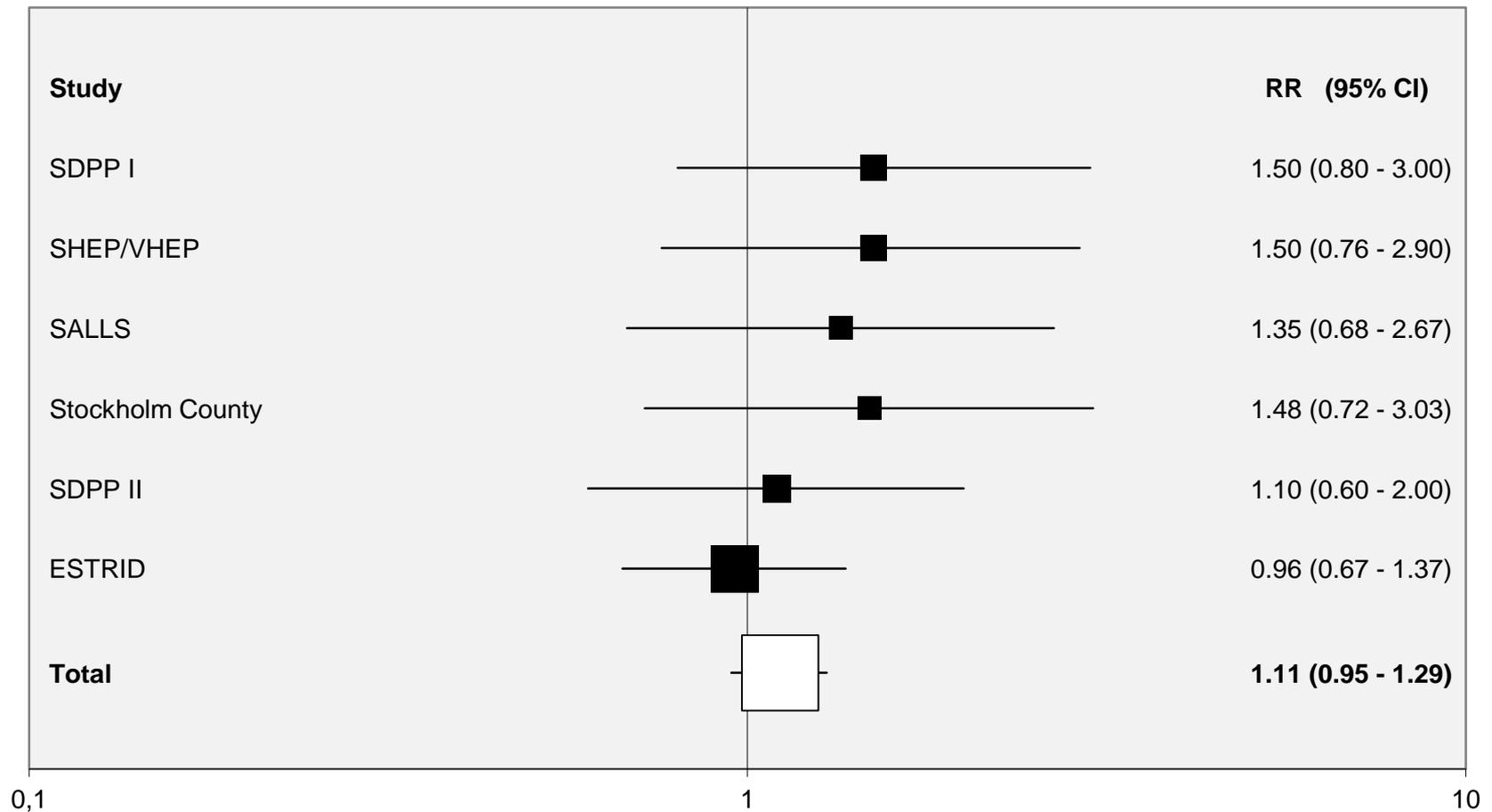
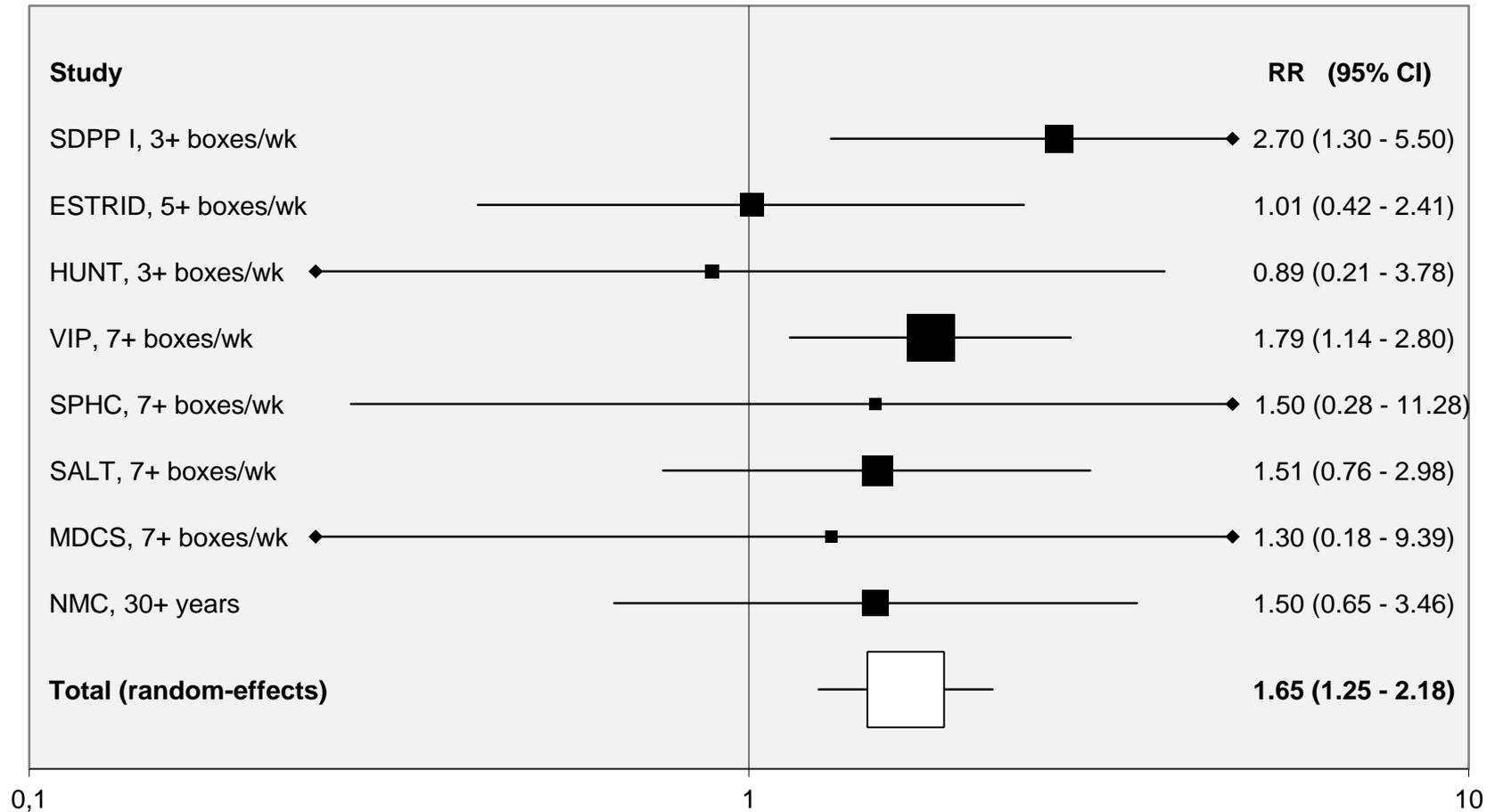


Figure 4. Diabetes and highest snus use in never smokers



Effect of snus on smoking habits

- There is no good evidence that snus acts as a “gateway” to smoking.
- Indeed, the fact that smoking is less common in Sweden than elsewhere in Europe argues against this.
- There are no reports that snus use discourages quitting and limited evidence from clinical trials that it might help quitting.

Conclusions

- If snus has any adverse effects on health, they are very minor compared to those from cigarette smoking.
- There is no good evidence it encourages smoking or discourages quitting.
- For smokers who still want their nicotine dose, snus is a very much safer alternative.
- Although other nicotine delivery systems that avoid inhalation of combusted material (such as e-cigarettes) may also be a much safer alternative to cigarettes, it is only for snus that there is good epidemiological evidence of reduced harm.
- The situation in the EU, where snus may be sold only in Sweden, but cigarettes can be sold everywhere, is ridiculous.

Other references cited (1)

- Araghi, M., et al., 2017. Use of moist oral snuff (snus) and pancreatic cancer: Pooled analysis of nine prospective observational studies. *Int. J. Cancer*. Epub ahead of print May 8.
- Arefalk, G., Hambræus, K., Lind, L., Michaëlsson, K., Lindahl, B., Sundström, J., 2014. Discontinuation of smokeless tobacco and mortality risk after myocardial infarction. *Circulation*. 130, 4, 325-332.
- Arefalk, G., et al., 2012. Smokeless tobacco (snus) and risk of heart failure: results from two Swedish cohorts. *Eur. J. Prev. Cardiol*. 19, 5, 1120-1127.
- Bertuccio, P., et al., 2011. Cigar and pipe smoking, smokeless tobacco use and pancreatic cancer: an analysis from the International Pancreatic Cancer Case-Control Consortium (PanC4). *Ann. Oncol*. 22, 6, 1420-1426.
- Burkey, M.D., Feirman, S., Wang, H., Choudhury, S.R., Grover, S., Johnston, F.M., 2014. The association between smokeless tobacco use and pancreatic adenocarcinoma: a systematic review. *Cancer Epidemiol*. 38, 6, 647-653.

Other references cited (2)

- Carlsson, S., et al., 2017. Smokeless tobacco (snus) is associated with an increased risk of type 2 diabetes: results from five pooled cohorts. *J. Intern. Med.* 281, 4, 398-406.
- Hansson, J., et al., 2012. Use of snus and acute myocardial infarction: pooled analysis of eight prospective observational studies. *Eur. J. Epidemiol.* 27, 10, 771-779.
- Hansson, J., et al., 2014. Snus (Swedish smokeless tobacco) use and risk of stroke: pooled analyses of incidence and survival. *J. Intern. Med.* 276, 1, 87-95.
- Hergens, M.P., et al., 2014. Use of Scandinavian moist smokeless tobacco (snus) and the risk of atrial fibrillation. *Epidemiology.* 25, 6, 872-876.
- Sundström, D., Waldenborg, M., Magnuson, A., Emilsson, K., 2013. Chronic nicotine effects on left ventricular function in healthy middle-aged people: an echocardiographic study. *Clin. Physiol. Funct. Imaging.* 33, 4, 317-24.