

## Snus and the risk of cancer of the mouth, lung, and pancreas

Juhua Luo and colleagues (June 16, p 2015)<sup>1</sup> state: "Our study is at odds with the perception that use of Swedish moist snus has no demonstrable carcinogenic risk." This statement is attributed to a publication of which I was the first author.<sup>2</sup> However, I wrote in that article that Swedish moist snuff is associated with no demonstrable risk of oral cancer. I am delighted to learn that Luo and colleagues agree, since their study "did not detect any excess risk for cancer of the oral cavity" among Swedish snus users.

Their current study has two important ramifications for tobacco users, neither of which was discussed. First, Luo and colleagues excluded Swedish construction workers enrolled in their cohort from 1971 to 1975 because of "ambiguities" in questionnaire coding. This presents a challenge to the credibility of an earlier report by Bolinder and colleagues,<sup>3</sup> which stands almost alone in linking snus use with cardiovascular diseases. The Bolinder study involved only workers enrolled in the years excluded by Luo and colleagues (1971–74), and questions about its findings were raised shortly after its publication.<sup>4</sup> Luo and colleagues should disclose more information about deficiencies in this cohort, and about the decision to restrict their analysis to workers enrolled from 1978 to 1992.

Second, the study by Luo and colleagues has implications for cancer mortality patterns not only in Sweden, but in smoking-dominated societies. The table shows mortality rates for cancers of the oral cavity, lung, and pancreas in Luo and colleagues' study population according to tobacco use. No tobacco product is demonstrably safe, but these data show that snus use is 97% less harmful than smoking

	Smokers who quit smoking	Smokers who switch to snus†	Smokers who switch to snus‡	Current smokers who continue to smoke
<b>Men's age (years)*</b>				
35	0.37 (0.34–0.40)	0.63 (0.56–0.69)	0.78 (0.70–0.86)	5.02 (4.72–5.35)
45	0.77 (0.71–0.83)	0.99 (0.91–1.08)	1.12 (1.03–1.22)	5.03 (4.72–5.36)
55	1.40 (1.29–1.52)	1.71 (1.56–1.87)	1.81 (1.66–1.97)	4.80 (4.49–5.13)
65	1.81 (1.65–1.99)	2.01 (1.83–2.21)	2.14 (1.96–2.35)	3.95 (3.65–4.26)
75	1.47 (1.29–1.68)	1.55 (1.35–1.75)	1.60 (1.41–1.81)	2.36 (2.11–2.62)
<b>Women's age (years)*</b>				
35	0.26 (0.24–0.29)	0.44 (0.40–0.49)	0.57 (0.50–0.65)	4.10 (3.85–4.35)
45	0.47 (0.43–0.51)	0.63 (0.58–0.69)	0.76 (0.68–0.84)	4.05 (3.80–4.30)
55	0.77 (0.71–0.83)	1.03 (0.94–1.12)	1.14 (1.04–1.25)	3.78 (3.54–4.03)
65	1.06 (0.97–1.15)	1.26 (1.15–1.37)	1.36 (1.23–1.48)	3.22 (2.98–3.46)
75	1.01 (0.88–1.13)	1.12 (0.98–1.25)	1.19 (1.03–1.33)	1.92 (1.69–2.13)

Data are years lost (95% CI). \*Age at baseline year (2000); smokers who switch to snus and smokers who quit smoking, switch, or quit in the baseline year. †Original model with snus use assumed to have 10% of smokers' cardiovascular disease mortality risk. ‡Amended model with snus use assumed to have 100% of smokers' cardiovascular disease mortality risk.

**Table: Years of healthy life lost compared with people who have never used tobacco**

research into how attractive current smokers find snus as an alternative to smoking and how likely smokers are to engage in long-term dual use with cigarettes.

McKee and Gilmore suggest that our model underestimated the risk of death from cardiovascular disease caused by snus because one study reported a 40% increase in cardiovascular death in snus users compared with non-smokers.<sup>3</sup> We reran the simulation, with snus use assigned the same risk of death from cardiovascular disease as smoking. Large health gains were still seen if smokers switched to snus (table). Even assuming a greater effect of snus on cardiovascular disease, the difference in health-adjusted life expectancy between lifelong non-tobacco-users and snus users who never smoked ranged from 0.3 to 0.6 years, whereas that between quitting tobacco use and switching to snus ranged from 0.1 to 0.4 years, depending on the age at which the smoker quit or switched to snus.

We wholeheartedly agree that the regulation of nicotine products should be proportional to the harm that they cause. In Australia, pharmaceutical nicotine replacement therapy that is much like cigarettes is available in supermarkets, but snus is completely

banned from sale. Yet new tobacco products can be introduced to the market so long as they are smoked. Philip Morris has recently received a green light from the Australian government to sell a potential reduced-exposure cigarette which it claims reduces second-hand smoke emissions by 90%.<sup>4</sup> A continuation of bans on snus means that smokers interested in reduced-harm products can only use putatively reduced-risk products that have at best uncertain health risks and probably higher ones than those of snus.

We declare that we have no conflict of interest.

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- 1 Ramström LM, Foulds J. Role of snus in initiation and cessation of tobacco smoking in Sweden. *Tob Control* 2006; **15**: 210–14.
- 2 Bolliger CT, Zellweger JP, Danielsson T, et al. Smoking reduction with oral nicotine inhalers: double-blind randomised clinical trial of efficacy and safety. *BMJ* 2000; **321**: 329–33.
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- 4 Houston C. Revealed: tobacco giant's secret new weapon in the age of smoking bans. *The Age* July 27, 2007.

	Oral cavity	Lung	Pancreas	All
Never-users	1.3	7.3	3.7	12.3
Current smokers	2.8	70.0	12.4	85.2
Current snus users	1.1	5.1	8.4	14.6

\*Deaths per 100 000 human-years. Data based on incidence rates from Luo and others<sup>1</sup> and 5-year case-fatality rates: oral cavity (41%), lung (85%), and pancreas (95%) from US National Cancer Institute Surveillance, Epidemiology and End Results Program.<sup>5</sup>

**Table: Mortality rate\* for cancers of oral cavity, lung, and pancreas in Swedish male construction workers, according to tobacco use**

with respect to cancers of the oral cavity, lung, and pancreas.

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- 1 Luo J, Ye W, Zendehelel K, et al. Oral use of Swedish moist snuff (snus) and risk for cancer of the mouth, lung, and pancreas in male construction workers: a retrospective cohort study. *Lancet* 2007; **370**: 2015–20.
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- 4 Rodu B, Cole P. Excess mortality in smokeless tobacco users not meaningful. *Am J Public Health* 1995; **85**: 118.
- 5 US National Cancer Institute Surveillance, Epidemiology and End Results Program. Cancer Stat Fact Sheets. <http://seer.cancer.gov/statfacts/> (accessed May 18, 2007).

### Authors' reply

We apologise for misinterpreting the conclusion of the review paper by Brad Rodu and his colleague.<sup>1</sup> Our impression was based on Rodu's explicit suggestion that the International Agency for Research on Cancer's classification of all smokeless tobacco products as carcinogenic to human beings, and the requirement to place warning labels on such products, might have been too broad. We are glad to learn that Rodu's standpoint is more moderated.

A report showing similar urinary excretion of a biomarker of exposure to the carcinogenic tobacco-specific nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone in smokeless tobacco users and cigarette smokers<sup>2</sup> underscores the need for caution.

As regards the information collected in 1971–75, we noted that non-smokers could not actively deny smoking in the questionnaire. Instead, they were instructed to simply skip the smoking questions. All cohort members without answers to these questions were coded as non-users. Thus, the never-smoker category might have contained some smokers who skipped the smoking questions for other reasons. Because non-smokers were instructed to move directly to the snus questions, where absence of any response was likewise coded as non-use, it is conceivable that, of all those who skipped the smoking questions, the proportion of smokers who skipped it inappropriately was greater when both sets of questions were skipped than when the snus questions were answered in the affirmative. However, a subsequent sensitivity analysis using admittedly self-selected workers with information from one or several repeat visits<sup>3</sup> did not support this suspicion.

According to our observed data, the excess mortality from the three studied cancers among cohort members who were current smokers at entry but never used snus and those who were current snus users but never smoked was, respectively, 80.4 and 4.9 per 100 000 human-years. If all cancer sites were to be included in the calculations, the advantage for snus might be greater. However, given the two-fold excess incidence of pancreatic cancer<sup>4</sup> and a 40% excess mortality from the three studied cancers combined (data not shown), surely Rodu would agree that snus use should always be discouraged in never-smokers.

So the adequate comparison from a public-health perspective is between persistent smokers and ex-smokers who switched to snus use, or between ex-smokers who quitted with and without snus. Unfortunately, incomplete information on if and when smokers quitted has prohibited these comparisons.

We declare that we have no conflict of interest.

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- 1 Rodu B, Jansson C. Smokeless tobacco and oral cancer: a review of the risks and determinants. *Crit Rev Oral Biol Med* 2004; **15**: 252–63.
- 2 Hecht SS, Carmella SG, Murphy SE, et al. Similar exposure to a tobacco-specific carcinogen in smokeless tobacco users and cigarette smokers. *Cancer Epidemiol Biomarkers Prev* 2007; **16**: 1567–72.
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- 4 Luo J, Ye W, Zendehelel K, et al. Oral use of Swedish moist snuff (snus) and risk for cancer of the mouth, lung, and pancreas in male construction workers: a retrospective cohort study. *Lancet* 2007; **369**: 2015–20.

### Department of Error

*Light DW. Is G8 putting profits before the world's poorest children? Lancet* 2007; **370**: 297–98—In this Comment (July 28), the author's address should have been "University of Medicine and Dentistry of New Jersey, Stratford, NJ 08084, USA".

*Pitcock SJ. Interferon beta in multiple sclerosis: how much BENEFIT? Lancet* 2007; **370**: 363–64—In this Comment (Aug 4), the last sentence of paragraph 5 should have read: "Additionally, they have sought to address many concerns of previous trials by maintaining blinding for the initial randomisation for both patients and physicians, and had a lower drop-out rate (15% and 19% of original interferon and placebo groups, respectively) than did other reported studies."<sup>11</sup>