

Errors and omissions in the study of snuff use and hypertension

Dear Sir,

We are writing to point out that the study of high blood pressure and hypertension amongst Swedish male snuff users by Hergens *et al.* [1] contains several apparent errors. In addition, the study omits prevalence estimates for the 37 546 subjects who had an Inpatient Register diagnosis of hypertension prior to baseline, and it omits follow-up information on hypertension for 35 464 subjects who were healthy at baseline but did not have repeated measurements.

Errors

In Table 1 ('baseline-cohort' column) and Table 2 (all rows except '≥65'), the number of ever snuff users is larger than the sum of the numbers of former and current users (the largest discrepancy of 57 is in the 'baseline cohort' column in Table 1). Similarly, the number of all workers in the 'repeated-measurements' column of Table 1 ($n = 42\,005$) is larger than the sum of never- and ever-snuff users, and the percentages for the highest two dose categories, 5% and 3%, are incorrect. We also point out that the results in this manuscript differ from those in Table 10 of the original thesis of this work published by the Karolinska Institute [2]. There is an ambiguity in Tables 2 and 3, which report age-specific odds ratios (ORs) but contain footnotes describing age adjustment. It is highly unusual for age-adjustment to be carried out within 5-year age intervals, so the authors should either explain this logistic model or correct the footnote.

Omissions

Hergens *et al.* [1] present detailed information about the 5915 workers with high blood pressure at baseline, giving prevalence and OR estimates according to snuff use, age and consumption level (Tables 1–3).

But the authors provide no corresponding estimates for the 37 546 workers who had an Inpatient Register diagnosis of hypertension prior to baseline. As defined in this study, high blood pressure and hypertension are two separate case definitions for the same condition. Failure to provide the effect estimates for hypertension is incomprehensible, and the study must be considered incomplete until this important omission is corrected.

Hergens *et al.* [1] emphasize in the Abstract, Introduction and Discussion, the longitudinal nature of their study. However, the person-time contributed by cohort members is not mentioned anywhere in the manuscript. In addition, longitudinal data are presented only in Table 4, which also omits critical outcome data. The table lists relative risks (RRs) for an Inpatient Register diagnosis of hypertension during follow-up amongst all workers who were healthy at baseline ($n = 77\,469$), and amongst a subset of workers who had repeated measurements ($n = 42\,005$), but there is no RR information for a second subset of 35 464 workers who were healthy at baseline and did not have repeated measurements. The RRs for the repeated-measurement subset, regardless of snuff use (i.e. ever, former, current and all consumption levels) are higher than those for all workers, indicating that the former may have had other characteristics that contributed to these elevated risks. Hergens *et al.* [1] must provide RRs for hypertension amongst the 35 464 workers who were healthy at baseline and did not have repeated measurements. Otherwise, the authors' aim of assessing '...the risk of... hypertension amongst male long-term users of snuff, particularly based on longitudinal data', is not achieved.

Hergens *et al.* concluded that their 'results are of potential public health importance as the prevalence of snuff use is high in Sweden and that hypertension

is one of the major risk factors for cardiovascular disease'. The potential public health importance of this study is contingent upon the resolution of the errors and omissions that we have described.

Conflict of interest statement

Our research is supported by unrestricted grants from smokeless tobacco manufacturers to the University of Louisville (US Smokeless Tobacco Company and Swedish Match AB) and to the University of Alberta (USSTC). The terms of the grants assure that the grantors are unaware of this letter, and thus had no scientific input or other influence with respect to its design, analysis, interpretation or preparation. Neither of us has any financial or other personal relationship with regard to the grantors.

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References

- 1 Hergens M-P, Lambe M, Pershagen G, Ye W. Risk of hypertension amongst Swedish male snuff users: a prospective study. *J Intern Med* 2008; 264: 187–94.
- 2 Hergens M-P. *Swedish Moist Snuff and the Risk of Cardiovascular Diseases*. Doctoral thesis. Stockholm: Institute of Environmental Medicine, Karolinska Institute, 2007.

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Snuff use and hypertension: response to Rodu and Heavner

Dear Sir,

We thank Rodu and Heavner for their detailed reading of our paper and the opportunity to make some clarifications and corrections. However, we want to emphasize that this does not change the results or our interpretation of the findings.

As Rodu and Heavner points out there were some errors in the numbers of study subjects given in Tables 1 and 2. In Table 1, the following changes should be made: In the baseline cohort with 120 930 men, 85 470 (71%) (previously, 85 413) were never tobacco users. The healthy cohort with 42 005 men, 29 912 (71%) (previously 29 892) were never tobacco users. Furthermore, in Table 2 there were some minor errors when summing up the current and former snuff users into ever snuff users in all age groups. The previously given and correct numbers are presented in Table A.

Regarding the highest two dose categories in Table 1 amongst those with repeated measurements, the correct proportions are 5.6% and 2.3% (compared to 5% and 3% as given in our paper).

Age is an important confounder in our material. It is not unusual to adjust for age as a continuous variable even when stratified into age categories. Hence, this regression model does not need to be modified.

It appears that Rodu and Heavner misunderstood Tables 1–3. It is clearly stated in the table headings that these analyses comprise all 120 930 men at baseline and not only the 5 915 men with high blood pressure.

We did not present person-years in our paper. However, in the method section we stated that for longitudinal analyses we used the Cox proportional hazards

model which requires an estimation of follow-up time and person-years. For the benefit of the readers, we present person-years in the different subsets in Table B. In this table we have also added the relative risk of hypertension amongst the subset of workers who were healthy at baseline and did not have repeated measurements ($n = 35\,464$). In this subset, a total of 250 men with a diagnosis of hypertension were identified in the Inpatient Register during follow-up. The proportion of ever snuff users was 36% in this subset. Amongst the former snuff users, only five men were found to have a diagnosis of hypertension in the Inpatient Register during follow-up and amongst current snuff users the corresponding number was 61 cases.

Finally, some preliminary results were published in an original thesis by Karolinska Intitutet 2007 [1]. Due to some changes in the final analyses, minor discrepancies in the results exist between Table 10 in the thesis version and in the final paper [2]. However, the interpretation of the results remains the same: there appears to be a moderately increased risk of hypertension related to the use of Swedish

Table A Corrected numbers of ever snuff users in the different age strata. Baseline cohort ($n = 120\,930$)

Age at baseline (years)	Previously Ever used snuff n	Corrected Ever used snuff n
All	1106	1100
<45	529	528
45–49	110	109
50–54	116	115
55–59	168	167
60–64	176	174
≥65	7	7

	Healthy at baseline (<i>n</i> = 77 469)	Healthy at baseline with repeated measurements (<i>n</i> = 42 005)	Healthy at baseline without repeated measurements (<i>n</i> = 35 464)
		High blood	
Outcome	Hypertension	pressure	Hypertension
Follow-up period	1978–2004	1978–1993	1978–2004
Person years	1 411 922	449 883	847 222
			564 799
Relative Risk ^a (95% CI)			
Ever snuff use			1.28 (0.96–1.72)
Former snuff use			0.97 (0.40–2.37)
Current snuff use			1.32 (0.98–1.79)

^aDerived from Cox proportional hazards regression model; CI, confidence interval; adjusted for age (age at follow-up was used as time scale), body mass index [weight(kg)/height(m²)], categorized into <20, 20.24.9, 25–29.9 and ≥30 and region of residence northern, middle and southern Sweden.

Table B Follow-up periods and accumulated person-years amongst Swedish male construction workers

moist snuff, which may be of public health importance.

Conflict of interest statement

No conflict of interest was declared.

2 Hergens M-P, Lambe M, Pershagen G, Ye W. Risk of hypertension amongst Swedish male snuff users: a prospective study. *J Intern Med* 2008; 264: 187–194.

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- 1 Hergens M-P. *Swedish Moist Snuff and the Risk of Cardiovascular Diseases*. Stockholm: Institute of Environmental Medicine, Karolinska Institutet, 2007.