Author’s response to reviews

Title: No connection between the level of exposition to statins in the population and the incidence/mortality of acute myocardial infarction: An ecological study based on Sweden’s municipalities.

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Author’s response to reviews: see over
Dear Editor!
The reviewer has made important and constructive remarks on the manuscript, *No connection between the level of exposition to statins in the population and the incidence/mortality of acute myocardial infarction: An ecological study based on Sweden’s municipalities*. Taking those remarks in account we think the manuscript has improved substantially and hope you will now consider it for publication in Journal of Negative Results in Biomedicine. Indeed, we are somewhat late according to the time limit set in your e-mail from the 13th of December. However we assume you got the e-mail sent on the 4th of March asking for some extension of time limit. According to your instruction for authors the order of the sections is changed i.e. Methods comes after Conclusions and a list of abbreviations has been added.

Sincerely
Staffan Nilsson
PhD, General practitioner

All changes are highlighted in the document.

**Background**
1. The first sentence has been replaced according to the referee’s suggestion. Consequently reference number 1 has been changed.

**Methods**
2. The importance of coronary revascularization is now mentioned in the Methods section. Consequently a new reference, number 20, has been added. Antihypertensive drugs as beta-blockers, ace-inhibitors and calcium channel blockers are also given for several other indications than hypertension e.g. angina pectoris, cardiac arrhythmias post AMI and heart failure. Therefore we chose not to adjust for the use of antihypertensive drugs in the statistical analyses.
3. ”−” means subtraction. The mathematical formulas are clarified in the text and highlighted.
4. The range of inhabitants are now included in the text for municipality groups 1, 3, 4, 7, 8 and 9. In group 2 more than 50 % of the resident population commutes to work in another municipality. In group 5 more than 40 % of the resident population are employed within the industrial sector and in group 6 more than 6.4 % within agriculture and forestry. A group 6 municipality has a population density below 70 % and is not a sparsely populated district. The exact range of inhabitants is not given for municipality groups 2, 5 and 6.
5. Since there is a considerable delay in the national registers and when the study was planned in 2005, 2002 was the last complete year. For the calculation of yearly AMI-incidence and mortality in each of the 289 municipalities the population sizes in the middle year i.e. 2000 were used. The socioeconomic deprivation index was calculated for each municipality for the year 2000 assuming no changes of importance during the studied five-year period.
6. The arguments are developed in the text, Discussion section paragraph four. In order to clarify “a few” has been changed to “two”.

**Results**
7. In section Statins, standard deviation (±SD) has been added. In section Mortality of AMI the exact figures and standard deviations of AMI mortality for men 70-79 years old in 1998 and 2002 has been added. In section Coronary revascularisation
the exact figures of mean revascularisation rates and standard deviations for men and women 70-79 years old in 1998 and 2002 has been added.
In section Socio-economic deprivation index, now ±SD is included in the text (page 5).
In the section Bivariate correlation and multivariate analysis (page 5) the exact correlation coefficients (r), regression coefficients (β) and p-values have been added.
In the end of section Statistical methods two sentences are added and highlighted.
We have discussed to insert ±SD in tables 1 and 2 instead of range. However, we think that range together with ±SD in the text is more informative.
8. SD within brackets has been replaced by ±SD to clarify it is standard deviation (page 4).
9. The remark is correct. “Statin utilization” has been skipped.
10. “Statistically” has been used and highlighted.

Discussion
11. May be “drawback” is better than complication.
12. The sentence has been changed according to the referee’s remark.
13. An explanation of NNT is added.

Conclusions
14. In order to be sharper “seems” has been replaced by “is” in section Conclusions, last sentence.

Tables
15. Explanations of abbreviations are now in tables 1-3.

Figure
16. Explanations of abbreviations are now in figure 1.
17. The incidence of AMI, attack rate, comprised fatal as well as non-fatal AMIs during each year. The same person could contribute by more than one AMI during the same year. Therefore we don’t think that person-year is relevant but rather AMI-incidence per 1000 inhabitants.
18. The text and explanations in figure 2 has been revised substantially in order to clarify the message.