Reviewer's report

Title: Statin use and association with colorectal cancer survival and risk: case control study with prescription data linkage

Version: 1 Date: 13 February 2012

Reviewer: Yana Vinogradova

Reviewer's report:

Research on associations between statin use and cancer risk has been active for years and a great number of epidemiological studies have been undertaken, yet there is still no definitive opinion about the effect of statins on the development of colorectal cancer.

The Introduction describes in details the mechanism suggested to reduce the risk of cancer but only briefly mentions epidemiological studies tabulating some of them in the Supplement. There is no explanation why the authors have conducted a study which is much less powerful than the previous ones. What is special about Scottish population and what additional knowledge might be useful to the reader? Are there particular factors associated with the risk of CRC and use of statins which were not available in previous studies?

Methods describe the study quite vaguely. What was the study period? What is the study type? How were outcomes defined? How was validity for recruited participants defined? Some details, at least an outline of the relevant parts of the food questionnaire, would be useful to see in the text. A full name for AJCC should be given. I am not clear what the authors mean by 'similarly for post-diagnosis' when defining use of statins.

The statistical analysis is also not well described. If each case was matched to one control there should be equal numbers of cases and controls as not matched observations would be dropped before running a conditional logistic regression. I am not clear what model was used for survival analysis – in page 8 paragraph 5 line 1 the authors say that it was Cox’s hazard model but in the next sentence they say that conditional logistic models were used in both survival and risk analysis. How was family history of CRC defined, particularly the categories low and medium/high? How was ‘regular intake’ of NSAIDs defined? How were missing values analysed?

Results. The reader wouldn’t expect to see significant differences in age and sex as the participants were supposed to be matched by these parameters. New factors, not described in Methods, appear in Results: physical activity, energy intake, HRT and contraception. It is not clear how the OR for BMI was obtained, in Methods BMI was defined as continuous variable and the OR should be given for an increment. For reported association in page 11 first line, the authors should at least mention whether it was positive or negative, and not just quote the P-value. No information about statin use is provided: descriptive statistics for number of prescriptions, duration of use and possibly types of statin. There is
also no information about how many observations were valid for multivariate analyses!

Discussion. Instead of concentrating on discussion of their own results the authors focus on speculations about limitations of other studies. The last sentence in paragraph 1 page 15 seems to be irrelevant. Apart from ‘some’ selection bias, which was in fact quite significant and which might warrant further investigation, there was also a volunteer bias (for control selection) which has not been mentioned as a limitation at all.

The authors suggest that small studies of this kind might contribute to some future meta-analysis, but the current quality of this paper would in my view make it an unlikely candidate for any such approach.

In summary, I would consider the two following points to be Major Compulsory Revisions:

1. To describe the study in full detail: the design, the study period, inclusions/exclusions, analysed variables, exposure to statins and other drugs, approach to missing values.

2. To analyse the difference between responders and non-responders and, for multivariate analyses, to provide the exact number of analysed observations.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.