

## ANSWERING REVIEWERS



September 11, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 4232-revision.doc).

**Title:** Statin use and the risk of liver cancer: a meta-analysis of 7 studies involving more than 4.7 million patients

**Author:** Hui Zhang, Chun Gao, Long Fang, Shu-Kun Yao

**Name of Journal:** *World Journal of Meta-Analysis*

**ESPS Manuscript NO:** 4232

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) The authors conducted the meta-analysis of 7 studies on statin use and its association with liver cancer risk in 4,725,593 people and 9,875 liver cancer cases. They showed that statin use was significantly associated with a 36-39% reduction of liver cancer risk. I have a few suggestions and comments; 1. The duration of literature search was not consistent. Please make the correction.

ANSWER: Thank you for your suggestion, the duration of literature search has been corrected.

(2) It must be better if the authors could provide the flow chart of the selection for inclusion in their meta-analysis.

ANSWER: Thank you for your good suggestion, the flow chart of the selection for inclusion in our meta-analysis has been provided as Figure 1.

(3) Discussion section: "Our result from liver cancer was not supported by another meta-analysis which was performed to determine the association between statins use and the risk of colorectal cancer.[24] This study involved eighteen studies and more than 1.5 million participants. The authors found that there was no evidence of an association between statin use and risk of colorectal cancer either among RCTs (RR 0.95, 95%CI 0.80-1.13, n=6) or among cohort studies (RR 0.96, 95%CI 0.84-1.11, n=3), although statin use was associated with a modest reduction in the risk of colorectal cancer among case-control studies. It seems that more studies are required in more kinds of malignancies." should be deleted since it is irrelevant to liver cancer.

ANSWER: Thank you for your suggestion, discussion about this article has been deleted.

(4) Similar to this study, there are two recent studies regarding statins and association with a reduced risk of liver cancer in which the authors should discuss their study in detail with those observations. Danitza P, et al. Statins and primary liver cancer: a meta-analysis of observational studies. *Eur J Cancer Prev* 2013; 22:229-34. Singh S, et al. Statins are associated with a reduced risk of hepatocellular cancer: A systemic review and meta-analysis. *Gastroenterol* 2013; 144:323-32.

ANSWER: Thank you for your suggestion, these two articles was published after our paper was submitted. They were performed independently and could be regarded as beneficial supplement.

(5) Zhang H, et al. reported that the association between statin use and the risk of liver cancer was determined by a meta-analysis. This analysis was involved in 7 studies, 4,725,593 people and 9,785 liver cancer cases from 2005 to 2013. The result showed a 36-39% reduction in liver cancer risk when used statin. This study is very interesting. However, authors may add a figure of the quality of reporting of meta- analyses statement to show how to select 7 studies.

ANSWER: Thank you for your good suggestion, the flow chart of the selection for inclusion in our meta-analysis has been provided as Figure 1.

(6) In addition, there have some information needed to check whether they are consistent. For example, in the abstract, authors stated that "A computerized literature search was conducted to identify those relevant studies between January 1966 and March 2013" and the result section "These studies involved 4,725,593 people and 9,785 liver cancer cases. They were published between the year of 2005 and 2013." Please check this information; in introduction section, it should be 4.9 per 100,000 people; give full name of "HCV", etc.

ANSWER: Thank you for your suggestion, the duration of literature search has been corrected. In addition, 4.9 per 100,000 people and the full name of "HCV" have been revised.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Meta-Analysis*.

Sincerely yours,

A handwritten signature in black ink that reads "Chun Gao". The script is cursive and fluid, with the first and last letters of each name being capitalized and prominent.

Chun Gao, MD  
Department of Gastroenterology  
China-Japan Friendship Hospital, Ministry of Health  
No.2 Yinghua East Road  
Beijing 100029, PR China  
Tel.: +86 10 84205313; +86 13520363898  
E-mail: gaochun@hsc.pku.edu.cn, gaochun@bjmu.edu.cn