Author's response to reviews

Title: The association between serum uric acid levels, metabolic syndrome and cardiovascular disease in middle aged and elderly Chinese: results from the DYSlipidemia International Study

Authors:

Yongfeng Tian (tianyf1988@163.com)
Kang Chen (cycon_ck@yeah.net)
Zongyan Xie (xiezongy@163.com)
Yuan Fang (angela0932@163.com)
Haibin Wang (wanghaibin2307@126.com)
Yi Nie (nieyi0730@163.com)
Dayi Hu (dayi.hu@medmail.com.cn)
Yiming Mu (yimingmu301@126.com)

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Author's response to reviews:

Dear Prof. Tony Merriman and Prof. Barry Palmer:

Thank you very much for your comments and suggestions.

As suggested, we have revised the manuscript, according to the comments and suggestions of reviewers and editor, and responded, point by point to. Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. I would like to re-submit this revised manuscript to BMC Cardiovascular Disorders, and hope it is acceptable for publication in the journal.

Looking forward to hearing from you soon.

With kindest regards,

Yours Sincerely

Yiming Mu

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The main corrections in the paper and the responds to the reviewer’s comments are as flowing:

Reviewer Comments:

Reviewer Tony Merriman:

[POINT 1]
The discussion on page 11 is based on the assumption that urate is causal of InsR, MetS and CVD. It is simply not possible to make this assumption on the basis of observational data. These two paragraphs should be deleted and the authors should, rather, discuss the limitations of the study in making causal inferences. They definitely need to discuss and cite Mendelian randomization studies showing no evidence for a causal link between urate and prevalent heart disease (Palmer et al BMJ 2012 and Kleber et al JASN 2015). Regarding beneficial effects of urate lowering by allopurinol, these could be mediated by the inhibition of xanthine oxidase. Finally, there may be important confounders (for eg dietary fructose), that are unmeasured and therefore unaccounted for, that could explain the observational relationship between urate and MetS and CVD.

Response:
We accept the reviewer’s suggestion. We have deleted these mentioned two paragraphs. Moreover, we also have discussed the limitations of making causal inferences in our present study.

[POINT 2]
Please change the final sentence of the abstract to read: "Elevated SU levels were positively related independently of measured confounders to CHD and HF."
Response:
We accept the reviewer’s suggestion. We have modified the sentences to read:"Elevated SU levels were positively related independently of measured confounders to CHD and HF."

[POINT 3]
In plasma/serum urate is present in the ionic form. It is only in the acidic environment of the urine that it is present as uric acid. The authors should therefore refer to urate (rather than uric acid) throughout.
Response:
Thanks for making this constructive comment. However, serum uric acid was widely used in those present articles. We think it also might be suitable here in our present study.

Reviewer Barry Palmer

[POINT 1]
Abstract
Method:
documented with SUA # with recorded SUA ???
Response:
Thanks for the comment. We have added the words accordingly.

[POINT 2]
Thanks for the comment. We have modified the vocabulary accordingly.

Thanks for the making the comment. We have added the punctuation accordingly.

Thanks for the comment. We have modified the word accordingly.

Thanks for the comment. We have modified the vocabulary accordingly.

Thanks for the comment. We have added the words accordingly.

Thanks for the comment. We have modified the word accordingly.

These two authors contribute equally to this work # These two authors
contributed equally to this work
Response:
Thanks for the comment. We have modified the word accordingly.