

Authors' Point-by-Point Response to Reviewers' comments

Dear Dr. Ma,

Thank you and the Reviewers for all your invaluable comments. We have carefully read and revised this manuscript. We believe this revised version has been significantly improved. Thanks!

Our Point-by-Point Response to Reviewers' comments (*in Italic*) are followed as below. Please let me know if you have any further questions.

Best wishes

Longjian Liu, MD, PhD

Reviewer #1:

Scientific Quality: Grade A (Excellent) 2

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: The Impact of Diabetes Mellitus and Cardiometabolic Syndrome on the Risk of Alzheimer's Disease Among Postmenopausal Women This study described the epidemiology of Diabetes Mellitus (DM) and cardiometabolic syndrome (CMS) and their associations with risk of incident Alzheimer's Disease (AD) among postmenopausal women, which is very interesting, and is one of the first reports on the association of DM and CMS with the risk of the development of AD among postmenopausal women. The sample size is very big and the follow-up duration is quite long. The analysis is reasonable, and the conclusion has been drawn carefully. The paper has been written qualified and the tables and figures are well presented.

Some suggestions:

1. Such a big project just has been finished by one person (only one author) seems not so proper. Usually at least 3: one-person designs, the second processes and the third one statistics.

Authors' Response: Thank you.

Drs. Ed Gracely, PhD, Xiaoyan Yin, MD and Howard J Eisen, MD have given critically comments, edited and contributed to the final manuscript. They are included as coauthors.

2. "Discussion" of "Abstract" should be "Conclusion".

Authors' Response: Thank you. we have corrected this in the resubmission (page 2).

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors: This paper is well written and interesting. It is potentially eligible for the publication in this journal. However, a major drawback is the use of self-reports of physician-diagnosis of some disease conditions, because this may lead to inaccurate diagnosis. Therefore, I recommend

- 1. To perform further subgroup analysis of only accurate and reliable diagnosis after excluding self-reports of physician-diagnosis.***

Authors' response: We fully understand the Reviewer's concerns. However, like most large-scale population-based observational studies, the WHI Observational Study used a self-administered questionnaire to collect participants' medical conditions, including Alzheimer's disease. The survey questionnaire was mailed to each participant. To minimize potential information bias, a "self-report" with help or completed by a family member and friend of the WHI study participant, or by a health care provider of the study participant or those who knew the participant's health conditions was collected and used to classify the disease status. In the resubmission, we added to a sensitivity analysis by testing the associations of AD reported from the different resource with DM and CMS. The overall results are consistent. We present and discussed the findings in the re-submission (pages 9 and 11-12, and Supplementary Table 1).

- 2. There are some mistakes in grammar, such as "Participants' marital status, education levels, family annual incomes, health insurance of Medicare, hormone therapy use, and medical history of hypertension, myocardial infarction, angina, stroke and peripheral artery disease were significant differences ..." and "... had fully access to the dataset".***

Authors response: Thank you. We have corrected this (page 8).

- 3. The paper should be carefully checked. As shown in the title of the Table 1, the participants are divided by cardiometabolic syndrome status. However, in the first paragraph of the Results section, the authors divided the patients by DM. A new table regarding difference in characteristics of patients by DM.***

Authors response: Thanks for the important suggestion. We have added a new Table on the baseline characteristics of participants by DM status.

- 4. More words should be added to describe the current Table 1 regarding difference in characteristics of patients by cardiometabolic syndrome status.***

Authors response: Yes, we have added in the revised version (page 10).