PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	The impact of secondhand smoke exposure on cognitive function among middle-aged and older women in China: Findings from 3-waves of the China Health and Retirement Longitudinal Study
AUTHORS	Bai, Anying; Jin, Yinzi; Huang, Yangmu

VERSION 1 – REVIEW

REVIEWER	Rachel Tham Australian Catholic University, Australia
REVIEW RETURNED	02-Jul-2020

GENERAL COMMENTS	Manuscript ID bmj-2020-039824 This is an interesting piece of research which aims to add to the current literature relating to the impact of exposure to second-hand tobacco smoke in non-smoking middle-aged to older-aged Chinese women and their cognitive function. Overall it is quite well written but would benefit from some professional English editing to enhance the meaning of the writing and to become grammatically correct throughout. Before considering this manuscript to be ready for acceptance I believe the authors need to address a range of important issues that arose for me when I read it. These issues are: • Abstract: The authors state that it is a cohort study but they have not demonstrated that all the women included in the final study sample were all “cognitively healthy” at baseline. Their methodological approach appears cross-sectional in nature but with 3 waves of cohort data pooled – their methodology is not described in the Abstract. In the Results they report the 95%CI but not the effect estimates from their statistical analysis. • The authors have had access to 3 waves of longitudinal cohort data but do not appear to have analysed the changes to cognitive function over those 3 waves as the length of exposure to second hand smoke increased. I am not convinced that the study design is appropriate for the research question. • Methods: Could the authors please confirm how Figure drawing is confirmed by telephone interview? This section needs to be clarified. • Research ethics: There is no mention of the ethical approvals for this study. • Statistics: The statistical methods are not clearly described and I apologise in advance if I have misunderstood their approach – lagged-dependent variable regression models – as it is not a method that I am familiar with in analysing longitudinal epidemiological data. If the authors wanted to look at change in risk over time why did they not consider generalised estimating equations or mixed effects regression? I recommend that an external statistician provide input into reviewing this component of

	the study. The authors did report multivariable linear regression but they did not include confounding variables in their analyses of the impact of second-hand smoke on the cognitive function outcomes. Hence these models are unadjusted for important contributing covariates. • The results tables are fairly well presented but some formatting of the listed variables could make the tables easier to read e.g. "More than 25 years less than 30 years" could be written as "25 to <30 years"; "More than 30 years to less than 40 years" could be written as "≥30 to <40 years" . Also, I do not understand why analyses of "missing" covariates are included. • I am unable to say that the Discussion and Conclusion are justified by the Results as I am not convinced that the Results are fully adjusted for all key covariates. • The authors do provide a good discussion of the study's limitations. • The Supplementary reporting is inappropriate – they have selected a report for qualitative studies instead of quantitative studies. They should refer to the STROBE Statement for reporting on observational studies. • Other minor issues: The terms second-hand smoke (SHS), environmental tobacco smoke and passive smoking have been used interchangeably throughout – I recommend that the authors use one term consistently to reduce confusion. I think this research is important but the authors need to make major revisions before it can be considered to be ready for acceptance for publication.

REVIEWER	Lucy Stirland University of Edinburgh, UK
REVIEW RETURNED	08-Jul-2020

GENERAL COMMENTS	This is a well thought-out observational study of the association between second-hand smoke and cognitive function in a large, robust cohort study. It has a clear structure and is suitably detailed. The paper requires some language editing and there are occasional places where language obscures meaning. I have the following specific comments for the authors: ABSTRACT In the first sentence of "results", please mention the direction of the significant association. In "conclusions", you mention education and depression screening interventions which were not part of your study design. I suggest you change this sentence to focus on conclusions that are more directly related to your study. INTRODUCTION The content of the introduction is good, but the section is too long overall. The initial paragraphs could be summarised into one sentence each. The final paragraph of the introduction, where you discuss other studies, might be better in the Discussion under "Comparison to other literature". METHODS Please provide a sentence explaining the recruitment process of CHARLS.

	The Methods section also requires an ethics statement. Please explain why this study was limited to married women, not unmarried/cohabiting women or men. If there are cultural reasons for assuming that the household of a married heterosexual couple is the norm for an environment with SHS exposure, please expand on this for your international audience. On Page 10, line 49 you mention “non-smokers” but later refer to “never smokers”. There is a difference here, as ex-smokers (who may be current non-smokers) may be at similar risks to current smokers. If you mean never smokers throughout, please change this wording. When outlining the cognitive tests used, please state which test you used to examine which cognitive domain, as this may not be clear to all readers. On page 13, line 27, please expand on the abbreviation “CES-D” or just refer to a pause when participants took another test. Please give further justification for your categorisation into four levels of passive smoking exposure (“Never/less than 25 years, 25-30 years, 30-40 years and over 40 years”). Firstly, why not use a continuous variable of number of years exposed to passive smoke and secondly, why these uneven cut-off boundaries? You refer to diabetes and hypertension as covariates. Please clarify in the text the levels used here (I see from Table 1 that you mean none/diagnosed without treatment/diagnosed with treatment) and whether this is self-reported. Page 15 line 14 – please specify what you mean by “average”. Page 15 line 22 – I think the word “symptoms” is an error here – perhaps you mean diagnoses. RESULTS Please consider re-phrasing the results on page 17, lines 38-48 and line 56 onwards, as the sentences are not clear. Page 17 line 9 – you do not know if participants “suffer from” cognitive decline. Please consider using the words “have” or “demonstrate” instead. DISCUSSION Page 17 line 40 – I suggest replacing the word “creative” with “novel” or similar. The paragraph about diabetes at the top of page 18 is not clearly related to your study question and should probably be either removed or its relevance explained. Page 18 line 48 – I did not understand the conclusions in the following sentence: “Compared with prior research(Pan, Luo et al. 2018), the coefficients were significant”. The phrase “Secondhand smoke seems to be a stronger indicator of cognitive decline than aging” implies some causality. Perhaps “strongly associated” would be clearer. ADDITIONAL FILE

	I was not sure why you included a sample qualitative research checklist when this is not qualitative research. A completed STROBE checklist would be useful instead.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1 (Tham, Rachel)
Please leave your comments for the authors below
Manuscript ID bmj-2020-039824
This is an interesting piece of research which aims to add to the current literature relating to the impact of exposure to second-hand tobacco smoke in non-smoking middle-aged to older-aged Chinese women and their cognitive function.
Overall it is quite well written but would benefit from some professional English editing to enhance the meaning of the writing and to become grammatically correct throughout.
Before considering this manuscript to be ready for acceptance I believe the authors need to address a range of important issues that arose for me when I read it. These issues are:

(1)Abstract: The authors state that it is a cohort study but they have not demonstrated that all the women included in the final study sample were all “cognitively healthy” at baseline. Their methodological approach appears cross-sectional in nature but with 3 waves of cohort data pooled – their methodology is not described in the Abstract. In the Results they report the 95%CI but not the effect estimates from their statistical analysis.
Response: Thank you very much for your suggestions. We have added few sentences in the abstract to demonstrate the baseline characteristic of our studied sample as following:
“Data from a total of 6875 Chinese women with normal cognitive function in baseline were selected for analysis, including 2981 who were interviewed in 2011, 2471 in 2013, and 1894 in 2015.”
Besides, we added some sentences in the methods description to make our approach more understandable,
“We pooled the three waves of data by using dummy variable to differentiate between 2-year and 4-year, and used lagged dependent variable models to examine independent associations between secondhand smoking and cognitive function.Demographic factors, socioeconomic factors, baseline cognitive functioning and health conditions were controlled in our models.”
And we have also reported the effect estimates in the results section.

(2)The authors have had access to 3 waves of longitudinal cohort data but do not appear to have analysed the changes to cognitive function over those 3 waves as the length of exposure to second hand smoke increased. I am not convinced that the study design is appropriate for the research question.
Response: Thank you very much for your insights. Since we firstly generated the SHS variable separately in different year(2011 and 2013), and then pooled them together to analyze the effect of secondhand smoke on cognitive function, the length of exposure to second hand smoke had already been considered and was different in each wave. Besides, we could see from Table 1 that the baseline characteristics of length of secondhand smoking is different among the three waves.

(3)Methods: Could the authors please confirm how Figure drawing is confirmed by telephone interview? This section needs to be clarified.
Response: Thank you for the question. CHARLS included items for cognitive function similar to those used in the Health and Retirement Study, a nationally representative longitudinal survey of more than 37 000 individuals over age 50 in 23 000 households in the
USA (Sonnega A, Faul JD, Ofstedal MB, Langa KM, Phillips JW, Weir DR. Cohort Profile: the Health

and Retirement Study (HRS). Int J Epidemiol. 2014;43(2):576-585. doi:10.1093/ije/dyu067). These items were components of the Telephone Interview of Cognitive Status battery. However, the field investigation in CHARLS used the face-to-face computer-assisted personal interview (CAPI) so all the information was obtained personally.
We have also added a few sentences in methods section to clarify the measures of cognitive function, "The cognitive function of the respondents in CHARLS questionnaires was measured through a question-and-answer interview instrument, and the respondents would be followed every two years using a face-to-face, computer-aided personal interview (CAPI). Cognitive subdomains including visuospatial ability, orientation and attention, and episodic memory could be assessed by these various sections of questionnaire. Figure drawing was tested by asking the participants to reproduce a picture of two overlapped pentagons in CHARLS questionnaires, and was used to measure a person's ability to identify visual and spatial relationships among objects. The Telephone Interview of Cognitive Status (TICS) was a screening test including serial subtractions of 7 from 100 (up to 5 times), date (month, day, and year and season), and the day of the week. To assess orientation and attention function, the number of correct answers to above questions in TICS was scored and summed up (range 0 to 10). Participants who successfully completed the task received a score of 1, and those who failed received 0 "

(4)Research ethics: There is no mention of the ethical approvals for this study.
Response: Thank you for your suggestion. We have added the sentence in the methods section to make a clearer statement:
"CHARLS had passed the ethical review before field investigation and we used data from 3 waves of the China Health and Retirement Longitudinal Study (CHARLS,2011-2013-2015), which was publicly available at http://charls.pku.edu.cn.".

(5)Statistics: The statistical methods are not clearly described and I apologise in advance if I have misunderstood their approach – lagged-dependent variable regression models – as it is not a method that I am familiar with in analysing longitudinal epidemiological data. If the authors wanted to look at change in risk over time why did they not consider generalised estimating equations or mixed effects regression? I recommend that an external statistician provide input into reviewing this component of the study. The authors did report multivariable linear regression but they did not include confounding variables in their analyses of the impact of second-hand smoke on the cognitive function outcomes. Hence these models are unadjusted for important contributing covariates.
Response: Thank you for the insight and suggestions. Lagged variables were generated to represent the time lag effect in some economic operation process. Some economic variables are not only affected by various factors in the same period, but also affected by various factors in some periods in the past and even their own past values. Generally, the variable with lag effect in the past period is called lagged variable, and the model with lag variable is called lag variable model. The lagged-dependent variable model takes into account the effect of time, which makes the problem of static analysis possible to become dynamic analysis. It is often used when the dependent variable is affected by the previous values of itself or another explanatory variable. It is superior for analyzing the effects of predictor variables on an outcome with 2-wave panel data while controlling for the influence of time-invariant variables (Johnson D. Two-wave panel analysis: comparing statistical methods for studying the effects of transitions. J Marriage Fam. 2005;67(4):1061–1075.)(Dong C, Xie K, Zeng J, Li X. Multivariate dynamic Tobit models with lagged observed dependent variables: An effectiveness analysis of highway safety laws. Accid Anal Prev. 2018;113:292-302. doi:10.1016/j.aap.2018.01.039). Participants' cognitive function was progressive and not only affected by external factors like demographic and socioeconomic characteristics, so it is necessary and reliable to add the baseline cognitive function into our models to estimate the robust effect of secondhand smoking on women's cognitive function. Regarding the second question, we had already included some confounders to adjust for important contributing covariates in the multivariable linear regression, including demographic factors, socioeconomic status and health condition.

(6)The results tables are fairly well presented but some formatting of the listed variables could make the tables easier to read e.g. “More than 25 years less than 30 years” could be written as “25 to <30 years”; “More than 30 years to less than 40 years” could be written as “≥30 to <40 years” . Also, I do not understand why analyses of “missing” covariates are included.
Response: Thank you very much for the suggestions. We have changed the format of the listed variables as advised. The missing group referred to participants who did not answer the questions related to their chronic disease conditions.

(7)I am unable to say that the Discussion and Conclusion are justified by the Results as I am not convinced that the Results are fully adjusted for all key covariates.The authors do provide a good discussion of the study’s limitations.
Response: Thank you for the comment. We have included some confounders to adjust for important contributing covariates in the multivariable linear regression, including demographic factors, socioeconomic status and health condition, so that our results might be robust. In the discussion section, we firstly compared our results in direction and magnitude with previous studies.
Seondly, we analyzed the possible reasons of the discrepancy between our conclusions and others, for instance, the different detecting methods of cognitive function and the studied population. Thirdly ,we hypothesized about the mechanisms underlying links between SHS exposure and poorer cognitive performance. Finally, we came to the strength and limitation of our study. We have also taken some nessesary changes in the manuscript to make our results and discussion more logically related for readers to capture what we want to show. Thnaks again for your questions.

(8)The Supplementary reporting is inappropriate – they have selected a report for qualitative studies instead of quantitative studies. They should refer to the STROBE Statement for reporting on observational studies.
Response: Thank you for your suggestions. We have referred to the STROBE Statement for reporting the observational studies.

(9)Other minor issues: The terms second-hand smoke (SHS), environmental tobacco smoke and passive smoking have been used interchangeably throughout – I recommend that the authors use one term consistently to reduce confusion.
Response: Thank you for your suggestions. We decided to use second-hand smoke consistently throughout.

I think this research is important but the authors need to make major revisions before it can be considered to be ready for acceptance for publication.

Reviewer: 2 (Stirland, Lucy)

Please leave your comments for the authors below
This is a well thought-out observational study of the association between second-hand smoke and cognitive function in a large, robust cohort study. It has a clear structure and is suitably detailed. The paper requires some language editing and there are occasional places where language obscures meaning.

I have the following specific comments for the authors:

(1)ABSTRACT
In the first sentence of “results”, please mention the direction of the significant association. In “conclusions”, you mention education and depression screening interventions which were not part of your study design. I suggest you change this sentence to focus on conclusions that are more directly

related to your study.
Response: Thank you for your suggestions. We have changed the first sentence of “results” in abstract to “Secondhand smoking was found to be inversely and significantly associated with cognitive function”. And we have changed our conclusions to,
“Secondhand smoking within households is a risk factor for cognitive decline among Chinese non-smoking women. Being exposed to secondhand smoke for more than 40 years was associated with greater decline in global cognitive function, visuospatial ability and episodic memory function, but not in orientation and attention among elder Chinese women”.

(2)INTRODUCTION
The content of the introduction is good, but the section is too long overall. The initial paragraphs could be summarised into one sentence each. The final paragraph of the introduction, where you discuss other studies, might be better in the Discussion under “Comparison to other literature”.
Response: Thank you for the suggestions. We have simplified the initial paragraphs and used sentences “Several studies have shown being exposed to SHS and cognitive impairment are interrelated (Yolton, Dietrich et al. 2005, Llewellyn, Lang et al. 2009, Heffernan and O'Neill 2013)” to summarize the results of previous studies in the final paragraph and put the discussions of other studies in the Discussion section.

(3)METHODS
Please provide a sentence explaining the recruitment process of CHARLS.
Response: Thank you for your advice. We provided one sentence as,
“Samples were chosen through multistage probability sampling. After excluding empty or non-resident dwellings, final interviews were conducted on 17,708 respondents from 10,257 households, which completed at least one module of the survey beyond the cover screening for age eligibility” to explain the recruitment process of CHARLS.”
We have also cited a paper that introducted the recruitment process of CHARLS to make it more easier for the readers to check for more detailed information. Zhao Y, Hu Y, Smith JP, et al. Cohort Profile: The China Health and Retirement Longitudinal Study (CHARLS). International Journal of Epidemiology 2012;43(1):61-68. doi: 10.1093/ije/dys20, in this article it mentioned that
In the first stage, 150 county-level units were randomly chosen with a probability-proportional-to-size (PPS) sampling technique from a sampling frame containing all county-level units with the exception of Tibet. The sample was stratified by region and within region by urban districts or rural counties and per capita statistics on gross domestic product (GDP). The final sample of 150 counties fell within 28 provinces. Our sample used the lowest level of government organization, consisting of administrative villages (cun) in rural areas and neighborhoods (shequ or juweihui) in urban areas, as primary sam- pling units (PSUs). We selected 3 PSUs within each county-level unit, using PPS sampling. Because no pre-existing sampling frame of residents existed, we conducted mapping and listing operations within each village-level unit to obtain the sampling frame for CHARLS. If more than one household was found within each dwelling unit, we randomly selected a household with a member 39 years of age or older. If the chosen household had more than one age-eligible member, we randomly selected one of them. If the selected person was between 39 and 45 years of age that person was designated for inclusion in a future re- freshment sample and was not interviewed. If the chosen person was 45 years of age or older, we interviewed both that person and his or her spouse. All stages of the sampling were conducted by computer to avoid human manipulation.

The Methods section also requires an ethics statement.
Response: Thank you for your suggestion. We have added the sentence：“CHARLS had passed the ethical review before field investigation and we used publicly available deidentified data at http://charls.pku.edu.cn .”in the methods section.

Please explain why this study was limited to married women, not unmarried/cohabiting women or men. If there are cultural reasons for assuming that the household of a married heterosexual couple is the norm for an environment with SHS exposure, please expand on this for your international audience.
Response: Thank you for your question. Secondhand smoking mainly affects married women in China. Though unmarried/cohabiting women can possibly be affected by household SHS, this kind of influence remains scarce. Moreover, our data could not distinguish the unmarried/cohabiting women from those who were unmarried and living alone in our research, since the investigation on marital status in CHARLS questionnairs only contains these questions: (1)Married with spouse present; (2)Married but not living with spouse temporarily for reasons such as work;(3)Separated;(4) Divorced;(5) Widowed; and (6) Never married.

On Page 10, line 49 you mention “non-smokers” but later refer to “never smokers”. There is a difference here, as ex-smokers (who may be current non-smokers) may be at similar risks to current smokers. If you mean never smokers throughout, please change this wording.
Response: Thank you for your suggestion. We already changed all the “non-smokers” to “never smokers”.

When outlining the cognitive tests used, please state which test you used to examine which cognitive domain, as this may not be clear to all readers. On page 13, line 27, please expand on the abbreviation “CES-D” or just refer to a pause when participants took another test.
Response: Thank you for your advice. We have added a few sentences in the methods section, “Cognitive subdomains including visuospatial ability, orientation and attention, and episodic memory could be assessed by these various sections of questionnaire. Figure drawing was tested by asking the participants to reproduce a picture of two overlapped pentagons in CHARLS questionnaires[18], and was used to measure a person’s ability to identify visual and spatial relationships among objects. The Telephone Interview of Cognitive Status (TICS) was a screening test including serial subtractions of 7 from 100 (up to 5 times), date (month, day, and year and season), and the day of the week. To assess orientation and attention function, the number of correct answers to above questions in TICS was scored and summed up (range 0 to 10). Participants who successfully completed the task received a score of 1, and those who failed received 0. In addition, the word recall test was consisted of 2 components, immediate recall and delayed recall, and evaluated episodic memory. Participants were required to immediately repeat 10 Chinese nouns just read to them, and after 20 questions concerning Center for Epidemiologic Studies Depression Scale (CES-D, approximately 4 to 10 minutes), they were again asked to recall as many of the original words as possible. The item was coded as 1 if recalled by the respondent, and as 0 if not. Scores for immediate and delayed recall both varied from 0 to 10. An evaluated episodic memory score was calculated using the mean of scores in immediate and delayed word recall(range 0 to 10).The overall cognition scores were the sum of the three different domains (range 0 to 21).”
We have also expanded the abbreviation to Center for Epidemiologic Studies Depression Scale (CES-D) in the appointed place.

Please give further justification for your categorisation into four levels of passive smoking exposure (“Never/less than 25 years, 25-30 years, 30-40 years and over 40 years”). Firstly, why not use a continuous variable of number of years exposed to passive smoke and secondly, why these uneven cut-off boundaries?
Resposne: Thank you for your suggestions. Firstly, we wanted to differentiate between different levels of secondhand smoking on women’s cognitive status, so we used categoried variable to measure SHS exposure, which represented more meanings of public health than continuous variable. Besides, some previous studies investigating the dose-response relationship between smoking and RA risk have suggested that the impact of smoking on RA is limited to those

with a cumulative exposure exceeding 10 pack years. (Hedström, A. K., Klareskog, L., & Alfredsson, L. (2018). Exposure to passive smoking and rheumatoid arthritis risk: results from the Swedish EIRA study. Annals of the rheumatic diseases, 77(7), 970–972. https://doi.org/10.1136/annrheumdis-2018-212973)(Costenbader KH, Feskanich D, Mandl LA, Karlson EW. Smoking intensity, duration, and cessation, and the risk of rheumatoid arthritis in women. Am J Med. 2006;119(503):e501–e509).Therefore, since most of the women were not exposed to secondhand smoking, the effect of SHS might be neglected if we only used continuous variable to represent exposure. Secondly, the cut-off boundaries of SHS exposure were decided to realize the relatively balanced population distribution frequency among different levels of exposure year. Thus,…..

You refer to diabetes and hypertension as covariates. Please clarify in the text the levels used here (I see from Table 1 that you mean none/diagnosed without treatment/diagnosed with treatment) and whether this is self-reported.
Response: Thank you for your advice. We have already clarified in the text in the methods section, as "Thus, the baseline chronic disease of hypertension and diabetes were classified as three types based on self-reported conditions on whether the participants were being treated: having hypertension/diabetes with treatment, having hypertension/diabetes without treatment and not having hypertension/diabetes."

Page 15 line 14 – please specify what you mean by "average".
Response: Thank you for your question. In Table1, we provides a descriptive summary of all the variables for participants from each panel of three different waves, and the continuous data were described as mean and standard deviations. Therefore, the average scores of baseline cognition and Center for Epidemiologic Studies Depression Scale (CES-D) scores could indicate the baseline condition of participants.

Page 15 line 22 – I think the word "symptoms" is an error here – perhaps you mean diagnoses.
Response: Thank you for your advice. We already changed the word from symptoms to diagnoses.

(4)RESULTS
Please consider re-phrasing the results on page 17, lines 38-48 and line 56 onwards, as the sentences are not clear.
Response: Thank you for you suggestion. We have already rephrased the sentence to:
"Scores of episodic memory, orientation and attention and visuospatial among respondents at baseline were strong predictors of their corresponding cognitive function measures after 2 or 4 years. Based on the analysis controlling age, annual household expenditure, education, baseline cognitive function and other chronic health status, we found that only being exposed to SHS for more than 40 years significantly resulted in a decline in visuospatial abilities, episodic memory and overall cognition scores for all respondents. Compared with respondents who were not exposed to SHS or exposed to it for less than 25 years, those who have exposed to SHS for more than 40 years was associated with 0.04-point decline in visuospatial abilities(95%CI, -0.08--0.01 P <0.1), 0.16-point decline in episodic memory(95%CI, -0.31--0.01 P <0.05), and 0.33-point decline in overall cognition functions(95%CI, -0.66--0.01 P <0.01). In addition, age was also negatively associated with cognitive function. Each one-year older resulted in 0.01-point, 0.01-point, 0.03-point,and 0.05-point decrease in visuospatial(95%CI, -0.01--0.00 P <0.01), orientation(95%CI, -0.03---0.01 P <0.01), memory(95%CI, -0.31---0.01 P <0.05) and overall cognition scores(95%CI, -0.66---0.01 P <0.01), respectively. High education level was associated with better cognitive performance, especially in orientation and attention. What's more, one-point increase in CESD scores was associated with 0.02-point decrease in scores of orientation and attention (95%CI, -0.03--0.00 P <0.05), showing that respondents with depressive symptoms were more likely to demonstrate cognitive decline in specific functions".

Page 17 line 9 – you do not know if participants “suffer from” cognitive decline. Please consider using the words “have” or “demonstrate” instead.
Response: Thank you for your advice. We already changed the word from “suffer from” to “demonstrate”.
(5)DISCUSSION
Page 17 line 40 – I suggest replacing the word “creative” with “novel” or similar.
Response: Thank you for your advice. We already changed the word from “creative” to “novel”.

The paragraph about diabetes at the top of page 18 is not clearly related to your study question and should probably be either removed or its relevance explained.
Response: Thank you for your suggeation. We removed the paragraph about diabetes.

Page 18 line 48 – I did not understand the conclusions in the following sentence: “Compared with prior research(Pan, Luo et al. 2018), the coefficients were significant”.
Response: Thank you for your question. We have already changed the sentence as:
“Our results were quite similar in magnitude to prior research on the relationship between SHS and cognitive function (Pan, Luo et al. 2018).”

The phrase “Secondhand smoke seems to be a stronger indicator of cognitive decline than aging” implies some causality. Perhaps “strongly associated” would be clearer.
Response: Thank you for your suggestion. We have already changed the sentence as:
“Secondhand smoke seems to be more strongly associated with cognitive decline than aging.”

ADDITIONAL FILE
I was not sure why you included a sample qualitative research checklist when this is not qualitative research. A completed STROBE checklist would be useful instead.
Response: Thank you for your suggestions. We have dropped the sample qualitative research checklist and referred to the STROBE Statement for reporting the observational studies instead.

VERSION 2 – REVIEW

REVIEWER	Rachel Tham Australian Catholic University, Australia
REVIEW RETURNED	07-Sep-2020

GENERAL COMMENTS	Reviewer comments I thank the authors for their comprehensive responses to the comments raised by the reviewers of this paper. This manuscript is now much clearer and I can make the linkages between the parts of the research. This research is important and provides an important basis to continuing with further longitudinal research with larger study samples. Before considering this manuscript to be ready for publication I recommend the authors undertake some minor revisions as outlined below. Abstract Results: The ‘negative symbol [-]’ is difficult to see in the reporting of Results. I suggest reporting the 95%CI for the beta coefficients as “(β=-0.33; 95%CI -0.66 to -0.01, p < 0.01), visuospatial ability (β=-0.04; -0.08 to-0.01, p < 0.05) and episodic memory function (β=-0.16; -0.31 to -0.01, p = 0.031).” This would apply to the Results section in the Main text (page 11).

	Conclusion: I suggest editing this section slightly to “Household second-hand smoke exposure for more than 40 years was associated with greater decline in global cognitive function, visuospatial ability and episodic memory function, but not in orientation and attention function among older Chinese women.” Please note, there is no need to underline ‘older’ but this is a better term than ‘elder’ for this sentence. Main Text Please check the correct spelling of ‘ageing/aging’ for the BMJ and use the correct spelling consistently throughout. I think the BMJ would prefer ‘ageing’ . Also please use the acronym SHS consistently throughout – sometimes the authors write “secondhand smoke”and sometimes “SHS” after they have defined the acronym on page 4. Page 8 Line 1: “would be followed” should be “were followed”. Page 10, last paragraph: “diagnose” should be “diagnoses”. The authors have established the acronym CES-D on page 8, there is no need to keep writing “Center for Epidemiologic Studies Depression Scale” on pages following (Page 9, page 11) Page 12, First line: “What’s more,” is not appropriate English grammar for a journal article – I suggest replacing this phrase with “In addition,” Page 13, last paragraph: The authors refer to another study (Burk et al 2018) but it is not clearly written – I do not understand what point of difference or similarity from their results they are trying to make here. Are they stating that the Burk et al study reported a decline in attention and orientation, but this study did not? Or are they defining what is meant by the terms ‘attention’ and ‘orientation’? Could this be clarified please? Page 14, The authors state “Previous study proved that the onset of memory decline may vary among different memory types, with episodic memory lasting lifelong [22]. Our study could not prove the onset age of memory decline without doing regression among different age groups, while the memory decline caused by SHS could be presented by the significant coefficient.” Unfortunately, observational studies cannot actually ‘prove cause and effect’ – I suggest the authors rewrite this section: “Previous research has indicated that the onset of memory decline may vary among different memory types, with episodic memory decline possibly being lifelong [22]. Our study could not explore the onset age of memory decline without doing regression among different age groups. Memory decline associated with SHS exposure could be indicated by the significant coefficient.” Page 15: “an animal research” should be written as “research on laboratory animals”. Page 15: The sentence ” A longitudinal design could elucidate this association by observing long-term exposure to SHS and a potential build-up of CVD as well as how these correlates with performance upon a range of cognitive measures.” is not technically correct – I suggest rewriting as “A longitudinal design may elucidate any associations by observing long-term exposure to SHS and the incidence of CVD and whether these CVD may mediate or interact with SHS exposure to impact cognitive function.” Tables The layout of the Tables needs to be improved for easier reading. Table 3 – the “Socres” is misspelt and is not needed – I think this can be removed.

	Tables 2 and 3: I encourage the authors to state exactly which independent covariates were used in the SHS exposure model for adjustment for potential confounding. I don't think it is enough to simply state in the Methods that the multivariate regression models were adjusted for "all demographic and socioeconomic characteristics." This detail can be provided as a footnote to the Tables. If the models are adjusted then they should state that the models are adjusted in the Title for the Tables.

REVIEWER	Lucy Stirland University of Edinburgh, UK
REVIEW RETURNED	25-Aug-2020

GENERAL COMMENTS	I thank the authors for their response. They have paid close attention to my comments and responded to them in detail. However, some of the responses were not demonstrated in changes to the manuscript. Overall, I still think the manuscript needs further language editing, so if this is not provided by BMJ Open copywriters, the authors should consult a professional language editing service. I have the following specific comments: METHODS Thank you for expanding on why the study only included married women. Please add a sentence to the manuscript to explain why you chose this study population for this research question. Please add to the manuscript an explanation for the cut-offs of levels of passive smoking exposure ("Never/less than 25 years, 25-30 years, 30-40 years and over 40 years") and justification for not using a continuous variable. You have used the word "average" several times – if you used the mean (not median or mode), please use the word "mean" instead. RESULTS Thank you for rewriting the section of Results to make it clearer. There are three instances in the Results (copied below) where you use the word "resulted", which implies causality. Please rephrase these to reflect that your analyses can only comment on associations. "we found that only being exposed to SHS for more than 40 years significantly resulted in a decline in visuospatial abilities…"; "Besides, each one-year increase in age resulted in a 0.01-point…" "Each one-year older resulted in 0.01-point…"

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Rachel Tham

Institution and Country: Australian Catholic University, Australia

Please state any competing interests or state 'None declared':None declared

Please leave your comments for the authors below

Reviewer comments

I thank the authors for their comprehensive responses to the comments raised by the reviewers of this paper. This manuscript is now much clearer and I can make the linkages between the parts of the research.

This research is important and provides an important basis to continuing with further longitudinal research with larger study samples.

Before considering this manuscript to be ready for publication I recommend the authors undertake some minor revisions as outlined below.

(1)Abstract

Results: The 'negative symbol [-]' is difficult to see in the reporting of Results. I suggest reporting the 95%CI for the beta coefficients as "(β=-0.33; 95%CI -0.66 to -0.01, p < 0.01), visuospatial ability (β=-0.04; -0.08 to-0.01, p < 0.05) and episodic memory function (β=-0.16; -0.31 to -0.01, p = 0.031)." This would apply to the Results section in the Main text (page 11).

Conclusion: I suggest editing this section slightly to "Household second-hand smoke exposure for more than 40 years was associated with greater decline in global cognitive function, visuospatial ability and episodic memory function, but not in orientation and attention function among older Chinese women." Please note, there is no need to underline 'older' but this is a better term than 'elder' for this sentence.

Response: Thank you very much for your suggestions. We have changed the results and conclusion in abstracts as:

"Results: Secondhand smoke was found to be inversely and significantly associated with cognitive function. Compared with those had not been exposed to household secondhand smoke, women who had lived with a smoking husband had significantly faster cognition decline, especially in global cognitive function (β=-0.33, 95%CI= -0.66 to -0.01, P < 0.01), visuospatial ability (β=-0.04, 95%CI=-0.08 to -0.01 P < 0.05) and episodic memory function (β=-0.16, 95%CI= -0.31 to -0.01 P = 0.031).

Conclusions: Household secondhand smoke exposure for more than 40 years was associated with a more significant decline in global cognitive function, visuospatial ability and episodic memory function, but not in orientation and attention function among older Chinese women."

(2)Main Text

Please check the correct spelling of 'ageing/aging' for the BMJ and use the correct spelling consistently throughout. I think the BMJ would prefer 'ageing' .

Also please use the acronym SHS consistently throughout – sometimes the authors write "secondhand smoke"and sometimes "SHS" after they have defined the acronym on page Page 8 Line 1: "would be followed" should be "were followed".

Page 10, last paragraph: "diagnose" should be "diagnoses".

The authors have established the acronym CES-D on page 8, there is no need to keep writing "Center for Epidemiologic Studies Depression Scale" on pages following (Page 9, page 11)

Page 12, First line: "What's more," is not appropriate English grammar for a journal article – I suggest replacing this phrase with "In addition,"

Response: Thank you for your suggestions. We have changed the aging/secondhand smoke/Center for Epidemiologic Studies/What's more to ageing/SHS/CES-D/In addition, and changed the grammar error in page 8 and page 10 accordingly.

Page 13, last paragraph: The authors refer to another study (Burk et al 2018) but it is not clearly written – I do not understand what point of difference or similarity from their results they are trying to make here. Are they stating that the Burk et al study reported a decline in attention and orientation, but this study did not? Or are they defining what is meant by the terms 'attention' and 'orientation'? Could this be clarified please?

Response: Thank you for your suggestions. We have changed the sentence as the following:

"Attention referred to the ability to concentrate and focus on specific stimuli slightly declined in later life [13]"

to clarify that we referred to the Burk's study to define the terms of "attention".

Page 14, The authors state "Previous study proved that the onset of memory decline may vary among different memory types, with episodic memory lasting lifelong [22]. Our study could not prove the onset age of memory decline without doing regression among different age groups, while the memory decline caused by SHS could be presented by the significant coefficient." Unfortunately, observational studies cannot actually 'prove cause and effect' – I suggest the authors rewrite this section: "Previous research has indicated that the onset of memory decline may vary among different memory types, with episodic memory decline possibly being lifelong [22]. Our study could not explore the onset age of memory decline without doing regression among different age groups. Memory decline associated with SHS exposure could be indicated by the significant coefficient."

Response: Thank you very much for your advice. We have changed the article as "Previous research has indicated that the onset of memory decline may vary among different memory types, with episodic memory decline possibly being lifelong [24]. Our study could not explore the onset age of memory decline without doing regression among different age groups. The significant coefficient could indicate momory decline associated with SHS exposure."

Page 15: "an animal research" should be written as "research on laboratory animals".

Page 15: The sentence " A longitudinal design could elucidate this association by observing long-term exposure to SHS and a potential build-up of CVD as well as how these correlates with performance upon a range of cognitive measures." is not technically correct – I suggest rewriting as "A longitudinal

design may elucidate any associations by observing long-term exposure to SHS and the incidence of CVD and whether these CVD may mediate or interact with SHS exposure to impact cognitive function."

Response: Thank you very much for your suggestions. We have changed the article accordingly.

Tables

The layout of the Tables needs to be improved for easier reading.

Table 3 – the "Socres" is misspelt and is not needed – I think this can be removed.

Tables 2 and 3: I encourage the authors to state exactly which independent covariates were used in the SHS exposure model for adjustment for potential confounding. I don't think it is enough to simply state in the Methods that the multivariate regression models were adjusted for "all demographic and socioeconomic characteristics." This detail can be provided as a footnote to the Tables. If the models are adjusted then they should state that the models are adjusted in the Title for the Tables.

Response: Thank you very much for your suggestions. We have removed the misspelting words, added the details of adjusted covariates as a footnote to the tables, and changed the title for the tables as " Adjusted Multivariable linear regression analysis of the relationship between smoking exposure and Visuospatial function and Orientation and Attention among older Chinese women (N = 6875), 2011-2013-2015" .

Reviewer: 2

Reviewer Name: Lucy Stirland

Institution and Country: University of Edinburgh, UK

Please state any competing interests or state 'None declared':None declared

Please leave your comments for the authors below

I thank the authors for their response. They have paid close attention to my comments and responded to them in detail. However, some of the responses were not demonstrated in changes to the manuscript.

Overall, I still think the manuscript needs further language editing, so if this is not provided by BMJ Open copywriters, the authors should consult a professional language editing service.

I have the following specific comments:

METHODS

Thank you for expanding on why the study only included married women. Please add a sentence to the manuscript to explain why you chose this study population for this research question.

Response：Thank you for your suggestions. We have added a few sentence in the Methods section as

“CHARLS involved participants with a nationally representative survey of adults aged 45 years or older, as well as their spouses when possible, and included assessments of social, economic, and health circumstances of community-residents.”

P

Please add to the manuscript an explanation for the cut-offs of levels of passive smoking exposure (“Never/less than 25 years, 25-30 years, 30-40 years and over 40 years”) and justification for not using a continuous variable.

Response：Thank you for your suggestions. We have added a few sentences in the Methods section that:

“Since the impact of SHS might be neglected if we only used a continuous variable to represent exposure; moreover, compared with continuous variables, the use of categorical variables has greater public health significance.”

You have used the word “average” several times – if you used the mean (not median or mode), please use the word “mean” instead.

Response：Thank you for your advice. I have used the "mean" word instead of " average" when I referred to the mean (not median or mode).

RESULTS

Thank you for rewriting the section of Results to make it clearer. There are three instances in the Results (copied below) where you use the word “resulted”, which implies causality. Please rephrase these to reflect that your analyses can only comment on associations.

“we found that only being exposed to SHS for more than 40 years significantly resulted in a decline in visuospatial abilities…”;

“Besides, each one-year increase in age resulted in a 0.01-point…”

“Each one-year older resulted in 0.01-point…”

Response：Thank you very muchfor your advice. We have changed the sentence to:

“We found that only being exposed to SHS for more than 40 years was significantly associated with a decline in visuospatial abilities……”

“Our results suggested that for each one-year increase in age, there were additional 0.01-point, 0.02-point, 0.04-point and 0.06-point decline in visuospatial, orientation, memory and overall cognition scores, respectively.”

“Each one-year older was associated with 0.01-point, 0.01-point, 0.03-point, and 0.05-point decrease in visuospatial (95%CI, -0.01 to -0.00 P <0.01), orientation (95%CI, -0.03 to -0.01 P <0.01), memory (95%CI, -0.31 to-0.01 P <0.05) and overall cognition scores (95%CI, -0.66 to -0.01 P <0.01), respectively. ”