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|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2020-039824 |
| Article Type: | Original research |
| Date Submitted by the Author: | 27-Apr-2020 |
| Complete List of Authors: | Bai, Anying; Peking University Health Science Centre, School of Public Health;<br>Jin, Yinzi; Peking University, School of Public Health<br>Huang, Yangmu; Peking University Health Science Centre, School of Public Health; |
| Keywords: | EPIDEMIOLOGY, Dementia < NEUROLOGY, PUBLIC HEALTH |
| | |

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**Title**

# Exposure to Secondhand Smoke and Cognitive Function Among Middle-aged and Older Women in China: Findings of 3-waves of the China Health and Retirement Longitudinal Study

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**Abstract**

**Objectives:** To examine the association between passive smoking and women's global cognitive function and cognitive subdomains.

**Design:** Cohort study

**Participants:** Data for this study were obtained from the China Health and Retirement Longitudinal Study (CHARLS), and panel data analysis was applied to wave 1and wave 2(2011-2013) ,wave 2 and wave 3(2013-2015) and wave 1 and wave 3(2011-2015). Data from a total of 6875 Chinese women were selected for analysis, including 2981 who were interviewed in 2011, 2471 in 2013, and 1894 in 2015.

**Primary and secondary outcome measures:**

Global cognitive function, domains of cognitive function including visuospatial ability, orientation and attention, and episodic memory could be assessed by various sections of CHARLS questionnaire.

**Results:** Passive smoking was found to be significantly associated with cognitive function. Compared with those had not been exposed to household secondhand smoking, women who had lived with a smoking husband for over 40

years had significantly faster cognition decline, especially in visuospatial ability(95%CI, -0.08--0.01 P < 0.05) and episodic memory function(95%CI, -0.31-- -0.01 P = 0.031). In addition, compared with individuals with lower educational levels, and residing in rural area, those with more education or living in urban area had higher cognitive scores, although exposed to SHS.

**Conclusions:** Passive smoking within households is a risk factor for cognitive decline among Chinese non-smoking women. Provision of more educational opportunities and screening for depressive symptoms in advance for Chinese women should be promoted, as these will also help to protect them against the negative effects brought on by passive smoking.

**Key words:** aging; passive smoking; panel analysis; visuospatial ability; memory

**Strengths and limitations of this study:**

- The first study to investigate on the association between secondhand smoke exposure and women's different domains of cognitive functions in China using a 4-year longitudinal national representative data.
- Addressed the issue of reverse causation in observational cohort studies by used

lagged dependent variable models and adjust for baseline cognition scores

- The exposure to secondhand smoke was evaluated based on self-report measures.
- The analyses only contained household SHS exposure and excluding environmental exposure.

**Word Count: 3361**

**Number of references:30**

**Number of data elements :1**



## Introduction

China's population has been ageing rapidly. By 2050, there will be 400 million Chinese citizens aged over 65 years old, and 150 million of whom will be older than 80 years old(Fang, Scheibye-Knudsen et al. 2015), which brought about formidable healthcare challenges. It will become increasingly important to understand the cognitive changes that accompany aging, both normally and pathologically(Harada, Natelson Love et al. 2013).

Cognitive impairment, described as a decline in intellectual functions(Robertson, Savva et al. 2013), ranges from mild forms of forgetfulness to severe and debilitating dementia and is common among the elderly (Yin, Ma et al. 2016). The prevalence of cognitive impairment is rising, with national figures estimating that around 9% of older persons in China had cognitive impairment in 2011(Yin, Ma et al. 2016).

Numerous determinants such as environmental, individual, and genetic factors could favor evolution toward cognitive impairment, and both age and late-life hypertension increase the risk of dementia over time (Bernardin, Maheut-Bosser et al. 2014). The mechanism lies in age-related functional and structural changes in cerebrovascular small and large blood vessels(Tadic, Cuspidi et al. 2016). Besides chronic diseases factors, depression has long been known to affect memory and other neurocognitive domains, and be associated with an increased risk of developing mild cognitive impairment(MCI) in cognitively normal elderly people(Taivalantti, Barnett et al. 2019).

Passive smoking is a heated public health issue in China. Exposure to secondhand smoke (SHS), also known as "passive

smoking," refers to a situation where a non-smoker inhales another person's smoke either by exposure to side stream smoke or mainstream smoke(Ling and Heffernan 2016). Current smoking prevalence in China decreased from 31.1% in 2002 to 28.1% in 2010; however, the number of adults exposed to secondhand smoking during this period still increased from 540 million to 556 million(Harada, Natelson Love et al. 2013). The negative health effects of high levels of exposure to SHS may be close to those of active smoking, including inferior performance on measures of general intelligence, visuospatial learning and memory and fine motor dexterity(Durazzo, Meyerhoff et al. 2012).·Given the association between exposure to SHS and risk factors for cognitive impairment such as cardiovascular disease(Teo, Ounpuu et al. 2006), hypertension (Kim, 2019) , and stroke (Malek, 2015) it is possible that high level of exposure may be a preventable risk factor for cognitive impairment or dementia(Heffernan and O'Neill 2013). A cross-sectional research including 150 samples conducted in the North East of England revealed that participants who had no history of smoking and averagely exposed to SHS for around 6 years, showed significantly reduced performance in processing

speed (i.e. how quickly one can process information and perform tasks) and executive function(i.e. the ability to organize memory, cognitive flexibility, and problem-solving ability) as compared with non-exposed people(Heffernan and O'Neill 2013). Such an inversed relationship between environment tobacco smoke exposure and visuospatial reasoning skills were also reported among children and adolescents(Yolton, Dietrich et al. 2005). Besides, a longitudinal aging study concerning 4809 samples(aged 50 years or older) had found that participants were about 30 percent more likely to develop dementia when exposed to SHS over a period of six years, compared with those who never having been exposed; while this association did not reach statistical significance after adjusting for age, sex, and education (P>0.05)(Llewellyn, Lang et al. 2009).

·Few studies, however, have investigated the relationship between household SHS exposure and different domains of cognitive function among elders. Previous studies of active smoking and cognitive impairment among the Chinese population suggested that older current smokers(aged 63 years old on average)(Yolton, Dietrich et

al. 2005)or those being exposed to SHS (aged between 55-64 years old)(Pan, Luo et al. 2018) were more likely to develop cognitive impairment compared with never-smokers. Nevertheless, both of them used only a 2-wave longitudinal data and did not control for baseline cognition score. Therefore, the primary aim of this study was to investigate the relationship between secondhand smoking and cognitive function among older non-smoking Chinese women, using a 3-wave longitudinal national representative data. Through the classification of respondents by different years of secondhand smoke exposure in a 4-year panel, we identified whether certain high SHS exposure groups were at higher risk of cognitive decline than others after controlling for demographic and socioeconomic factors. Besides, we aimed to examine the association between secondhand smoke exposure and cognitive subdomains. This is especially important given the escalating aging trend and increasing prevalence of SHS exposure in China.

## Methods

### Data

We used data from 3 waves of the China Health and Retirement Longitudinal Study(CHARLS, 2011-2013-2015), which involved participants with a nationally representative survey of adults aged 45 years or older, as well as their spouses when possible. The CHARLS includes assessments of social, economic, and health circumstances of community-residents. The national baseline survey was conducted between June 2011 and March 2012 and included 17,708 respondents from 10,257 households. CHARLS respondents were followed every 2 years, using a face-to-face computer-assisted personal interview (CAPI)(Zhao, Hu et al. 2012). At baseline there was 3381 married women who never smoked cigarettes and lived with spouses who had either smoked cigarettes in the past or smoked at the time of interview. Besides, all the data for each variable have been collected for those respondents. Our final sample was composed of 6875 respondents, among them 2802 were interviewed again during the second wave of data collection in 2013, and 2247were interviewed again during the third wave in 2015. The similar sample selection process was conducted for participants in the second wave in 2013 as baseline, and final sample was consisted of 1799 women who

were investigated again in 2015 as participants.

## Measures

### *Secondhand Smoke*

Based on standardized CHARLS questionnaire, the exposure to SHS among Chinese women was assessed through several surveys, asking the participants about their current marital status, the exact year they got married, and the years the husband in each household has begun or ceased smoking at home.

The smoking status section contained four questions: "Have you ever chewed tobacco, smoked a pipe, smoked self-rolled cigarettes, or smoked cigarettes/cigars?", "Do you still have the habit or have you totally quit?", "At what age did you totally quit smoking?" and "At what age did you start to smoke on a regular basis?". If the answer to the first question was "yes", they were defined as "current smokers". Our analysis of SHS exposure focused only on nonsmokers excluding the "current smokers", because of the difficulty to differentiate the negative effects of active smoking on health condition from that of SHS exposure. The length of SHS exposure was calculated and expressed as the total number of years that never-smoking women spent living

with their spouses who smoked cigarettes at home. Based on the constructed SHS exposure variable, the participants were classified into four different groups: Never or being exposed to secondhand smoke for less than 25 years, more than 25 years and less than 30 years, more than 30 years and less than 40 years and over 40 years.

***Cognitive function***

Cognitive functions were measured from Telephone Interview of Cognition Status form (self-rated memory, today's date, day of the week, and current season); recall and delayed recall test of memory of 10 words; test of serial subtractions of 7 from 100; ability to reproduce a picture of two overlapped pentagons in CHARLS questionnaires (Zhao, 2012. Cognitive subdomains including visuospatial ability, orientation and attention, and episodic memory (Ge, Wei et al. 2018) could be assessed by these various sections of questionnaire. The Telephone Interview of Cognitive Status (TICS) is a 10-item screening test for the assessment of cognitive function in patients with Alzheimer's disease who are unwilling or unable to be examined in person. To assess orientation and attention function, the number of correct answers to above questions

was scored and summed up (range 0 to 10). Figure drawing was used to measure a person's ability to identify visual and spatial relationships among objects. Participants who successfully completed the task received a score of 1, and those who failed received 0(Ge, Wei et al. 2018).

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 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)(Li, Cacchione et al. 2017).

The overall cognition scores were the sum of the three different domains (range 0 to 21).

***Control variables***

Given that cognitive function may vary across demographic and socioeconomic status, we thus included age,

urban/rural residence, education, annual household expenditures, chronic diseases and depressive symptoms as control variables. Education was categorized into 3 groups: “illiterate”, “primary education” and “secondary education or above”. Arterial hypertension and diabetes mellitus are separately strong independent risk factors for the development of cognitive impairment and dementia(Tadic, Cuspidi et al. 2016) (Moheet, Mangia et al. 2015). Thus, the baseline condition of hypertension and diabetes were included, in addition to whether the participants were being treated. The measure of depressive symptoms was based on the 10-item version of the Center for Epidemiologic Studies Depression Scale(CES-D) short form, and each of the 4-option response to item was scored ranging from 0 to 3. The total score is the sum of points for all 10 items, and a score of 10 or higher suggests the presence of depressive symptoms(Cheng, Chen et al. 2016).

**Analysis**

All analyses were conducted with STATA, version 14.0 (Stata, College Station, TX, USA).We used lagged dependent-variable regression models with ordinary least squares

estimation. In the LDV method, covariation both between and within waves is used to estimate the coefficients, yielding more stable estimates and lower standard errors than those found in other methods, such as the change score (CS) methods(Johnson 2005). After pooling the three sets of panel data into one through using the "year" dummy variable to differentiate between change in 2 years or in 4 years, we have 6875 respondents who have complete data on all variables. The overall cognitive scores, episodic memory scores, visuospatial ability scores and orientation and attention scores were 4 separate outcome variables. The different groups of SHS exposure years were the predictor variable, and other independent variables included all demographic and socioeconomic characteristics. Prior to fitting the regression models, descriptive analyses were conducted to estimate the mean and standard deviations for continuous data and frequencies and percentages for categorical data.

**Results**

Table 1 provides a descriptive summary of all the variables for participants from each panel of three different waves: 2011-2013, 2011-2015 and 2013-2015. High

prevalence of SHS exposure between 30 to 40 years were seen in different panels, accounting for 32.51%, 35.18% and 42.69% respectively.

The participants were over 45 years old, with the average age of 56, 56 and 58 years old, respectively in those waves . Participants were more likely to live in rural area, have lower education background and do not have hypertension or diabetes symptoms at baseline. In addition, our results indicated that the average baseline cognition scores were higher than wave-2 and wave-3 cognition scores. The average scores of CES-D indicated high prevalence of depression among Chinese middle-aged and old-aged women in those years. Other socio-demographic characteristics of the respondents are shown in Table 1

Results from the regression models for the relationship between SHS exposure and each domain of cognitive function and overall cognition scores are reported in Table 2 and Table 3. Scores of episodic memory, orientation and attention and visuospatial among respondents at baseline were strong predictors of their corresponding cognitive function measures 2 or 4 years later. 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 being exposed to it for less than 25 years, those who have exposed to SHS for more than 40 years suffered a 0.04-point decline in visuospatial abilities(95%CI, -0.08--0.01 P <0.1), a 0.16-point decline in episodic memory(95%CI, -0.31--0.01 P <0.05), and a 0.33-point decline in overall cognition functions(95%CI, -0.66--0.01 P <0.01). In addition, age was also a strong indicator. Each one-year older resulted in a 0.01-point, 0.01-point, 0.03-point, 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, a one-point increase in CESD scores decrease 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 suffer from cognitive decline in specific functions.

**Discussion**

Results from this longitudinal study with a large, representative sample of middle-aged and older women in China indicated that exposure to secondhand smoke for over 40 years was associated with significantly poorer performance of global cognition and cognitive subdomains. It is the first examination of cognitive subdomains in relation to household SHS exposure using a 4-year longitudinal data in China. The inferior performance of passive smokers on measures of visuospatial abilities, episodic memory and orientation and attention abilities are creative as these domains were not specifically evaluated in earlier studies with middle-aged and older samples who never smoke(Durazzo, Meyerhoff et al. 2012).Previous study only suggested that secondhand smoke was associated with poorer cognitive performance specifically in children, adolescents and adults(Yolton, Dietrich et al. 2005). Besides, we found that having a high educational level, living in urban area and having better baseline cognitive

function would improve their cognitive performance. Compared with those without diabetes, participants with diabetes in baseline were found to have a 0.172-point decline in episodic memory scores, whereas the exact type of diabetes could not be examined in our study. An early finding showed that people with both type 1 and type 2 diabetes had mild to moderate reductions in cognitive function compared to non-diabetic controls as measured by neuropsychological testing, while type 2 diabetes (T2DM), but not type 1 diabetes, has been associated with 50% increased risk of dementia (Moheet, Mangia et al. 2015).

Our results showed that compared with women who have never been exposed to SHS or being exposed for less than 20 years, those who was exposed to SHS for more than 40 years have experienced, on average, 0.04-point, 0,16-point and 0.33-point decline in scores of visuospatial function, episodic memory and overall cognitive scores, respectively. Compared with prior research(Pan, Luo et al. 2018), the coefficients were significant. Besides, each one-year increase in age resulted in a 0.01-point, 0.02-point, 0.04-point, 0.06-point decrease in visuospatial, orientation, memory and overall cognition scores, respectively.

Secondhand smoke seems to be a stronger indicator of cognitive decline than aging. Study had reported that attention referred to the ability to concentrate and focus on specific stimuli slightly declined in later life (Lezak, M; Howieson, D, 2012), and orientation was one's ability to identify exact date, month, day and season of the year. Our results did not signify the relationship between SHS and orientation and attention ability may due to the relatively small size of sample and short period of cohort study after controlling for all demographic and socioeconomic confounders. Visuospatial abilities involve the ability to understand space in two and three dimensions. A nationally representative data concerning 5683 children and adolescents who were 6–16 years in America showed that years of SHS exposure was significantly associated with lower scores for reading, math, and visuospatial skills, after adjusting for covariates (Yolton, Dietrich et al. 2005). In our study, an inversed relationship between SHS exposure and visuospatial abilities among middle-aged and older adults was also presented, showing a 0.04-point decline in their visuospatial scores. As one of the most common cognitive complaints among elders, episodic memory

refers to personally experienced events which could be measured by stories, word lists or figures. Previous study proved that the onset of memory decline may vary among different memory types, with episodic memory lasting lifelong (Rönnlund, M; Nyberg, L.2005). 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.

The inconsistent conclusions between our studies and prior ones may probably due to the relatively simplified version of cognition test procedure in CHARLS questionnaires compared with the MoCA(Li, Jia et al. 2018) and MMSE(Trzepacz, Hochstetler et al. 2015). Some studies also used clinical or magnetic resonance imaging (MRI) evidence of neurologic damage to detect cognitive impairment (Kalb R, et al 2018). Best adapted to a screening test, the MoCA exhibited excellent sensitivity in identifying MCI and AD(Alzheimer's disease) by 90% and 100%, respectively (Ziad S. Nasreddine 2005).

The most popular hypothesis about the mechanisms underlying the links between SHS exposure and poorer

cognitive performance lies in the notion that the carbon monoxide (CO) in tobacco smoke may interfere with the oxygen being delivered to the brain via the blood system, which could be tested by measuring levels of CO in the blood of never smokers who have been exposed to SHS and comparing these with never smokers with no history of such exposure. However, the reasons behind different effect on various domains of brain function are far from clear. One possible explanation derives from an animal research. It may lead to reduced neuronal mass in specific regions of the brain associated with learning and memory after exposing animals to varying degrees of toxic mixtures of chemicals found in tobacco smoke. Since the hippocampal region of the brain is known to be involved in the mediation of memory(Staples and Mandyam 2016) and learning, further research should be conducted in other regions dominating visuospatial and orientation ability. Another possible mechanism is that prolonged exposure to SHS may be a significant risk factor for cardiovascular disease (Yankelevitz, Henschke et al. 2013), which may therefore lead to a range of health and cognitive problems in later life. 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.

Several limitations need to be considered when interpreting this study and designing future studies. Firstly, the exposure to secondhand smoke was evaluated based on self-report measures. This might be subject to recall bias and led to over-or-underestimation of exposure(Ling and Heffernan 2016). Therefore, further studies could include more biological assays, for example, cotinine residue levels or nicotine residue in saliva or hair samples (Akhtar, Andresen et al. 2013). Previous research using serum cotinine as a biomarker of exposure to SHS found that higher levels of serum cotinine were associated with significant reductions in performance in reading, mathematics, and visual and spatial abilities in children and adolescents (Yolton, Dietrich et al. 2005). However, no studies had used a combination of biomarker and self-report yet (Stirland, O'Shea et al. 2018). Cognitive impairment could also be detected by the effect of apolipoprotein ε4 (Apo ε4) polymorphism, which was a known risk factor for dementia. Secondly, it may be impossible

to control for all potentially confounding variables. After adjusting for age, household expenditure, education, area, chronic health condition and depressive symptoms, some other demographic or socioeconomic confounders may be neglected. Nevertheless, this did not appear to affect the magnitude of the association between SHS exposure and cognition(Chen, Clifford et al. 2013).Besides, the analyses only contained household SHS exposure, which precludes the analyses of the influence of environment smoke inhale on smoking proclivity. Whether exposure to household SHS can hasten the onset of cognitive impairment for older Chinese women could by further proved by running regression models in different age groups.

**Acknowledgments :**

We would like to thank the professor Yaohui Zhao at Centre for Chinese Economic Research, Peking University for her thoughtful contributions to this study.

**Conflict of Interest**

The authors have no conflicts of interest to declare.

**Author's Contribution**

Anying Bai wrote and participated in all aspects of this research, including the field investigation. Dr Yangmu Huang reviewed and supervised this research. Yinzi Jin participated in the statistical analysis of this work and reviewed the final article.

**Data sharing statement**

CHARLS data is available to the public online : http://charls.pku.edu.cn

**Funding Resources**

This is a self-funded research.



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Table1.Characteristics of the Participants from 3 waves of CHARLS, 2011-2013-2015

| | 2011-2013 (N=2802) | | 2011-2015 (N=2274) | | 2013-2015 (N=1799) | |
|---|---|---|---|---|---|---|
| **Variable** | Count | Frequency | Count | Frequency | Count | Frequency |
| **Area** | | | | | | |
| Urban | 981 | 35.01% | 730 | 32.10% | 556 | 30.91% |
| Rural | 1821 | 64.99% | 1544 | 67.90% | 1243 | 69.09% |
| **Secondhand Smoke** | | | | | | |
| Less than 25 years | 759 | 27.09% | 531 | 23.35% | 262 | 14.56% |
| More than 25 years and less than 30 years | 634 | 22.63% | 573 | 25.20% | 385 | 21.40% |
| More than 30 years and less than 40 years | 911 | 32.51% | 800 | 35.18% | 768 | 42.69% |
| More than 40 years | 498 | 17.77% | 370 | 16.27% | 384 | 21.35% |
| **Education** | | | | | | |
| Illiterate | 1552 | 55.39% | 1309 | 57.56% | 1004 | 55.81% |
| Primary education | 512 | 18.27% | 414 | 18.21% | 336 | 18.68% |
| Secondary or above | 738 | 26.34% | 551 | 24.23% | 459 | 25.51% |
| **Hypertension** | | | | | | |
| No hypertension | 2124 | 75.80% | 1720 | 75.64% | 1365 | 75.88% |
| Hypertension with treatment | 522 | 18.63% | 1720 | 75.64% | 358 | 19.90% |
| Hypertension without treatment | 156 | 5.57% | 130 | 5.72% | 76 | 4.22% |
| **Diabetes** | | | | | | |
| No Diabetes in baseline | 2643 | 94.33% | 2140 | 94.11% | 1704 | 94.72% |

| | | | | | | |
|---|---|---|---|---|---|---|
| Have Diabetes with treatment | 143 | 5.10% | 120 | 5.28% | 86 | 4.78% |
| Have Diabetes without treatment | 16 | 0.57% | 14 | 0.62% | 9 | 0.50% |
| | Count | Mean(SD) | Count | Mean(SD) | Count | Mean(SD) |
| Age | 2802 | 55.84(8.22) | 2274 | 56.19(7.75) | 1799 | 57.90(7.43) |
| Annual Household Expenditure, yuan[a] | 2802 | 13786.99(14197.29) | 2274 | 13060.14(13639.33) | 1799 | 16632.84(18568.24) |
| Visuospatial ability[b] | 2802 | 0.51(0.50) | 2274 | 0.48(0.50) | 1799 | 0.49(0.50) |
| Orientation and attention[c] | 2802 | 5.87(3.29) | 2274 | 5.84(3.19) | 1799 | 5.97(3.14) |
| Memory Scores[d] | 2802 | 3.33(1.96) | 2274 | 3.04(1.93) | 1799 | 3.15(1.91) |
| Baseline Visuospatial ability | 2802 | 0.57(0.50) | 2274 | 0.55(0.50) | 1799 | 0.54(0.50) |
| Baseline Orientation and attention | 2802 | 6.39(2.92) | 2274 | 6.25(2.90) | 1799 | 6.16(3.00) |
| Baseline Memory Scores | 2802 | 3.27(1.98) | 2274 | 3.23(1.92) | 1799 | 3.50(1.78) |
| Baseline CES-D Score[e] | 2802 | 12.09(5.38) | 2274 | 12.13(5.45) | 1799 | 10.90(5.14) |

Abbreviation: SHS, secondhand smoke.

a 1 US dollar = 6.3 yuan.

b The score range for visuospatial ability was 0–1.

c The score range for orientation and attention was 0–10. Higher scores indicate better mental status.

d The score range for episodic memory was 0–10. Higher scores indicate better memory function.

e A score of 10 or greater indicated the presence of depressive symptoms.

Table2.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

| | Visuospatial Scores | | | Orientation and Attention | | |
|---|---|---|---|---|---|---|
| VARIABLES | β coefficient | 95%CI | t | β coefficient | 95%CI | t |
| **Age** | -0.01[a] | -0.01,-0.00 | -6.73 | -0.02[a] | -0.03, -0.01 | -4.34 |
| **Expenditure** | 0.00 | 0.00, 0.00 | 0.01 | 0.00[a] | 0.00, 0.00 | 0.77 |
| **Secondhand Smoke Exposure[d]** | | | | | | |
| **More than 25 years less than 30 years** | -0.01 | -0.04, 0.02 | -0.72 | 0.05 | -0.12, 0.21 | 0.56 |
| **More than 30 years less than 40 years** | -0.02 | -0.05, 0.02 | -0.95 | -0.03 | -0.20, 0.13 | -0.38 |
| **More than 40 years** | -0.04[c] | -0.08, 0.01 | -1.67 | -0.15 | -0.38, 0.09 | -1.24 |
| **Baseline Visuospatial Scores** | 0.23[a] | 0.21, 0.26 | 17.93 | | | |
| **Baseline Orientation Socres** | | | | 0.55[a] | 0.53, 0.57 | 44.86 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Urban**[e] | 0.06[a] | 0.04, 0.09 | 5.27 | 0.38[a] | 0.25, 0.51 | 5.72 |
| **Education**[f] | | | | | | |
| **Primary** | 0.23[a] | 0.20, 0.26 | 14.00 | 1.11[a] | 0.94, 1.27 | 12.91 |
| **Secondary or Above** | 0.29[a] | 0.26, 0.32 | 18.51 | 1.18[a] | 1.01, 1.36 | 13.44 |
| **Hypertension**[g] | | | | | | |
| **With Treatment** | -0.03 | -0.09, 0.02 | -1.20 | 0.06 | -0.24, 0.35 | -0.38 |
| **Without Treatment** | -0.02 | -0.06, 0.03 | -0.69 | 0.06 | -0.11, 0.24 | 0.04 |
| **Missing Group** | -0.05[c] | -0.12, 0.01 | -1.67 | 0.06 | -0.19, 0.30 | -0.01 |
| **Diabetes**[h] | | | | | | |
| **With Treatment** | 0.02 | -0.03, 0.07 | 0.90 | 0.25[c] | -0.03, 0.52 | -1.77 |
| **Without Treatment** | 0.03 | -0.04, 0.09 | 0.82 | 0.21 | -0.06, 0.48 | -0.23 |
| **Missing Group** | 0.07 | -0.08, 0.21 | 0.88 | 0.50 | -0.22, 1.23 | 0.67 |
| **Baseline CES-D Score** | -0.00[c] | -0.00, 0.00 | -1.71 | -0.02[b] | -0.03, -0.00 | -2.57 |
| **year = 2** | -0.02 | -0.04, 0.01 | -1.58 | 0.09 | -0.05, 0.22 | 1.29 |

Abbreviations: CI, confidence interval; SHS, secondhand smoke.

a. p<0.01

b. p<0.05

c. p<0.1

d. Referent: No SHS exposure or Less than 25 years.

e. Expenditure is expressed as the natural log of the annual household expenditure

f. Referent: Illiterate

g. Referent: Without hypertension

h. Referent: Without diabetes

Table3.Multivariable linear regression analysis of the relationship between smoking exposure and Episodic memory and Overall cognitive function among older Chinese women (N = 6875), 2011-2013-2015

| | Episodic Memory | | | Overall Cognition Socres | | |
|---|---|---|---|---|---|---|
| VARIABLES | β coefficient | 95%CI | t | β coefficient | 95%CI | t |
| **Age** | -0.04[a] | -0.05,-0.03 | -11.37 | -0.06[a] | -0.07, -0.04 | -7.87 |
| **Expenditure** | 0.00 | 0.00, 0.00 | 1.30 | 0.00[a] | 0.00, 0.00 | 0.32 |
| **Secondhand Smoke Exposure[d]** | | | | | | |
| **More than 25 years less than 30 years** | -0.04 | -0.16, 0.08 | -0.67 | -0.01 | -0.25, 0.25 | -0.01 |
| **More than 30 years less than 40 years** | 0.02 | -0.09, 0.13 | 0.36 | -0.05 | -0.29, 0.19 | -0.41 |
| **More than 40 years** | -0.16[b] | -0.31, -0.01 | -2.06 | -0.33[a] | -0.66, 0.01 | -1.93 |
| **Baseline Memory Scores** | 0.30[a] | 0.28, 0.32 | 25.22 | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Baseline Cognition Scores** | | | | 0.55[a] | 0.46, 0.83 | 44.95 |
| **Urban[e]** | 0.25[a] | 0.16, 0.34 | 5.60 | 0.65[a] | 0.46, 0.83 | 6.68 |
| **Education[f]** | | | | | | |
| **Primary** | 0.70[a] | 0.58, 0.80 | 12.42 | 1.77[a] | 1.53, 2.02 | 14.28 |
| **Secondary or Above** | 0.97[a] | 0.86, 1.08 | 17.29 | 2.00[a] | 1.74, 2.26 | 15.24 |
| **Hypertension[g]** | | | | | | |
| **With Treatment** | 0.04 | -0.16, 0.23 | 0.35 | 0.13 | -0.29, 0.56 | 0.62 |
| **Without Treatment** | 0.06 | -0.06, 0.17 | 0.95 | 0.12 | -0.14, 0.38 | 0.93 |
| **Missing Group** | 0.07 | -0.12, 0.25 | 0.70 | 0.10 | -0.27, 0.47 | 0.52 |
| **Diabetes[h]** | | | | | | |
| **With Treatment** | -0.20[b] | -0.38, 0.02 | -2.20 | -0.04 | -0.43, 0.36 | 0.62 |
| **Without Treatment** | -0.07 | -0.25, 0.11 | -0.77 | 0.08 | -0.30, 0.47 | 0.43 |
| **Missing Group** | 0.32 | -0.16, 0.80 | 1.30 | 0.87 | -0.11, 1.84 | 1.75 |
| **Baseline CES-D Score** | -0.01[b] | -0.01, 0.00 | -1.59 | -0.01 | -0.03, 0.00 | -2.57 |
| **year = 2** | -0.24 | -0.33, -0.15 | -5.21 | -0.17 | -0.37, 0.03 | -1.70 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Constant** | 0.63 | 0.53, 0.74 | 11.54 | 6.48[a] | 5.59, 7.37 | 14.28 |

Abbreviations: CI, confidence interval; SHS, secondhand smoke.

a. p<0.01

b. p<0.05

c. p<0.1

d. Referent: No SHS exposure or Less than 25 years.

e. Expenditure is expressed as the natural log of the annual household expenditure

f. Referent: Illiterate

g. Referent: Without hypertension

h. Referent: Without diabetes

# Reporting checklist for qualitative study.

Based on the SRQR guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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| | | Reporting Item | Page Number |
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| **Title** | | | |
| | #1 | Concise description of the nature and topic of the study identifying the study as qualitative or indicating the approach (e.g. ethnography, grounded theory) or data collection methods (e.g. interview, focus group) is recommended | 1 |
| **Abstract** | | | |
| | #2 | Summary of the key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results and conclusions | 2 |
| **Introduction** | | | |
| Problem formulation | #3 | Description and signifcance of the problem / phenomenon studied: review of relevant theory and empirical work; problem statement | 4 |
| Purpose or research question | #4 | Purpose of the study and specific objectives or questions | 5 |

**Methods**

| | | | |
|---|---|---|---|
| Qualitative approach and research paradigm | #5 | Qualitative approach (e.g. ethnography, grounded theory, case study, phenomenolgy, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g. postpositivist, constructivist / interpretivist) is also recommended; rationale. The rationale should briefly discuss the justification for choosing that theory, approach, method or technique rather than other options available; the assumptions and limitations implicit in those choices and how those choices influence study conclusions and transferability. As appropriate the rationale for several items might be discussed together. | 6 |
| Researcher characteristics and reflexivity | #6 | Researchers' characteristics that may influence the research, including personal attributes, qualifications / experience, relationship with participants, assumptions and / or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results and / or transferability | 6 |
| Context | #7 | Setting / site and salient contextual factors; rationale | 2 |
| Sampling strategy | #8 | How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g. sampling saturation); rationale | 7 |
| Ethical issues pertaining to human subjects | #9 | Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues | 2 |
| Data collection methods | #10 | Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources / methods, and modification of procedures in response to evolving study findings; rationale | 7 |
| Data collection instruments and technologies | #11 | Description of instruments (e.g. interview guides, questionnaires) and devices (e.g. audio recorders) used for data collection; if / how the instruments(s) changed over the course of the study | 7 |

| | | | |
|---|---|---|---|
| Units of study | #12 | Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results) | 7 |
| Data processing | #13 | Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymisation / deidentification of excerpts | 10 |
| Data analysis | #14 | Process by which inferences, themes, etc. were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale | 11 |
| Techniques to enhance trustworthiness | #15 | Techniques to enhance trustworthiness and credibility of data analysis (e.g. member checking, audit trail, triangulation); rationale | 10 |
| **Results/findings** | | | |
| Syntheses and interpretation | #16 | Main findings (e.g. interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory | 11 |
| Links to empirical data | #17 | Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings | 11 |
| **Discussion** | | | |
| Intergration with prior work, implications, transferability and contribution(s) to the field | #18 | Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application / generalizability; identification of unique contributions(s) to scholarship in a discipline or field | 13 |
| Limitations | #19 | Trustworthiness and limitations of findings | 15 |
| **Other** | | | |
| Conflicts of interest | #20 | Potential sources of influence of perceived influence on study conduct and conclusions; how these were managed | 17 |
| Funding | #21 | Sources of funding and other support; role of funders in data collection, interpretation and reporting | 17 |

BMJ Open

# Exposure to Secondhand Smoke and Cognitive Function Among Middle-aged and Older Women in China: Findings of 3-waves of the China Health and Retirement Longitudinal Study

| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2020-039824.R1 |
| Article Type: | Original research |
| Date Submitted by the Author: | 22-Aug-2020 |
| Complete List of Authors: | Bai, Anying; Peking University Health Science Centre, School of Public Health;<br>Jin, Yinzi; Peking University, School of Public Health<br>Huang, Yangmu; Peking University Health Science Centre, School of Public Health; |
| Primary Subject Heading: | Epidemiology |
| Secondary Subject Heading: | Smoking and tobacco, Public health, Mental health |
| Keywords: | EPIDEMIOLOGY, Dementia < NEUROLOGY, PUBLIC HEALTH |
| | |

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**Title**

# Exposure to Secondhand Smoke and Cognitive Function Among Middle-aged and Older Women in China: Findings of 3-waves of the China Health and Retirement Longitudinal Study

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**Abstract**

**Objectives:** To examine the association between secondhand smoke and women's global cognitive function and cognitive subdomains.

**Design:** Cohort study

**Participants:** Data for this study were obtained from the China Health and Retirement Longitudinal Study (CHARLS, 2011-2013-2015), and pooled analysis was applied to wave 1 and wave 2(2011-2013), wave 2 and wave 3(2013-2015) and wave 1 and wave 3(2011-2015). 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.

**Main outcome measures and methods:** Secondhand smoke was classified based on length of exposed years (<25years, ≥ 25 to <30 years, ≥30 to <40 years, ≥40 years). Global cognitive function, visuospatial ability, orientation and attention, and episodic memory function were used as measures of cognitive function. We pooled the three waves of data by using dummy variable to differentiate between

2-year and 4-year. Lagged dependent variable models were used to examine independent associations between secondhand smoke and cognitive function. Demographic factors, socioeconomic factors, baseline cognitive functioning and health conditions were controlled in our models.

**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--0.01, $P < 0.01$), visuospatial ability (β=-0.04, 95%CI, -0.08--0.01 P < 0.05) and episodic memory function (β=-0.16, 95%CI, -0.31--0.01 P = 0.031).

**Conclusions:** Secondhand smoke within household 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 function among elder Chinese women.

**Key words:** aging; passive smoking; panel analysis; visuospatial ability; memory

**Strengths and limitations of this study:**

- This is the first study to investigate on the association between secondhand smoke exposure and women's different domains of cognitive functions in China using a 4-year longitudinal national representative data.
- This study addressed the issue of reverse causation in observational cohort studies by used lagged dependent variable models and adjust for baseline cognition scores
- The exposure to secondhand smoke was evaluated based on self-report measures.
- The analyses only contained household SHS exposure and excluding environmental exposure.

**Word Count: 3214**

**Number of references:31**

**Number of data elements :1**

## Introduction

China's population has been ageing rapidly. By 2050, there will be 400 million Chinese citizens aged over 65 years old, and 150 million of whom will be older than 80

years old[1]. It will become increasingly important to understand the cognitive changes that accompany aging[2]. Cognitive impairment, described as a decline in intellectual functions [3], ranges from mild forms of forgetfulness to severe and debilitating dementia [4]. The prevalence of cognitive impairment is rising, with national figures estimating that around 9% of older persons in China had cognitive impairment in 2011 [4].

Numerous determinants such as environmental, individual, and genetic factors could favor evolution toward cognitive impairment, and both age and late-life hypertension increase the risk of dementia over time [5]. The mechanism lies in age-related functional and structural changes in cerebrovascular small and large blood vessels [6]. Besides chronic diseases factors, depression has long been known to affect memory and other neurocognitive domains, and be associated with an increased risk of developing mild cognitive impairment (MCI) in cognitively normal elderly people [7].

Exposure to secondhand smoke (SHS), also known as "passive smoking," refers to a situation where a never-smoker inhales another person's smoke either by exposure

to side stream smoke or mainstream smoke [8]. Current smoking prevalence in China decreased from 31.1% in 2002 to 28.1% in 2010; however, the number of adults exposed to secondhand smoke during this period still increased from 540 million to 556 million [2]. The negative health effects of high levels of exposure to SHS may be close to those of active smoking, including inferior performance on measures of general intelligence, visuospatial learning and memory and fine motor dexterity [9].· Given the association between exposure to SHS and risk factors for cognitive impairment such as cardiovascular disease [10], hypertension [11], and stroke [12] , it is possible that high level of exposure may be a preventable risk factor for cognitive impairment or dementia [13].

Several studies have shown that exposure of SHS and cognitive impairment are interrelated [13-15]. However, much less is known about whether and to what extent SHS is associated with global and subdomains of cognitive function among elder women in China. Previous studies of active smoking and cognitive impairment among the Chinese population suggested that older current smokers(aged 63 years old on average) [14] or those being exposed to SHS

(aged between 55-64 years old) [16] were more likely to develop cognitive impairment compared with never-smokers. Nevertheless, both of them used only a 2-wave longitudinal data and did not control for baseline cognition. Therefore, the primary aim of this study was to investigate the relationship between secondhand smoke and cognitive function among older non-smoking Chinese women, using a 3-wave longitudinal national representative data. Through the classification of respondents by different years of secondhand smoke exposure in a 4-year panel, we identified whether certain high SHS exposure groups were at higher risk of cognitive decline than others after controlling for confounders. Besides, we aimed to examine the association between secondhand smoke exposure and cognitive subdomains. This is especially important given the escalating aging trend and increasing prevalence of SHS exposure in China.

## Methods

### Data

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. 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. The national baseline survey was conducted between June 2011 and March 2012 and 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. CHARLS respondents were followed every 2 years, using a face-to-face computer-assisted personal interview (CAPI) [17]. At baseline there was 3381 married women who never smoked cigarettes and lived with spouses who had either smoked cigarettes in the past or smoked at the time of interview. Besides, all the data for each variable have been collected for those respondents. Our final sample was composed of 6875 respondents, among them 2802 were interviewed again during the second wave of data collection in 2013, and 2247 were interviewed again during the third wave in 2015. The similar sample selection process was conducted for participants in the second wave in 2013 as baseline, and

final sample was consisted of 1799 women who were investigated again in 2015 as participants.

**Measures**

***Secondhand Smoke***

Based on standardized CHARLS questionnaire, the exposure to SHS among Chinese women was assessed through several surveys, asking the participants about their current marital status, the exact year they got married, and the year the husband in each household has begun or ceased smoking at home.

The smoking status section contained four questions: "Have you ever chewed tobacco, smoked a pipe, smoked self-rolled cigarettes, or smoked cigarettes/cigars?", "Do you still have the habit or have you totally quit?", "At what age did you totally quit smoking?" and "At what age did you start to smoke on a regular basis?". If the answer to the first question was "yes", they were defined as "current smokers". Our analysis of SHS exposure focused only on never smokers excluding the "current smokers", because of the difficulty to differentiate the negative effects of active smoking on health condition from that of SHS exposure. The length of SHS exposure was calculated and

expressed as the total number of years that never-smoking women spent living with their spouses who smoked cigarettes at home. Based on the constructed SHS exposure variable, the participants were classified into four different groups: Never or being exposed to secondhand smoke for less than 25 years, more than 25 years and less than 30 years, more than 30 years and less than 40 years and over 40 years.

***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[17], 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 [18].

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) [19].

The overall cognition scores were the sum of the three different domains (range 0 to 21).

***Control variables***

Given that cognitive function may vary across demographic and socioeconomic status, we thus included age, urban/rural residence, education, annual household expenditures, chronic diseases and depressive symptoms as

control variables. Education was categorized into 3 groups: "illiterate", "primary education" and "secondary education or above". Arterial hypertension and diabetes mellitus are separately strong independent risk factors for the development of cognitive impairment and dementia[6] [20]. 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. The measure of depressive symptoms was based on the 10-item version of the Center for Epidemiologic Studies Depression Scale (CES-D) short form, and each of the 4-option response to item was scored ranging from 0 to 3. The total score is the sum of points for all 10 items, and a score of 10 or higher suggests the presence of depressive symptoms .

***Patient and Public Involvement***

No patient involved.

**Analysis**

All analyses were conducted with STATA, version 14.0 (Stata, College Station, TX, USA).We used lagged dependent-

variable regression models with ordinary least squares estimation. LDV models were 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 [16]. It adjusted for baseline cognitive conditions for all participants, therefore provided more robust estimates of the effects of independent variables. After pooling the three sets of panel data into one through using the "year" dummy variable to differentiate between change in 2 years or in 4 years, we have 6875 respondents who have complete data on all variables. The overall cognitive scores, episodic memory scores, visuospatial ability scores and orientation and attention scores were 4 separate outcome variables. The different groups of SHS exposure years were the predictor variable, and other independent variables included all demographic and socioeconomic characteristics. Prior to fitting the regression models, descriptive analyses were conducted to estimate the mean and standard deviations for continuous data and frequencies and percentages for categorical data.

**Results**

Table 1 provides a descriptive summary of all the

variables for participants from each panel of three different waves: 2011-2013, 2011-2015 and 2013-2015. High prevalence of SHS exposure between 30 to 40 years were seen in different panels, accounting for 32.51%, 35.18% and 42.69% respectively.

The participants were over 45 years old, with the average age of 56, 56 and 58 years old, respectively in those waves. Participants were more likely to live in rural area, have lower education background and do not have hypertension or diabetes diagnose at baseline. In addition, our results indicated that the average baseline cognition scores were higher than cognition scores after 2 or 4 years. The average scores of Center for Epidemiologic Studies Depression Scale (CES-D) indicated that the prevalence of depression among Chinese middle-aged and old-aged women were high in those years. Other socio-demographic characteristics of the respondents are shown in Table 1

Results from the regression models for the relationship between SHS exposure and each domain of cognitive function and overall cognition scores are reported in Table 2 and Table 3. 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 adjusted for 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 been 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 function (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.

**Discussion**

Results from this longitudinal study with a large, representative sample of middle-aged and older women in China indicated that exposure to secondhand smoke for over 40 years was significantly associated with poorer performance of global cognition and cognitive subdomains. It is the first examination of cognitive subdomains in relation to household SHS exposure using a 4-year longitudinal data in China. The inferior performance of secondhand smoke on visuospatial abilities, episodic memory and orientation and attention abilities are novel as these domains were not specifically evaluated in earlier studies among middle-aged and older women who never smoke [9].Previous study only suggested that secondhand smoke was

associated with poorer cognitive performance, specifically in children, adolescents and adults [14]. Besides, we found that having a high educational level, living in urban area and having better baseline cognitive function would improve their cognitive performance. Compared with those without diabetes, participants with diabetes in baseline were found to have a 0.172-point decline in episodic memory scores, which is similar to the previous findings [20].

Our results showed that compared with women who have never been exposed to SHS or have been exposed for less than 20 years, those who have been exposed to SHS for more than 40 years experienced 0.04-point, 0,16-point and 0.33-point of decline in scores of visuospatial function, episodic memory and overall cognitive scores, respectively. Our results were quite similar in magnitude to prior research on the relationship between SHS and cognitive function [16]. A cross-sectional research including 150 samples conducted in the North East of England revealed that participants who had no history of smoking and being averagely exposed to SHS for around 6 years showed significantly reduced performance in processing speed (i.e. how quickly one can process information and perform tasks)

and executive function (i.e. the ability to organize memory, cognitive flexibility, and problem-solving ability) as compared with non-exposed people[13]. Another longitudinal aging study concerning 4809 samples (aged 50 years or older) found that never smokers exposed to the highest levels of SHS (salivary cotinine concentrations 0.8-13.5 ng/ml) were more likely to be cognitively impaired (odds ratio 1.70, 1.03 to 2.80) than those exposed to little or no SHS[15].

Besides, each one-year increase in age resulted in a 0.01-point, 0.02-point, 0.04-point, 0.06-point decrease in visuospatial, orientation, memory and overall cognition scores, respectively. Secondhand smoke seems to be more strongly associated with cognitive decline than aging. Study had reported that attention referred to the ability to concentrate and focus on specific stimuli slightly declined in later life [21], and orientation was one's ability to identify exact date, month, day and season of the year. Our results did not observe the relationship between SHS and orientation and attention ability, which may due to the relatively small size of sample and short period of cohort study after controlling for all demographic and socioeconomic confounders. Visuospatial

abilities involve the ability to understand space in two and three dimensions. In our study, an inversed relationship between SHS exposure and visuospatial abilities among middle-aged and older adults was presented, showing a 0.04-point decline in their visuospatial scores. Such an inversed relationship between SHS exposure and visuospatial reasoning skills were also reported among 5683 children aged 6–16 years in America, showing that years of SHS exposure was significantly associated with lower scores for reading, math, and visuospatial skills, after adjusting for covariates [14]. As one of the most common cognitive complaints among elders, episodic memory refers to personally experienced events which could be measured by stories, word lists or figures. 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.

The inconsistent conclusions between our studies and prior ones may probably due to the relatively simplified

version of cognition test procedure in CHARLS questionnaires compared with the MoCA [23] and MMSE [24]. Some studies also used clinical or magnetic resonance imaging (MRI) evidence of neurologic damage to detect cognitive impairment [25]. Best adapted to a screening test, the MoCA exhibited excellent sensitivity in identifying MCI and AD (Alzheimer's disease) by 90% and 100%, respectively [26].

The most popular hypothesis about the mechanisms underlying the links between SHS exposure and poorer cognitive performance lies in the notion that the carbon monoxide (CO) in tobacco smoke may interfere with the oxygen being delivered to the brain via the blood system. However, the reasons behind different effect on various domains of brain function are far from clear. One possible explanation derives from an animal research. Exposing animals to varying degrees of toxic mixtures of chemicals found in tobacco smoke may lead to reduced neuronal mass in specific regions of the brain associated with learning and memory. Since the hippocampal region of the brain is known to be involved in the mediation of memory[27] and learning, further research should be conducted in other regions dominating visuospatial and orientation ability.

Another possible mechanism is that prolonged exposure to SHS may be a significant risk factor for cardiovascular disease (CVD)[28], which may therefore lead to a range of health and cognitive problems in later life. 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.

Several limitations need to be considered when interpreting this study and designing future studies. Firstly, the exposure to secondhand smoke was evaluated based on self-report measures. This might be subject to recall bias and lead to over-or-underestimation of exposure [8]. Therefore, further studies could include more biological assays, for example, cotinine residue levels or nicotine residue in saliva or hair samples [29]. Previous research using serum cotinine as a biomarker of exposure to SHS found that higher levels of serum cotinine were associated with significant worse performance in reading, mathematics, and visual and spatial abilities in children and adolescents [14]. However, no studies had used a combination of biomarker and self-report yet [30]. Cognitive

impairment could also be detected by the effect of apolipoprotein ε4 (Apo ε4) polymorphism, which was a known risk factor for dementia. Secondly, it may be impossible to control for all potentially confounding variables. After adjusting for age, household expenditure, education, area, chronic health condition and depressive symptoms, some other demographic or socioeconomic confounders may be neglected. Nevertheless, this did not appear to affect the magnitude of the association between SHS exposure and cognition [31]. Besides, the analyses only contained household SHS exposure, which precluded the analyses of the influence of environment smoke inhale on smoking proclivity. Whether exposure to household SHS can hasten the onset of cognitive impairment for older Chinese women could be further proved by running regression models in different age groups.

**Acknowledgments :**

We would like to thank the professor Yaohui Zhao at Centre for Chinese Economic Research, Peking University for her thoughtful contributions to this study.

**Conflict of Interest**

The authors have no conflicts of interest to declare.

**Author's Contribution**

Anying Bai wrote and participated in all aspects of this research, including the field investigation. Dr Yangmu Huang reviewed and supervised this research. Yinzi Jin participated in the statistical analysis of this work and reviewed the final article.

**Data sharing statement**

CHARLS data is available to the public online : http://charls.pku.edu.cn

**Funding Resources**

This is a self-funded research.

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Table1.Characteristics of the Participants from 3 waves of CHARLS, 2011-2013-2015

| | 2011-2013 (N=2802) | | 2011-2015 (N=2274) | | 2013-2015 (N=1799) | |
|---|---|---|---|---|---|---|
| **Variable** | Count | Frequency | Count | Frequency | Count | Frequency |
| **Area** | | | | | | |
| Urban | 981 | 35.01% | 730 | 32.10% | 556 | 30.91% |
| Rural | 1821 | 64.99% | 1544 | 67.90% | 1243 | 69.09% |
| **Secondhand Smoke** | | | | | | |
| Less than 25 years | 759 | 27.09% | 531 | 23.35% | 262 | 14.56% |
| More than 25 years and less than 30 years | 634 | 22.63% | 573 | 25.20% | 385 | 21.40% |
| More than 30 years and less than 40 years | 911 | 32.51% | 800 | 35.18% | 768 | 42.69% |
| More than 40 years | 498 | 17.77% | 370 | 16.27% | 384 | 21.35% |
| **Education** | | | | | | |
| Illiterate | 1552 | 55.39% | 1309 | 57.56% | 1004 | 55.81% |
| Primary education | 512 | 18.27% | 414 | 18.21% | 336 | 18.68% |
| Secondary or above | 738 | 26.34% | 551 | 24.23% | 459 | 25.51% |
| **Hypertension** | | | | | | |
| No hypertension | 2124 | 75.80% | 1720 | 75.64% | 1365 | 75.88% |
| Hypertension with treatment | 522 | 18.63% | 1720 | 75.64% | 358 | 19.90% |
| Hypertension without treatment | 156 | 5.57% | 130 | 5.72% | 76 | 4.22% |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Diabetes** | | | | | | |
| No Diabetes in baseline | 2643 | 94.33% | 2140 | 94.11% | 1704 | 94.72% |
| Have Diabetes with treatment | 143 | 5.10% | 120 | 5.28% | 86 | 4.78% |
| Have Diabetes without treatment | 16 | 0.57% | 14 | 0.62% | 9 | 0.50% |
| | Count | Mean(SD) | Count | Mean(SD) | Count | Mean(SD) |
| Age | 2802 | 55.84(8.22) | 2274 | 56.19(7.75) | 1799 | 57.90(7.43) |
| Annual Household Expenditure, yuan[a] | 2802 | 13786.99(14197.29) | 2274 | 13060.14(13639.33) | 1799 | 16632.84(18568.24) |
| Visuospatial ability[b] | 2802 | 0.51(0.50) | 2274 | 0.48(0.50) | 1799 | 0.49(0.50) |
| Orientation and attention[c] | 2802 | 5.87(3.29) | 2274 | 5.84(3.19) | 1799 | 5.97(3.14) |
| Memory Scores[d] | 2802 | 3.33(1.96) | 2274 | 3.04(1.93) | 1799 | 3.15(1.91) |
| Baseline Visuospatial ability | 2802 | 0.57(0.50) | 2274 | 0.55(0.50) | 1799 | 0.54(0.50) |
| Baseline Orientation and attention | 2802 | 6.39(2.92) | 2274 | 6.25(2.90) | 1799 | 6.16(3.00) |
| Baseline Memory Scores | 2802 | 3.27(1.98) | 2274 | 3.23(1.92) | 1799 | 3.50(1.78) |
| Baseline CES-D Score[e] | 2802 | 12.09(5.38) | 2274 | 12.13(5.45) | 1799 | 10.90(5.14) |

Abbreviation: SHS, secondhand smoke.

a 1 US dollar = 6.3 yuan.

b The score range for visuospatial ability was 0–1.

c The score range for orientation and attention was 0–10. Higher scores indicate better mental status.

d The score range for episodic memory was 0–10. Higher scores indicate better memory function.

e A score of 10 or greater indicated the presence of depressive symptoms.

Table2.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

| | Visuospatial Scores | | | Orientation and Attention | | |
|---|---|---|---|---|---|---|
| VARIABLES | β coefficient | 95%CI | t | β coefficient | 95%CI | t |
| **Age** | -0.01[a] | -0.01,-0.00 | -6.73 | -0.02[a] | -0.03, -0.01 | -4.34 |
| **Expenditure** | 0.00 | 0.00, 0.00 | 0.01 | 0.00[a] | 0.00, 0.00 | 0.77 |
| **Secondhand Smoke Exposure[d]** | | | | | | |
| **25 to <30 years** | -0.01 | -0.04, 0.02 | -0.72 | 0.05 | -0.12, 0.21 | 0.56 |
| **≥30 to <40 years** | -0.02 | -0.05, 0.02 | -0.95 | -0.03 | -0.20, 0.13 | -0.38 |
| **≥ 40 years** | -0.04[c] | -0.08, 0.01 | -1.67 | -0.15 | -0.38, 0.09 | -1.24 |
| **Baseline Visuospatial Scores** | 0.23[a] | 0.21, 0.26 | 17.93 | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Baseline Orientation Socres** | | | | 0.55[a] | 0.53, 0.57 | 44.86 |
| **Urban[e]** | 0.06[a] | 0.04, 0.09 | 5.27 | 0.38[a] | 0.25, 0.51 | 5.72 |
| **Education[f]** | | | | | | |
| **Primary** | 0.23[a] | 0.20, 0.26 | 14.00 | 1.11[a] | 0.94, 1.27 | 12.91 |
| **Secondary or Above** | 0.29[a] | 0.26, 0.32 | 18.51 | 1.18[a] | 1.01, 1.36 | 13.44 |
| **Hypertension[g]** | | | | | | |
| **With Treatment** | -0.03 | -0.09, 0.02 | -1.20 | 0.06 | -0.24, 0.35 | -0.38 |
| **Without Treatment** | -0.02 | -0.06, 0.03 | -0.69 | 0.06 | -0.11, 0.24 | 0.04 |
| **Missing Group** | -0.05[c] | -0.12, 0.01 | -1.67 | 0.06 | -0.19, 0.30 | -0.01 |
| **Diabetes[h]** | | | | | | |
| **With Treatment** | 0.02 | -0.03, 0.07 | 0.90 | 0.25[c] | -0.03, 0.52 | -1.77 |
| **Without Treatment** | 0.03 | -0.04, 0.09 | 0.82 | 0.21 | -0.06, 0.48 | -0.23 |
| **Missing Group** | 0.07 | -0.08, 0.21 | 0.88 | 0.50 | -0.22, 1.23 | 0.67 |
| **Baseline CES-D Score** | -0.00[c] | -0.00, 0.00 | -1.71 | -0.02[b] | -0.03, -0.00 | -2.57 |
| **year = 2** | -0.02 | -0.04, 0.01 | -1.58 | 0.09 | -0.05, 0.22 | 1.29 |

Abbreviations: CI, confidence interval; SHS, secondhand smoke.

a. p<0.01

b. p<0.05

c. p<0.1

d. Referent: No SHS exposure or Less than 25 years.

e. Expenditure is expressed as the natural log of the annual household expenditure

f. Referent: Illiterate

g. Referent: Without hypertension

h. Referent: Without diabetes

Table3.Multivariable linear regression analysis of the relationship between smoking exposure and Episodic memory and Overall cognitive function among older Chinese women (N = 6875), 2011-2013-2015

| | Episodic Memory | | | Overall Cognition Socres | | |
|---|---|---|---|---|---|---|
| VARIABLES | β coefficient | 95%CI | t | β coefficient | 95%CI | t |
| **Age** | -0.04[a] | -0.05,-0.03 | -11.37 | -0.06[a] | -0.07, -0.04 | -7.87 |
| **Expenditure** | 0.00 | 0.00, 0.00 | 1.30 | 0.00[a] | 0.00, 0.00 | 0.32 |
| **Secondhand Smoke Exposure[d]** | | | | | | |
| **25 to <30 years** | -0.04 | -0.16, 0.08 | -0.67 | -0.01 | -0.25, 0.25 | -0.01 |
| **≥30 to <40 years** | 0.02 | -0.09, 0.13 | 0.36 | -0.05 | -0.29, 0.19 | -0.41 |
| **≥ 40 years** | -0.16[b] | -0.31, -0.01 | -2.06 | -0.33[a] | -0.66, 0.01 | -1.93 |
| **Baseline Memory Scores** | 0.30[a] | 0.28, 0.32 | 25.22 | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Baseline Cognition Scores** | | | | 0.55[a] | 0.46, 0.83 | 44.95 |
| **Urban[e]** | 0.25[a] | 0.16, 0.34 | 5.60 | 0.65[a] | 0.46, 0.83 | 6.68 |
| **Education[f]** | | | | | | |
| **Primary** | 0.70[a] | 0.58, 0.80 | 12.42 | 1.77[a] | 1.53, 2.02 | 14.28 |
| **Secondary or Above** | 0.97[a] | 0.86, 1.08 | 17.29 | 2.00[a] | 1.74, 2.26 | 15.24 |
| **Hypertension[g]** | | | | | | |
| **With Treatment** | 0.04 | -0.16, 0.23 | 0.35 | 0.13 | -0.29, 0.56 | 0.62 |
| **Without Treatment** | 0.06 | -0.06, 0.17 | 0.95 | 0.12 | -0.14, 0.38 | 0.93 |
| **Missing Group** | 0.07 | -0.12, 0.25 | 0.70 | 0.10 | -0.27, 0.47 | 0.52 |
| **Diabetes[h]** | | | | | | |
| **With Treatment** | -0.20[b] | -0.38, 0.02 | -2.20 | -0.04 | -0.43, 0.36 | 0.62 |
| **Without Treatment** | -0.07 | -0.25, 0.11 | -0.77 | 0.08 | -0.30, 0.47 | 0.43 |
| **Missing Group** | 0.32 | -0.16, 0.80 | 1.30 | 0.87 | -0.11, 1.84 | 1.75 |
| **Baseline CES-D Score** | -0.01[b] | -0.01, 0.00 | -1.59 | -0.01 | -0.03, 0.00 | -2.57 |
| **year = 2** | -0.24 | -0.33, -0.15 | -5.21 | -0.17 | -0.37, 0.03 | -1.70 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Constant** | 0.63 | 0.53, 0.74 | 11.54 | 6.48[a] | 5.59, 7.37 | 14.28 |

Abbreviations: CI, confidence interval; SHS, secondhand smoke.

a. p<0.01

b. p<0.05

c. p<0.1

d. Referent: No SHS exposure or Less than 25 years.

e. Expenditure is expressed as the natural log of the annual household expenditure

f. Referent: Illiterate

g. Referent: Without hypertension

h. Referent: Without diabetes

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

| | Item No | Recommendation | Page No |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract<br>(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 1-3 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 4 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 5 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 6 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>(*b*) For matched studies, give matching criteria and number of exposed and unexposed | 6 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 7-9 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 7-9 |
| Bias | 9 | Describe any efforts to address potential sources of bias | 9 |
| Study size | 10 | Explain how the study size was arrived at | 6 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 7-9 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding<br>(*b*) Describe any methods used to examine subgroups and interactions<br>(*c*) Explain how missing data were addressed<br>(*d*) If applicable, explain how loss to follow-up was addressed<br>(*e*) Describe any sensitivity analyses | 9-10 |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed<br>(b) Give reasons for non-participation at each stage<br>(c) Consider use of a flow diagram | 6 |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders<br>(b) Indicate number of participants with missing data for each variable of interest<br>(c) Summarise follow-up time (eg, average and total amount) | 10-11 |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time | 11 |

| | | | |
|---|---|---|---|
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included<br>(*b*) Report category boundaries when continuous variables were categorized<br>(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | 11 |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 11-12 |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 12 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 15-16 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 13-15 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 12 |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 17 |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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# Exposure to Secondhand Smoke and Cognitive Function Among Middle-aged and Older Women in China: Findings of 3-waves of the China Health and Retirement Longitudinal Study

| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2020-039824.R2 |
| Article Type: | Original research |
| Date Submitted by the Author: | 13-Sep-2020 |
| Complete List of Authors: | Bai, Anying; Peking University Health Science Centre, School of Public Health;<br>Jin, Yinzi; Peking University, School of Public Health<br>Huang, Yangmu; Peking University Health Science Centre, School of Public Health; |
| Primary Subject Heading: | Epidemiology |
| Secondary Subject Heading: | Smoking and tobacco, Public health, Mental health |
| Keywords: | EPIDEMIOLOGY, Dementia < NEUROLOGY, PUBLIC HEALTH |
| | |

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**Title**

# Exposure to Secondhand Smoke and Cognitive Function Among Middle-aged and Older Women in China: Findings of 3-waves of the China Health and Retirement Longitudinal Study

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**Abstract**

**Objectives:** To examine the association between secondhand smoke and women's global cognitive function and cognitive subdomains.

**Design:** Cohort study

**Participants:** Data for this study were obtained from the China Health and Retirement Longitudinal Study (CHARLS, 2011-2013-2015), and pooled analysis was applied to wave 1 and wave 2 (2011-2013), wave 2 and wave 3 (2013-2015) and wave 1 and wave 3 (2011-2015). 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.

**Main outcome measures and methods:** Secondhand smoke was classified based on the length of exposed years (<25years, ≥25 to <30 years, ≥30 to <40 years, ≥40 years). Global cognitive function, visuospatial ability, orientation and attention, as well as episodic memory function were used as measures of cognitive function. Three waves of data were pooled by using dummy variable

to differentiate between 2-year and 4-year. Lagged dependent variable models were used to examine independent associations between secondhand smoke and cognitive function. Demographic factors, socioeconomic factors, baseline cognitive functioning and health conditions were controlled in our models.

**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.

**Key words:** ageing; passive smoking; panel analysis;

visuospatial ability; memory

**Strengths and limitations of this study:**

- This is the first study to investigate on the association between secondhand smoke exposure and women's different domains of cognitive functions in China by using a 4-year longitudinal national representative data.
- This study addressed the issue of reverse causation in observational cohort studies by used lagged dependent variable models and adjust for baseline cognition scores
- The exposure to secondhand smoke was evaluated based on self-report measures.
- The analyses only contained household SHS exposure and excluding environmental exposure.

**Word Count: 3295**

**Number of references:32**

**Number of data elements:1**

## Introduction

China's population has been ageing rapidly. By 2050, there will be 400 million Chinese citizens aged over 65 years old, and 150 million of whom will be older than 80

years old[1]. It will become increasingly important to understand the cognitive changes that accompany ageing[2]. Cognitive impairment, described as a decline in intellectual functions[3], ranges from mild forms of forgetfulness to severe and debilitating dementia [4]. The prevalence of cognitive impairment is rising, with national figures estimating that over 9.4% of older persons in China had cognitive impairment in 2011 [4].

Numerous determinants such as environmental, individual, and genetic factors could favor evolution toward cognitive impairment, and both age and late-life hypertension increase the risk of dementia over time [5]. The mechanism lies in age-related functional and structural changes in cerebrovascular small and large blood vessels [6]. Besides chronic diseases factors, depression has long been known to affect memory and other neurocognitive domains. Previous studies have emphasized that depression could increase the risk of developing mild cognitive impairment (MCI) in cognitively normal elderly people[7] .

Exposure to secondhand smoke (SHS), also known as "passive smoking," refers to a situation where a never-smoker inhales another person's smoke either by exposure

to sidestream smoke or mainstream smoke [8]. Current smoking prevalence in China decreased from 31.1% in 2002 to 28.1% in 2010; however, the number of adults exposed to SHS during this period still increased from 540 million to 556 million [2]. The negative health effects of high levels of exposure to SHS may be close to those of active smoking, including inferior performance on measures of general intelligence, visuospatial learning and memory and fine motor dexterity[9] .· Given the association between exposure to SHS and risk factors for cognitive impairment such as cardiovascular disease[10] , hypertension[11], and stroke [12], it is possible that high level of exposure may be a preventable risk factor for cognitive impairment or dementia [11, 13].

There are some evidence to suggest that older current smokers (ages ≥63) [14] or those being exposed to SHS (aged 55-64) [13-16] were more likely to develop cognitive impairment compared with never-smokers. However, much less is known about whether and to what extent SHS is associated with global and subdomains of cognitive function among elder women in China. Previous studies in China indicated that SHS exposure increased the risk of cognitive impairment in older adults[17, 18]. Nevertheless, both of

these studies only used a 2-wave longitudinal data and did not control for baseline cognition[17, 18]. Therefore, the primary aim of this study was to investigate the relationship between SHS and cognitive function among older non-smoking Chinese women, using a 3-wave longitudinal national representative data. Through the classification of respondents by different years of SHS exposure in a 4-year panel, we identified whether certain high SHS exposure groups were at higher risk of cognitive decline than others after controlling for confounders. Besides, we aimed to examine the association between SHS exposure and cognitive subdomains. This is especially important given the escalating ageing trend and increasing prevalence of SHS exposure in China.

## Methods

### Data

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. 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. The national baseline survey was conducted between June 2011 and March 2012 and 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. CHARLS respondents were followed every 2 years, using a face-to-face computer-assisted personal interview (CAPI) [14]. At baseline, there were 3381 married women who never smoked cigarettes and lived with spouses who had either smoked cigarettes in the past or smoked at the time of interview. Besides, all the data for each variable have been collected for those respondents. Our final sample was composed of 6875 respondents. Among them, 2802 were interviewed again during the second wave of data collection in 2013, and 2247 were interviewed again during the third wave in 2015. The similar sample selection process was conducted for participants in the second wave in 2013 as a baseline. The final sample consisted of 1799 women who were investigated again in 2015 as participants.

**Measures**

***Secondhand Smoke***

In this study, the exposure to SHS among Chinese women was assessed through several surveys based on standardized CHARLS questionnaire. Questions about the participant's current marital status, the exact year they got married, and the year the husband in each household has begun or ceased smoking at home were asked.

The smoking status section contained four questions: "Have you ever chewed tobacco, smoked a pipe, smoked self-rolled cigarettes, or smoked cigarettes/cigars?", "Do you still have the habit or have you totally quit?", "At what age did you totally quit smoking?" and "At what age did you start to smoke on a regular basis?". If the answer to the first question was "yes", they were defined as "current smokers". Our analysis of SHS exposure focused only on never smokers excluding the "current smokers", because of the difficulty to differentiate the negative effects of active smoking on health condition from that of SHS exposure. The length of SHS exposure was calculated and expressed as the total number of years that never-smoking women spent living with their spouses who smoked cigarettes at home.

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. Based on the constructed SHS exposure variable, the participants were classified into four different groups: Never or being exposed to SHS for less than 25 years, more than 25 years and less than 30 years, more than 30 years and less than 40 years and over 40 years.

***Cognitive function***

The cognitive function of the respondents in CHARLS questionnaires was measured through a question-and-answer interview instrument, and the respondents were followed every two years using a face-to-face, computer-aided personal interview (CAPI). These various sections of the questionnaire could assess cognitive subdomains including visuospatial ability, orientation and attention, and episodic memory. Figure drawing was tested by asking the participants to reproduce a picture of two overlapped pentagons in CHARLS questionnaires[18]. It 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. In order to assess orientation and attention function, the number of correct answers to the 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 [19].

In addition, the word recall test was consisted of 2 components, immediate recall and delayed recall, and evaluated episodic memory. Participants were required to repeat 10 Chinese nouns just read to them immediately, 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) [19].

The overall cognition scores were the sum of the three different domains (range 0 to 21).

***Control variables***

Given that cognitive function may vary across demographic and socioeconomic status, we thus included age,

urban/rural residence, education, annual household expenditures, chronic diseases and depressive symptoms as control variables. Education was categorized into 3 groups: "illiterate", "primary education" and "secondary education or above". Arterial hypertension and diabetes mellitus are separately strong independent risk factors for the development of cognitive impairment and dementia[20] [21]. 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. The measure of depressive symptoms was based on the 10-item version of the CES-D short form, and each of the 4-option response to the item was scored ranging from 0 to 3. The total score is the sum of points for all 10 items, and a score of 10 or higher suggests the presence of depressive symptoms [6].

***Patient and Public Involvement***

No patient involved.

**Analysis**

All analyses were conducted with STATA, version 14.0 (Stata, College Station, TX, USA). The lagged dependent-variable regression models with ordinary least squares estimation were used during analysis. LDV models were 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[22]. It adjusted for baseline cognitive conditions for all participants, therefore provided more robust estimates of the effects of independent variables. After pooling the three sets of panel data into one through using the "year" dummy variable to differentiate between a change in 2 years or in 4 years, we have 6875 respondents who have complete data on all variables. The overall cognitive scores, episodic memory scores, visuospatial ability scores and orientation and attention scores were 4 separate outcome variables. The different groups of SHS exposure years were the predictor variable, and other independent variables included all demographic and socioeconomic characteristics. Prior to fitting the regression models, descriptive analyses were conducted to estimate the mean and standard deviations for continuous data and frequencies and percentages for

categorical data.

## Results

Table 1 provides a descriptive summary of all the variables for participants from each panel of three different waves: 2011-2013, 2011-2015 and 2013-2015. High prevalence of SHS exposure between 30 to 40 years was seen in different panels, accounting for 32.51%, 35.18% and 42.69% respectively.

The participants were over 45 years old, with the mean age of 56, 56 and 58 years old, respectively in those waves. Participants were more likely to live in a rural area, have a lower education background and do not have hypertension or diabetes diagnoses at baseline. In addition, our results indicated that the mean baseline cognition scores were higher than cognition scores after 2 or 4 years. The mean scores of CES-D suggested that the prevalence of depression among Chinese middle-aged and old-aged women was increased in those years. Other socio-demographic characteristics of the respondents are shown in Table 1

Results from the regression models for the relationship between SHS exposure and each domain of the cognitive function and overall cognition scores are

reported in Table 2 and Table 3. 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 adjusted for age, annual household expenditure, education, baseline cognitive function and another chronic health status, we found that only being exposed to SHS for more than 40 years was significantly associated with 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 been exposed to SHS for more than 40 years was associated with a 0.04-point decline in visuospatial abilities (95%CI, -0.08 to -0.01 P <0.1), a 0.16-point decline in episodic memory (95%CI, -0.31 to -0.01 P <0.05), and a 0.33-point decline in overall cognition function (95%CI, -0.66 to -0.01 P <0.01). In addition, age was also negatively associated with cognitive function. 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. High education level was associated with better cognitive performance, especially in orientation and attention. In addition, a one-point increase in CESD scores was associated with 0.02-point decrease in scores of orientation and attention (95%CI, -0.03 to 0.00 P <0.05), showing that respondents with depressive symptoms were more likely to demonstrate a cognitive decline in specific functions.

## Discussion

Results from this longitudinal study with a large, representative sample of middle-aged and older women in China indicated that exposure to SHS for over 40 years was significantly associated with the more unsatisfactory performance of global cognition and cognitive subdomains. It is the first examination of cognitive subdomains concerning household SHS exposure using a 4-year longitudinal data in China. The inferior performance of SHS on visuospatial abilities, episodic memory and orientation and attention abilities are novel. Because these domains

were not specifically evaluated in earlier studies among middle-aged and older women who never smoke. In addition to the previous findings that SHS was associated with poor cognitive performance, especially in children, adolescents and adults [18]. We found that having a high educational level, living in an urban area and having better baseline cognitive function would improve their cognitive performance. The episodic memory score of participants with diabetes at baseline decreased by 0.172 points compared with those without diabetes, which is similar to previous findings[9].

Moreover, our results showed that compared with women who have never been exposed to SHS or have been exposed for less than 20 years, those who have been exposed to SHS for more than 40 years have a significant decline in visuospatial function (0.04-point), episodic memory (0,16-point) and overall cognitive scores (0.33-point). These findings were quite similar in magnitude to prior research on the relationship between SHS and cognitive function [14]. Moheet and colleagues (2015) conducted a cross-sectional study in the North East of England to explore the impact of diabetes on cognitive function and brain structure

(N=150). Research suggested that compared with non-exposed people, participants who had no history of smoking and being averagely exposed to SHS for around 6 years showed significantly reduced performance in processing speed (i.e. how quickly one can process information and perform tasks) and executive function (i.e. the ability to organize memory, cognitive flexibility, and problem-solving ability)[22]. Another longitudinal ageing study in China (N=4809, ages ≥50) found that never smokers exposed to the highest levels of SHS (salivary cotinine concentrations 0.8-13.5 ng/ml) were more likely to be cognitively impaired (odds ratio =1.70) than those exposed to little or no SHS[18].

Attention referred to the ability to concentrate and focus on specific stimuli slightly declined in later life [13]. Orientation was one's ability to identify the exact date, month, day and season of the year[23]. 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. SHS seems to be more strongly associated with cognitive decline than ageing, since the magnitude of signitificant coefficient between

SHS and cognitive decline was almost four times the one in ageing. However, the relationship between SHS and orientation and attention ability was not observed. This may due to the size of the sample is relatively small, plus the period of cohort study after controlling for all demographic and socioeconomic confounders is relatively short.

Visuospatial abilities involve the ability to understand space in two and three dimensions. In our study, an inversed relationship between SHS exposure and visuospatial abilities among middle-aged and older adults was presented, showing a 0.04-point decline in their visuospatial scores. Such an inversed relationship between SHS exposure and visuospatial reasoning skills was also reported among American children (N=5683; ages 6–16), showing that years of SHS exposure was significantly associated with lower scores for reading, math, and visuospatial skills, after adjusting for covariates [15]. As one of the most common cognitive complaints among elders, episodic memory refers to personally experienced events which could be measured by stories, word lists or figures. 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.

The inconsistent conclusions between our studies and prior ones may probably due to the relatively simplified version of the cognition test procedure in CHARLS questionnaires compared with the MoCA [14] and MMSE [25]. Some studies also used clinical or magnetic resonance imaging (MRI) evidence of neurologic damage to detect cognitive impairment. Best adapted to a screening test, the MoCA exhibited excellent sensitivity in identifying MCI and AD (Alzheimer's disease) by 90% and 100%, respectively [26].

The most popular hypothesis about the mechanisms underlying the links between SHS exposure and more unsatisfactory cognitive performance lies in the notion that the carbon monoxide (CO) in tobacco smoke may interfere with the oxygen being delivered to the brain via the blood system. However, the reasons behind the different effect on various domains of brain function are far from clear. One possible explanation derives from

research on laboratory animals. Exposing animals to varying degrees of toxic mixtures of chemicals found in tobacco smoke may lead to reduced neuronal mass in specific regions of the brain associated with learning and memory. Since the hippocampal region of the brain is known to be involved in the mediation of memory [27] and learning, further research should be conducted in other regions dominating visuospatial and orientation ability. Another possible mechanism is that prolonged exposure to SHS may be a significant risk factor for cardiovascular disease (CVD)[28], which may therefore lead to a range of health and cognitive problems in later life. In the future, a longitudinal design may elucidate any associations by observing long-term exposure to SHS and the incidence of CVD, and whether this CVD may mediate or interact with SHS exposure to impact cognitive function.

Several limitations need to be considered when interpreting this study and designing future studies. Firstly, exposure to SHS was evaluated based on self-report measures. This might be subject to recall bias and lead to over-or-underestimation of exposure [29]. Therefore, further studies could include more biological assays, for example, cotinine

residue levels or nicotine residue in saliva or hair samples [30]. Previous research using serum cotinine as a biomarker of exposure to SHS found that higher levels of serum cotinine were associated with significantly worse performance in reading, mathematics, and visual and spatial abilities in children and adolescents [8]. However, no studies had used a combination of biomarker and self-report yet [31]. Some validated biomarkers could be used as proxies for AD neuropathological changes, such as cerebrospinal fluid (CSF) amyloid-beta (Aβ)42 concentrations or Aβ42/ Aβ40 ratio and amyloid load on positron emission tomography (PET) scans. These biomarkers could provide more reliable measures of cognitive impairment[32]. Secondly, it may be impossible to control for all potentially confounding variables. After adjusting for age, household expenditure, education, area, chronic health condition and depressive symptoms, some other demographic or socioeconomic confounders may be neglected. However, this did not appear to affect the magnitude of the association between SHS exposure and cognition [14]. Besides, the analyses only contained household SHS exposure, which precluded the analyses of the influence of environment smoke inhale on

smoking proclivity. Whether exposure to household SHS can hasten the onset of cognitive impairment for older Chinese women could be further proved by running regression models in different age groups.

**Acknowledgments :**

We would like to thank the professor Yaohui Zhao at Centre for Chinese Economic Research, Peking University for her thoughtful contributions to this study.

**Conflict of Interest**

The authors have no conflicts of interest to declare.

**Author's Contribution**

Anying Bai wrote and participated in all aspects of this research, including the field investigation. Dr Yangmu Huang reviewed and supervised this research. Yinzi Jin participated in the statistical analysis of this work and reviewed the final article.

**Data sharing statement**

CHARLS data is available to the public online: http://charls.pku.edu.cn

**Funding Resources**

This is a self-funded research.

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Table1.Characteristics of the Participants from 3 waves of CHARLS, 2011-2013-2015

| | 2011-2013 (N=2802) | | 2011-2015 (N=2274) | | 2013-2015 (N=1799) | |
|---|---|---|---|---|---|---|
| **Variable** | Count | Frequency | Count | Frequency | Count | Frequency |
| **Area** | | | | | | |
| Urban | 981 | 35.01% | 730 | 32.10% | 556 | 30.91% |
| Rural | 1821 | 64.99% | 1544 | 67.90% | 1243 | 69.09% |
| **SHS** | | | | | | |
| Less than 25 years | 759 | 27.09% | 531 | 23.35% | 262 | 14.56% |
| More than 25 years and less than 30 years | 634 | 22.63% | 573 | 25.20% | 385 | 21.40% |
| More than 30 years and less than 40 years | 911 | 32.51% | 800 | 35.18% | 768 | 42.69% |
| More than 40 years | 498 | 17.77% | 370 | 16.27% | 384 | 21.35% |
| **Education** | | | | | | |
| Illiterate | 1552 | 55.39% | 1309 | 57.56% | 1004 | 55.81% |
| Primary education | 512 | 18.27% | 414 | 18.21% | 336 | 18.68% |
| Secondary or above | 738 | 26.34% | 551 | 24.23% | 459 | 25.51% |
| **Hypertension** | | | | | | |
| No hypertension | 2124 | 75.80% | 1720 | 75.64% | 1365 | 75.88% |
| Hypertension with treatment | 522 | 18.63% | 1720 | 75.64% | 358 | 19.90% |
| Hypertension without treatment | 156 | 5.57% | 130 | 5.72% | 76 | 4.22% |
| **Diabetes** | | | | | | |
| No Diabetes in baseline | 2643 | 94.33% | 2140 | 94.11% | 1704 | 94.72% |

| | | | | | | |
|---|---|---|---|---|---|---|
| Have Diabetes with treatment | 143 | 5.10% | 120 | 5.28% | 86 | 4.78% |
| Have Diabetes without treatment | 16 | 0.57% | 14 | 0.62% | 9 | 0.50% |
| | Count | Mean(SD) | Count | Mean(SD) | Count | Mean(SD) |
| Age | 2802 | 55.84(8.22) | 2274 | 56.19(7.75) | 1799 | 57.90(7.43) |
| Annual Household Expenditure, yuan[a] | 2802 | 13786.99(14197.29) | 2274 | 13060.14(13639.33) | 1799 | 16632.84(18568.24) |
| Visuospatial ability[b] | 2802 | 0.51(0.50) | 2274 | 0.48(0.50) | 1799 | 0.49(0.50) |
| Orientation and attention[c] | 2802 | 5.87(3.29) | 2274 | 5.84(3.19) | 1799 | 5.97(3.14) |
| Memory Scores[d] | 2802 | 3.33(1.96) | 2274 | 3.04(1.93) | 1799 | 3.15(1.91) |
| Baseline Visuospatial ability | 2802 | 0.57(0.50) | 2274 | 0.55(0.50) | 1799 | 0.54(0.50) |
| Baseline Orientation and attention | 2802 | 6.39(2.92) | 2274 | 6.25(2.90) | 1799 | 6.16(3.00) |
| Baseline Memory Scores | 2802 | 3.27(1.98) | 2274 | 3.23(1.92) | 1799 | 3.50(1.78) |
| Baseline CES-D Score[e] | 2802 | 12.09(5.38) | 2274 | 12.13(5.45) | 1799 | 10.90(5.14) |

Abbreviation: SHS, secondhand smoke.

a 1 US dollar = 6.3 yuan.

b The score range for visuospatial ability was 0–1.

c The score range for orientation and attention was 0–10. Higher scores indicate better mental status.

d The score range for episodic memory was 0–10. Higher scores indicate better memory function.

e A score of 10 or greater indicated the presence of depressive symptoms.

Table2.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

| | Visuospatial Function | | | Orientation and Attention | | |
|---|---|---|---|---|---|---|
| VARIABLES | β coefficient | 95%CI | t | β coefficient | 95%CI | t |
| **Age** | -0.01[a] | -0.01,-0.00 | -6.73 | -0.02[a] | -0.03, -0.01 | -4.34 |
| **Expenditure** | 0.00 | 0.00, 0.00 | 0.01 | 0.00[a] | 0.00, 0.00 | 0.77 |
| **SHS Exposure[d]** | | | | | | |
| **25 to <30 years** | -0.01 | -0.04, 0.02 | -0.72 | 0.05 | -0.12, 0.21 | 0.56 |
| **≥30 to <40 years** | -0.02 | -0.05, 0.02 | -0.95 | -0.03 | -0.20, 0.13 | -0.38 |
| **≥ 40 years** | -0.04[c] | -0.08, 0.01 | -1.67 | -0.15 | -0.38, 0.09 | -1.24 |
| **Baseline Visuospatial Function** | 0.23[a] | 0.21, 0.26 | 17.93 | | | |
| **Baseline Orientation and Attention** | | | | 0.55[a] | 0.53, 0.57 | 44.86 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Urban**[e] | 0.06[a] | 0.04, 0.09 | 5.27 | 0.38[a] | 0.25, 0.51 | 5.72 |
| **Education**[f] | | | | | | |
| **Primary** | 0.23[a] | 0.20, 0.26 | 14.00 | 1.11[a] | 0.94, 1.27 | 12.91 |
| **Secondary or Above** | 0.29[a] | 0.26, 0.32 | 18.51 | 1.18[a] | 1.01, 1.36 | 13.44 |
| **Hypertension**[g] | | | | | | |
| **With Treatment** | -0.03 | -0.09, 0.02 | -1.20 | 0.06 | -0.24, 0.35 | -0.38 |
| **Without Treatment** | -0.02 | -0.06, 0.03 | -0.69 | 0.06 | -0.11, 0.24 | 0.04 |
| **Missing Group** | -0.05[c] | -0.12, 0.01 | -1.67 | 0.06 | -0.19, 0.30 | -0.01 |
| **Diabetes**[h] | | | | | | |
| **With Treatment** | 0.02 | -0.03, 0.07 | 0.90 | 0.25[c] | -0.03, 0.52 | -1.77 |
| **Without Treatment** | 0.03 | -0.04, 0.09 | 0.82 | 0.21 | -0.06, 0.48 | -0.23 |
| **Missing Group** | 0.07 | -0.08, 0.21 | 0.88 | 0.50 | -0.22, 1.23 | 0.67 |
| **Baseline CES-D Score** | -0.00[c] | -0.00, 0.00 | -1.71 | -0.02[b] | -0.03, -0.00 | -2.57 |
| **year = 2** | -0.02 | -0.04, 0.01 | -1.58 | 0.09 | -0.05, 0.22 | 1.29 |

Abbreviations: CI, confidence interval; SHS, secondhand smoke.

a. p<0.01

b. p<0.05

c. p<0.1

d. Referent: No SHS exposure or Less than 25 years.

e. Expenditure is expressed as the natural log of the annual household expenditure

f. Referent: Illiterate

g. Referent: Without hypertension

h. Referent: Without diabetes

I. This model adjusted for age, expenditure, living area, education, baseline hypertension, diabetes, depression status and baseline cognitive function.

Table3. Adjusted Multivariable linear regression analysis of the relationship between smoking exposure and Episodic memory and Overall cognitive function among older Chinese women (N = 6875), 2011-2013-2015

| | Episodic Memory | | | Overall Cognition | | |
|---|---|---|---|---|---|---|
| VARIABLES | β coefficient | 95%CI | t | β coefficient | 95%CI | t |
| **Age** | -0.04[a] | -0.05,-0.03 | -11.37 | -0.06[a] | -0.07, -0.04 | -7.87 |
| **Expenditure** | 0.00 | 0.00, 0.00 | 1.30 | 0.00[a] | 0.00, 0.00 | 0.32 |
| **SHS Exposure[d]** | | | | | | |
| **25 to <30 years** | -0.04 | -0.16, 0.08 | -0.67 | -0.01 | -0.25, 0.25 | -0.01 |
| **≥30 to <40 years** | 0.02 | -0.09, 0.13 | 0.36 | -0.05 | -0.29, 0.19 | -0.41 |
| **≥ 40 years** | -0.16[b] | -0.31, -0.01 | -2.06 | -0.33[a] | -0.66, 0.01 | -1.93 |
| **Baseline Episodic Memory** | 0.30[a] | 0.28, 0.32 | 25.22 | | | |
| **Baseline Overall Cognition** | | | | 0.55[a] | 0.46, 0.83 | 44.95 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Urban**[e] | 0.25[a] | 0.16, 0.34 | 5.60 | 0.65[a] | 0.46, 0.83 | 6.68 |
| **Education**[f] | | | | | | |
| **Primary** | 0.70[a] | 0.58, 0.80 | 12.42 | 1.77[a] | 1.53, 2.02 | 14.28 |
| **Secondary or Above** | 0.97[a] | 0.86, 1.08 | 17.29 | 2.00[a] | 1.74, 2.26 | 15.24 |
| **Hypertension**[g] | | | | | | |
| **With Treatment** | 0.04 | -0.16, 0.23 | 0.35 | 0.13 | -0.29, 0.56 | 0.62 |
| **Without Treatment** | 0.06 | -0.06, 0.17 | 0.95 | 0.12 | -0.14, 0.38 | 0.93 |
| **Missing Group** | 0.07 | -0.12, 0.25 | 0.70 | 0.10 | -0.27, 0.47 | 0.52 |
| **Diabetes**[h] | | | | | | |
| **With Treatment** | -0.20[b] | -0.38, 0.02 | -2.20 | -0.04 | -0.43, 0.36 | 0.62 |
| **Without Treatment** | -0.07 | -0.25, 0.11 | -0.77 | 0.08 | -0.30, 0.47 | 0.43 |
| **Missing Group** | 0.32 | -0.16, 0.80 | 1.30 | 0.87 | -0.11, 1.84 | 1.75 |
| **Baseline CES-D Score** | -0.01[b] | -0.01, 0.00 | -1.59 | -0.01 | -0.03, 0.00 | -2.57 |
| **year = 2** | -0.24 | -0.33, -0.15 | -5.21 | -0.17 | -0.37, 0.03 | -1.70 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Constant** | 0.63 | 0.53, 0.74 | 11.54 | 6.48[a] | 5.59, 7.37 | 14.28 |

Abbreviations: CI, confidence interval; SHS, secondhand smoke.

a. p<0.01

b. p<0.05

c. p<0.1

d. Referent: No SHS exposure or Less than 25 years.

e. Expenditure is expressed as the natural log of the annual household expenditure

f. Referent: Illiterate

g. Referent: Without hypertension

h. Referent: Without diabetes

I. This model adjusted for age, expenditure, living area, education, baseline hypertension, diabetes, depression status and baseline cognitive function.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

| | Item No | Recommendation | Page No |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract<br>(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 1-3 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 4 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 5 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 6 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>(*b*) For matched studies, give matching criteria and number of exposed and unexposed | 6 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 7-9 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 7-9 |
| Bias | 9 | Describe any efforts to address potential sources of bias | 9 |
| Study size | 10 | Explain how the study size was arrived at | 6 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 7-9 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding<br>(*b*) Describe any methods used to examine subgroups and interactions<br>(*c*) Explain how missing data were addressed<br>(*d*) If applicable, explain how loss to follow-up was addressed<br>(*e*) Describe any sensitivity analyses | 9-10 |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed<br>(b) Give reasons for non-participation at each stage<br>(c) Consider use of a flow diagram | 6 |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders<br>(b) Indicate number of participants with missing data for each variable of interest<br>(c) Summarise follow-up time (eg, average and total amount) | 10-11 |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time | 11 |

| | | | |
|---|---|---|---|
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included<br>(*b*) Report category boundaries when continuous variables were categorized<br>(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | 11 |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 11-12 |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 12 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 15-16 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 13-15 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 12 |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 17 |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

# 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

| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2020-039824.R3 |
| Article Type: | Original research |
| Date Submitted by the Author: | 30-Sep-2020 |
| Complete List of Authors: | Bai, Anying; Peking University Health Science Centre, School of Public Health;<br>Jin, Yinzi; Peking University, School of Public Health<br>Huang, Yangmu; Peking University Health Science Centre, School of Public Health; |
| Primary Subject Heading: | Epidemiology |
| Secondary Subject Heading: | Smoking and tobacco, Public health, Mental health |
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**Title**

# 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

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**Abstract**

**Objectives:** To examine the association between secondhand smoke and women's global cognitive function and cognitive subdomains.

**Design:** Cohort study

**Participants:** Data for this study were obtained from the China Health and Retirement Longitudinal Study (CHARLS, 2011-2013-2015), and pooled analysis was applied to wave 1 and wave 2 (2011-2013), wave 2 and wave 3 (2013-2015) and wave 1 and wave 3 (2011-2015). Data from a total of 6875 Chinese women with normal cognitive function at baseline were selected for analysis, including 2981 who were interviewed in 2011, 2471 in 2013, and 1894 in 2015.

**Main outcome measures and methods:** Secondhand smoke (SHS) was classified based on the number of exposed years (<25years, ≥25 to <30 years, ≥30 to <40 years, ≥40 years). Global cognitive function, visuospatial ability, orientation and attention, as well as episodic memory function were used as measures of cognitive function.

Three waves of data were pooled by using a dummy variable to differentiate between 2-year and 4-year groups. Lagged dependent variable models were used to examine independent associations between secondhand smoke and cognitive function. Demographic factors, socioeconomic factors, baseline cognitive functioning and health conditions were controlled for in our models.

**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 a 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.

**Key words:** ageing; passive smoking; panel analysis; visuospatial ability; memory

**Strengths and limitations of this study:**

- This is the first study to investigate the association between secondhand smoke exposure and different domains of women's cognitive function in China by using 4-year of longitudinal national representative data.
- This study addressed the issue of reverse causation in observational cohort studies by used lagged dependent variable models and adjust for baseline cognition scores
- The exposure to secondhand smoke was evaluated based on self-reported measures.
- The analyses only contained household SHS exposure and excluded environmental exposure.

**Word Count: 3352**

**Number of references:32**

**Number of data elements:1**

## Introduction

China's population has been ageing rapidly. By 2050, there will be 400 million Chinese citizens aged over 65 years old, 150 million of whom will be older than 80 years

old[1]. It will become increasingly important to understand the cognitive changes that accompany ageing[2]. Cognitive impairment, described as a decline in intellectual function[3], ranges from mild forms of forgetfulness to severe and debilitating dementia [4]. The prevalence of cognitive impairment is rising, with national figures estimating that over 9.4% of older persons in China had cognitive impairment in 2011 [4].

Numerous determinants such as environmental, individual, and genetic factors could favor evolution toward cognitive impairment, and both age and late-life hypertension increase the risk of dementia over time [5]. The mechanism lies in age-related functional and structural changes in cerebrovascular small and large blood vessels [6]. Besides chronic diseases factors, depression has long been known to affect memory and other neurocognitive domains. Previous studies have emphasized that depression could increase the risk of developing mild cognitive impairment (MCI) in cognitively normal elderly people[7] .

Exposure to secondhand smoke (SHS), also known as "passive smoking," refers to a situation where a never-smoker inhales another person's smoke either by exposure

to sidestream smoke or mainstream smoke [8]. Current smoking prevalence in China has decreased from 31.1% in 2002 to 28.1% in 2010; however, the number of adults exposed to SHS during this period still increased from 540 million to 556 million due to population growth [2]. The negative health effects of high levels of exposure to SHS may be close to those of active smoking, including inferior performance on measures of general intelligence, visuospatial learning and memory and fine motor dexterity[9] .· Given the association between exposure to SHS and risk factors for cognitive impairment such as cardiovascular disease[10] , hypertension[11], and stroke [12], it is possible that a high level of exposure may be a preventable risk factor for cognitive impairment or dementia [11, 13].

There is some evidence to suggest that older current smokers (ages ≥63) [14] or those being exposed to SHS (aged 55-64) [13-16] were more likely to develop cognitive impairment compared with never-smokers. However, much less is known about whether and to what extent, SHS is associated with global and subdomains of cognitive function among elder women in China. Previous studies in China indicated that SHS exposure increased the risk of cognitive

impairment in older adults[17, 18]. Nevertheless, both of these studies only used 2-wave longitudinal data and did not control for baseline cognition[17, 18]. Therefore, the primary aim of this study was to investigate the relationship between SHS and cognitive function among older non-smoking Chinese women, using a 3-wave longitudinal national representative data. Through the classification of respondents by different years of SHS exposure in a 4-year panel, we identified whether certain high SHS exposure groups were at higher risk of cognitive decline than others after controlling for confounders. Besides, we aimed to examine the association between SHS exposure and cognitive subdomains. This is especially important given the growing and ageing population, and increasing prevalence of SHS exposure in China.

## Methods

### Data

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.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. The national baseline survey was conducted between June 2011 and March 2012 and 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. CHARLS respondents were followed every 2 years, using a face-to-face computer-assisted personal interview (CAPI) [14]. SHS mainly affects married women in China. Though unmarried or cohabiting women can possibly be affected by household SHS, this kind of influence remains scarce. At baseline, there were 3381 married women who never smoked cigarettes and lived with spouses who had either smoked cigarettes in the past or smoked at the time of interview. Data for each variable was therefore collected for those respondents. Our final sample was composed of 6875 respondents. Among them, 2802 were interviewed again during the second wave of data collection in 2013, and 2247 were interviewed again during the third wave in 2015. The similar sample selection process was

conducted for participants in the second wave in 2013 as a baseline. The final sample consisted of 1799 women who were investigated again in 2015 as participants.

## Measures

### *Secondhand Smoke*

In this study, the exposure to SHS among Chinese women was assessed through several surveys based on the standardized CHARLS questionnaire. Questions about the participant's current marital status, the year they got married, and the year the husband in each household has begun or ceased smoking at home were asked.

The smoking status section contained four questions: "Have you ever chewed tobacco, smoked a pipe, smoked self-rolled cigarettes, or smoked cigarettes/cigars?", "Do you still have the habit or have you totally quit?", "At what age did you totally quit smoking?" and "At what age did you start to smoke on a regular basis?". If the answer to the first question was "yes", they were defined as "current smokers" or "ex-smokers". Our analysis of SHS exposure focused only on never smokers excluding the "current smokers" and "ex-smokers", because of the difficulty to differentiate the negative effects of active smoking on

health condition from that of SHS exposure. The length of SHS exposure was calculated and expressed as the total number of years that never-smoking women spent living with their spouses who smoked cigarettes at home.

Categorical classification of SHS was used because the impact of SHS might be neglected if we only used a continuous variable to represent exposure. Similarly compared with continuous variables categorical variables have greater public health significance. Based on the constructed SHS exposure variable, participants were classified into four different groups: Never or being exposed to SHS for less than 25 years, more than 25 years and less than 30 years, more than 30 years and less than 40 years and over 40 years. The cut-off boundaries of SHS exposure were decided to realize the relatively balanced population distribution frequency among different levels of exposure year.

***Cognitive function***

The cognitive function of the respondents in CHARLS questionnaires was measured through a question-and-answer interview instrument, and the respondents were followed every two years using a face-to-face, computer-aided

personal interview (CAPI). The various sections of the questionnaire could assess cognitive subdomains including visuospatial ability, orientation and attention, and episodic memory. Figure drawing was tested by asking the participants to reproduce a picture of two overlapped pentagons in CHARLS questionnaires[18]. It 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. In order to assess orientation and attention function, the number of correct answers to the 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 [19].

In addition, the word recall test consisted of 2 components, immediate recall and delayed recall, and evaluated episodic memory. Participants were required to repeat 10 Chinese nouns just read to them, and then 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) [19].

The overall cognition scores were the sum of the three different domains (range 0 to 21).

***Control variables***

Given that cognitive function may vary across demographic and socioeconomic status, we thus included age, urban/rural residence, education, annual household expenditures, chronic diseases and depressive symptoms as control variables. Education was categorized into 3 groups: "illiterate", "primary education" and "secondary education or above". Arterial hypertension and diabetes mellitus are separately strong independent risk factors for the development of cognitive impairment and dementia[20] [21]. 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. The measure of depressive symptoms was based on the 10-item version of the CES-D

short form, and each of the 4-option response to the item was scored ranging from 0 to 3. The total score is the sum of points for all 10 items, and a score of 10 or higher suggests the presence of depressive symptoms [6].

***Patient and Public Involvement***

No patient involved.

**Analysis**

All analyses were conducted with STATA, version 14.0 (Stata, College Station, TX, USA). The lagged dependent-variable (LDV) regression models with ordinary least squares estimation were used during analysis. LDV models were 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[22]. It adjusted for baseline cognitive conditions for all participants, therefore provided more robust estimates of the effects of independent variables. After pooling the three sets of panel data into one through using the "year" dummy variable to differentiate between a change in 2 years or in 4 years, we have 6875 respondents who have complete data on all variables. The overall cognitive

scores, episodic memory scores, visuospatial ability scores and orientation and attention scores were 4 separate outcome variables. The different groups of SHS exposure years were the predictor variable, and other independent variables included all demographic and socioeconomic characteristics. Prior to fitting the regression models, descriptive analyses were conducted to estimate the mean and standard deviations for continuous data and frequencies and percentages for categorical data.

**Results**

Table 1 provides a descriptive summary of all the variables for participants from each panel of three different waves: 2011-2013, 2011-2015 and 2013-2015. High prevalence of SHS exposure between 30 to 40 years was seen in different panels, accounting for 32.51%, 35.18% and 42.69% respectively.

The participants were over 45 years old, with the mean age of 56, 56 and 58 years old, respectively in those waves. Participants were more likely to live in a rural area, have a lower education background and not to have hypertension or diabetes diagnoses at baseline. In addition, our results indicated that the mean baseline cognition scores were

higher than cognition scores after 2 or 4 years. The mean scores of CES-D suggested that the prevalence of depression among Chinese middle-aged and old-aged women increased in those years. Other socio-demographic characteristics of the respondents are shown in Table 1

Results from the regression models for the relationship between SHS exposure and each domain of the cognitive function and overall cognition scores are reported in Table 2 and Table 3. 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 adjusted for age, annual household expenditure, education, baseline cognitive function and another chronic health status, we found that only being exposed to SHS for more than 40 years was significantly associated with 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 been exposed to SHS for more than 40 years was associated with a 0.04-point decline in

visuospatial abilities (95%CI, -0.08 to -0.01 P <0.1), a 0.16-point decline in episodic memory (95%CI, -0.31 to -0.01 P <0.05), and a 0.33-point decline in overall cognition function (95%CI, -0.66 to -0.01 P <0.01). In addition, age was also negatively associated with cognitive function. 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. High education level was associated with better cognitive performance, especially in orientation and attention. In addition, a one-point increase in CESD scores was associated with 0.02-point decrease in scores of orientation and attention (95%CI, -0.03 to 0.00 P <0.05), showing that respondents with depressive symptoms were more likely to demonstrate a cognitive decline in specific functions.

**Discussion**

Results from this longitudinal study with a large, representative sample of middle-aged and older women in

China indicated that exposure to SHS for over 40 years was significantly associated with declining performance of global cognition and cognitive subdomains. It is the first examination of cognitive subdomains concerning household SHS exposure using a 4-year longitudinal data in China. The inferior performance of SHS on visuospatial abilities, episodic memory and orientation and attention abilities are novel because these domains were not specifically evaluated in earlier studies among middle-aged and older women who never smoke. This study builds on previous findings that SHS was associated with poor cognitive performance, especially in children, adolescents and adults [18]. We found that having a high educational level, living in an urban area and having better baseline cognitive function would improve their cognitive performance. The episodic memory score of participants with diabetes at baseline decreased by 0.172 points compared with those without diabetes, which is similar to previous findings[9].

Moreover, our results showed that compared with women who have never been exposed to SHS or have been exposed for less than 20 years, those who have been exposed to SHS for more than 40 years have a significant decline in

visuospatial function (0.04-point), episodic memory (0,16-point) and overall cognitive scores (0.33-point). These findings were similar in magnitude to prior research on the relationship between SHS and cognitive function [14]. Moheet and colleagues (2015) conducted a cross-sectional study in the North East of England to explore the impact of diabetes on cognitive function and brain structure (N=150). Research suggested that compared with non-exposed people, participants who had no history of smoking and being averagely exposed to SHS for around 6 years showed significantly reduced performance in processing speed (i.e. how quickly one can process information and perform tasks) and executive function (i.e. the ability to organize memory, cognitive flexibility, and problem-solving ability)[22]. Another longitudinal ageing study in China (N=4809, ages ≥50) found that never smokers exposed to the highest levels of SHS (salivary cotinine concentrations 0.8-13.5 ng/ml) were more likely to be cognitively impaired (odds ratio =1.70) than those exposed to little or no SHS[18].

Attention referred to the ability to concentrate and focus on specific stimuli slightly declined in later life [13]. Orientation was one's ability to identify the exact

date, month, day and season of the year[23]. 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. SHS seems to be more strongly associated with cognitive decline than ageing, since the magnitude of signitificant coefficient between SHS and cognitive decline was almost four times the one in ageing. However, the relationship between SHS and orientation and attention ability was not observed. This may since the size of the sample is relatively small, plus the period of cohort study after controlling for all demographic and socioeconomic confounders is relatively short.

Visuospatial abilities involve the ability to understand space in two and three dimensions. In our study, an inversed relationship between SHS exposure and visuospatial abilities among middle-aged and older adults was observed, showing a 0.04-point decline in their visuospatial scores. Such an inversed relationship between SHS exposure and visuospatial reasoning skills was also reported among American children (N=5683; ages 6–16), showing that years

of SHS exposure was significantly associated with lower scores for reading, math, and visuospatial skills, after adjusting for covariates [15]. As one of the most common cognitive complaints among elders, episodic memory refers to personally experienced events which could be measured by stories, word lists or figures. 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 may indicate memory decline associated with SHS exposure.

The inconsistent conclusions between our studies and prior ones may be due to the relatively simplified version of the cognition test procedure in CHARLS questionnaires compared with the Montreal Congnitive Assessment (MoCA) [14] and Mini-Mental State Examination (MMSE) [25]. Some studies also used clinical or magnetic resonance imaging (MRI) evidence of neurologic damage to detect cognitive impairment. The MoCA functions best as a screening test, having exhibited excellent sensitivity in identifying MCI and AD (Alzheimer's disease) at 90% and 100%, respectively

[26].

The most popular hypothesis about the mechanisms underlying the links between SHS exposure and more unsatisfactory cognitive performance lies in the notion that the carbon monoxide (CO) in tobacco smoke may interfere with the oxygen being delivered to the brain via the blood. However, the reasons behind the different effect on various domains of brain function are far from clear. One possible explanation derives from research on laboratory animals. Exposing animals to varying degrees of toxic mixtures of chemicals found in tobacco smoke may lead to reduced neuronal mass in specific regions of the brain associated with learning and memory. Since the hippocampal region of the brain is known to be involved in the mediation of memory [27] and learning, further research should be conducted in other regions dominating visuospatial and orientation ability. Another possible mechanism is that prolonged exposure to SHS may be a significant risk factor for cardiovascular disease (CVD) [28], which may therefore lead to a range of health and cognitive problems in later life. In the future, a longitudinal design may elucidate any associations by

observing long-term exposure to SHS and the incidence of CVD, and whether this CVD may mediate or interact with SHS exposure to impact cognitive function.

Several limitations need to be considered when interpreting this study and designing future studies. Firstly, exposure to SHS was evaluated based on self-report measures. This might be subject to recall bias and lead to over-or-underestimation of exposure [29]. Therefore, further studies could include more biological assays, for example, cotinine residue levels or nicotine residue in saliva or hair samples [30]. Previous research using serum cotinine as a biomarker of exposure to SHS found that higher levels of serum cotinine were associated with significantly worse performance in reading, mathematics, and visual and spatial abilities in children and adolescents [8]. However, no studies have used a combination of biomarker and self-reporting yet [31]. Some validated biomarkers could be used as proxies for AD neuropathological changes, such as cerebrospinal fluid (CSF) amyloid-beta (Aβ)42 concentrations or Aβ42/ Aβ40 ratio and amyloid load on positron emission tomography (PET) scans. These biomarkers could provide more reliable measures of cognitive

impairment[32]. Secondly, it may be impossible to control for all potentially confounding variables. After adjusting for age, household expenditure, education, area, chronic health condition and depressive symptoms, some other demographic or socioeconomic confounders may still have been neglected. However, this did not appear to affect the magnitude of the association between SHS exposure and cognition [14]. Besides, the analyses only contained household SHS exposure, which precluded the analyses of the influence of environmental smoke inhalation on smoking proclivity. Whether exposure to household SHS can hasten the onset of cognitive impairment for older Chinese women could be further proved by running regression models in different age groups.

**Acknowledgments :**

We would like to thank the professor Yaohui Zhao at Centre for Chinese Economic Research, Peking University and Mr Benjamin Martin at Birmingham Women's and Children's Hospital for their thoughtful contributions to this study.

**Conflict of Interest**

The authors have no conflicts of interest to declare.

**Author's Contribution**

Anying Bai wrote and participated in all aspects of this research, including the field investigation. Dr Yangmu Huang reviewed and supervised this research. Yinzi Jin participated in the statistical analysis of this work and reviewed the final article.

**Data sharing statement**

CHARLS data is available to the public online: http://charls.pku.edu.cn

**Funding Resources**

This is a self-funded research.

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Table1.Characteristics of the Participants from 3 waves of CHARLS, 2011-2013-2015

| | 2011-2013 (N=2802) | | 2011-2015 (N=2274) | | 2013-2015 (N=1799) | |
|---|---|---|---|---|---|---|
| **Variable** | Count | Frequency | Count | Frequency | Count | Frequency |
| **Area** | | | | | | |
| Urban | 981 | 35.01% | 730 | 32.10% | 556 | 30.91% |
| Rural | 1821 | 64.99% | 1544 | 67.90% | 1243 | 69.09% |
| **SHS** | | | | | | |
| Less than 25 years | 759 | 27.09% | 531 | 23.35% | 262 | 14.56% |
| More than 25 years and less than 30 years | 634 | 22.63% | 573 | 25.20% | 385 | 21.40% |
| More than 30 years and less than 40 years | 911 | 32.51% | 800 | 35.18% | 768 | 42.69% |
| More than 40 years | 498 | 17.77% | 370 | 16.27% | 384 | 21.35% |
| **Education** | | | | | | |
| Illiterate | 1552 | 55.39% | 1309 | 57.56% | 1004 | 55.81% |
| Primary education | 512 | 18.27% | 414 | 18.21% | 336 | 18.68% |
| Secondary or above | 738 | 26.34% | 551 | 24.23% | 459 | 25.51% |
| **Hypertension** | | | | | | |
| No hypertension | 2124 | 75.80% | 1720 | 75.64% | 1365 | 75.88% |
| Hypertension with treatment | 522 | 18.63% | 1720 | 75.64% | 358 | 19.90% |
| Hypertension without treatment | 156 | 5.57% | 130 | 5.72% | 76 | 4.22% |
| **Diabetes** | | | | | | |
| No Diabetes in baseline | 2643 | 94.33% | 2140 | 94.11% | 1704 | 94.72% |

| | | | | | | |
|---|---|---|---|---|---|---|
| Have Diabetes with treatment | 143 | 5.10% | 120 | 5.28% | 86 | 4.78% |
| Have Diabetes without treatment | 16 | 0.57% | 14 | 0.62% | 9 | 0.50% |
| | Count | Mean(SD) | Count | Mean(SD) | Count | Mean(SD) |
| Age | 2802 | 55.84(8.22) | 2274 | 56.19(7.75) | 1799 | 57.90(7.43) |
| Annual Household Expenditure, yuan[a] | 2802 | 13786.99(14197.29) | 2274 | 13060.14(13639.33) | 1799 | 16632.84(18568.24) |
| Visuospatial ability[b] | 2802 | 0.51(0.50) | 2274 | 0.48(0.50) | 1799 | 0.49(0.50) |
| Orientation and attention[c] | 2802 | 5.87(3.29) | 2274 | 5.84(3.19) | 1799 | 5.97(3.14) |
| Memory Scores[d] | 2802 | 3.33(1.96) | 2274 | 3.04(1.93) | 1799 | 3.15(1.91) |
| Baseline Visuospatial ability | 2802 | 0.57(0.50) | 2274 | 0.55(0.50) | 1799 | 0.54(0.50) |
| Baseline Orientation and attention | 2802 | 6.39(2.92) | 2274 | 6.25(2.90) | 1799 | 6.16(3.00) |
| Baseline Memory Scores | 2802 | 3.27(1.98) | 2274 | 3.23(1.92) | 1799 | 3.50(1.78) |
| Baseline CES-D Score[e] | 2802 | 12.09(5.38) | 2274 | 12.13(5.45) | 1799 | 10.90(5.14) |

Abbreviation: SHS, secondhand smoke.

a 1 US dollar = 6.3 yuan.

b The score range for visuospatial ability was 0–1.

c The score range for orientation and attention was 0–10. Higher scores indicate better mental status.

d The score range for episodic memory was 0–10. Higher scores indicate better memory function.

e A score of 10 or greater indicated the presence of depressive symptoms.

Table2.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

| | Visuospatial Function | | | Orientation and Attention | | |
|---|---|---|---|---|---|---|
| VARIABLES | β coefficient | 95%CI | t | β coefficient | 95%CI | t |
| **Age** | -0.01[a] | -0.01,-0.00 | -6.73 | -0.02[a] | -0.03, -0.01 | -4.34 |
| **Expenditure** | 0.00 | 0.00, 0.00 | 0.01 | 0.00[a] | 0.00, 0.00 | 0.77 |
| **SHS Exposure[d]** | | | | | | |
| **25 to <30 years** | -0.01 | -0.04, 0.02 | -0.72 | 0.05 | -0.12, 0.21 | 0.56 |
| **≥30 to <40 years** | -0.02 | -0.05, 0.02 | -0.95 | -0.03 | -0.20, 0.13 | -0.38 |
| **≥ 40 years** | -0.04[c] | -0.08, 0.01 | -1.67 | -0.15 | -0.38, 0.09 | -1.24 |
| **Baseline Visuospatial Function** | 0.23[a] | 0.21, 0.26 | 17.93 | | | |
| **Baseline Orientation and Attention** | | | | 0.55[a] | 0.53, 0.57 | 44.86 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Urban**[e] | 0.06[a] | 0.04, 0.09 | 5.27 | 0.38[a] | 0.25, 0.51 | 5.72 |
| **Education**[f] | | | | | | |
| **Primary** | 0.23[a] | 0.20, 0.26 | 14.00 | 1.11[a] | 0.94, 1.27 | 12.91 |
| **Secondary or Above** | 0.29[a] | 0.26, 0.32 | 18.51 | 1.18[a] | 1.01, 1.36 | 13.44 |
| **Hypertension**[g] | | | | | | |
| **With Treatment** | -0.03 | -0.09, 0.02 | -1.20 | 0.06 | -0.24, 0.35 | -0.38 |
| **Without Treatment** | -0.02 | -0.06, 0.03 | -0.69 | 0.06 | -0.11, 0.24 | 0.04 |
| **Missing Group** | -0.05[c] | -0.12, 0.01 | -1.67 | 0.06 | -0.19, 0.30 | -0.01 |
| **Diabetes**[h] | | | | | | |
| **With Treatment** | 0.02 | -0.03, 0.07 | 0.90 | 0.25[c] | -0.03, 0.52 | -1.77 |
| **Without Treatment** | 0.03 | -0.04, 0.09 | 0.82 | 0.21 | -0.06, 0.48 | -0.23 |
| **Missing Group** | 0.07 | -0.08, 0.21 | 0.88 | 0.50 | -0.22, 1.23 | 0.67 |
| **Baseline CES-D Score** | -0.00[c] | -0.00, 0.00 | -1.71 | -0.02[b] | -0.03, -0.00 | -2.57 |
| **year = 2** | -0.02 | -0.04, 0.01 | -1.58 | 0.09 | -0.05, 0.22 | 1.29 |

Abbreviations: CI, confidence interval; SHS, secondhand smoke.

a. p<0.01

b. p<0.05

c. p<0.1

d. Referent: No SHS exposure or Less than 25 years.

e. Expenditure is expressed as the natural log of the annual household expenditure

f. Referent: Illiterate

g. Referent: Without hypertension

h. Referent: Without diabetes

I. This model adjusted for age, expenditure, living area, education, baseline hypertension, diabetes, depression status and baseline cognitive function.

Table3. Adjusted Multivariable linear regression analysis of the relationship between smoking exposure and Episodic memory and Overall cognitive function among older Chinese women (N = 6875), 2011-2013-2015

| | Episodic Memory | | | Overall Cognition | | |
|---|---|---|---|---|---|---|
| VARIABLES | β coefficient | 95%CI | t | β coefficient | 95%CI | t |
| **Age** | -0.04[a] | -0.05,-0.03 | -11.37 | -0.06[a] | -0.07, -0.04 | -7.87 |
| **Expenditure** | 0.00 | 0.00, 0.00 | 1.30 | 0.00[a] | 0.00, 0.00 | 0.32 |
| **SHS Exposure[d]** | | | | | | |
| **25 to <30 years** | -0.04 | -0.16, 0.08 | -0.67 | -0.01 | -0.25, 0.25 | -0.01 |
| **≥30 to <40 years** | 0.02 | -0.09, 0.13 | 0.36 | -0.05 | -0.29, 0.19 | -0.41 |
| **≥ 40 years** | -0.16[b] | -0.31, -0.01 | -2.06 | -0.33[a] | -0.66, 0.01 | -1.93 |
| **Baseline Episodic Memory** | 0.30[a] | 0.28, 0.32 | 25.22 | | | |
| **Baseline Overall Cognition** | | | | 0.55[a] | 0.46, 0.83 | 44.95 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Urban[e]** | 0.25[a] | 0.16, 0.34 | 5.60 | 0.65[a] | 0.46, 0.83 | 6.68 |
| **Education[f]** | | | | | | |
| **Primary** | 0.70[a] | 0.58, 0.80 | 12.42 | 1.77[a] | 1.53, 2.02 | 14.28 |
| **Secondary or Above** | 0.97[a] | 0.86, 1.08 | 17.29 | 2.00[a] | 1.74, 2.26 | 15.24 |
| **Hypertension[g]** | | | | | | |
| **With Treatment** | 0.04 | -0.16, 0.23 | 0.35 | 0.13 | -0.29, 0.56 | 0.62 |
| **Without Treatment** | 0.06 | -0.06, 0.17 | 0.95 | 0.12 | -0.14, 0.38 | 0.93 |
| **Missing Group** | 0.07 | -0.12, 0.25 | 0.70 | 0.10 | -0.27, 0.47 | 0.52 |
| **Diabetes[h]** | | | | | | |
| **With Treatment** | -0.20[b] | -0.38, 0.02 | -2.20 | -0.04 | -0.43, 0.36 | 0.62 |
| **Without Treatment** | -0.07 | -0.25, 0.11 | -0.77 | 0.08 | -0.30, 0.47 | 0.43 |
| **Missing Group** | 0.32 | -0.16, 0.80 | 1.30 | 0.87 | -0.11, 1.84 | 1.75 |
| **Baseline CES-D Score** | -0.01[b] | -0.01, 0.00 | -1.59 | -0.01 | -0.03, 0.00 | -2.57 |
| **year = 2** | -0.24 | -0.33, -0.15 | -5.21 | -0.17 | -0.37, 0.03 | -1.70 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Constant** | 0.63 | 0.53, 0.74 | 11.54 | 6.48[a] | 5.59, 7.37 | 14.28 |

Abbreviations: CI, confidence interval; SHS, secondhand smoke.

a. p<0.01

b. p<0.05

c. p<0.1

d. Referent: No SHS exposure or Less than 25 years.

e. Expenditure is expressed as the natural log of the annual household expenditure

f. Referent: Illiterate

g. Referent: Without hypertension

h. Referent: Without diabetes

I. This model adjusted for age, expenditure, living area, education, baseline hypertension, diabetes, depression status and baseline cognitive function.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

| | Item No | Recommendation | Page No |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract<br>(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 1-3 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 4 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 5 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 6 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>(*b*) For matched studies, give matching criteria and number of exposed and unexposed | 6 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 7-9 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 7-9 |
| Bias | 9 | Describe any efforts to address potential sources of bias | 9 |
| Study size | 10 | Explain how the study size was arrived at | 6 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 7-9 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding<br>(*b*) Describe any methods used to examine subgroups and interactions<br>(*c*) Explain how missing data were addressed<br>(*d*) If applicable, explain how loss to follow-up was addressed<br>(*e*) Describe any sensitivity analyses | 9-10 |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed<br>(b) Give reasons for non-participation at each stage<br>(c) Consider use of a flow diagram | 6 |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders<br>(b) Indicate number of participants with missing data for each variable of interest<br>(c) Summarise follow-up time (eg, average and total amount) | 10-11 |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time | 11 |

| | | | |
|---|---|---|---|
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included<br>(*b*) Report category boundaries when continuous variables were categorized<br>(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | 11 |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 11-12 |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 12 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 15-16 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 13-15 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 12 |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 17 |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.