

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Incidence and risk factors of depressive symptoms in four years of follow-up among mid-aged and elderly community-dwelling Chinese adults: Findings from the China health and Retirement Longitudinal Study
<b>AUTHORS</b>	Wen, Yue; Liu, Chunjuan; Liao, Jing; Yin, Yiqiong; Wu, Dongmei

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Scott Rozelle Stanford University, USA
<b>REVIEW RETURNED</b>	21-Feb-2019

<b>GENERAL COMMENTS</b>	<p>This is a simple but important paper that uses CHARLs, a national representative data set of elderly in China, to examine depression among urban and rural individuals over the age of 45 years old. The paper finds high rates of depression—especially among women and rural individuals. There are also a number of correlates of depression that are identified.</p> <p>While generally high quality, there are some comments and suggestions (many that have to do with writing more clearly / or explaining things more clearly) that may make the paper even stronger.</p> <ol style="list-style-type: none"><li>1. Throughout the paper the authors refer to different waves of the survey and this gets confusing. I believe in the methods section that they need to define the different waves and then use one and only one name per wave. Now they use language such as: Depressive Symptom in 2 years ... Depressive Symptom in 4 years ... Depressive symptoms in four years of follow up. These are confusing. I actually do not know what they mean.</li><li>2. On page 12 in the section on Incidence of Depressive Symptoms, there is a long paragraph that describes the way that incidence is calculated. Why is this done? Why not simple weighted average shares/ratios? This needs more explanation to allow the reader to follow the logic of the authors.</li><li>3. I would like to see the authors re-run their analysis with simple OLS rather than more complicated multivariate logistic analysis and put the results in an appendix and tell the reader if there are any differences. This will help with transparency.</li></ol>
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	<p>4. In the table that shows the simple incidence of depression (Table 2), I would like to see p-value on differences between some of the key groupings that are analyzed in the results section of the paper. The authors report differences, yet we do not know if these are statistically significant differences.</p> <p>5. I am confused about the sentence at the bottom of page 4 that compares the results of this paper with those of Li et al. (reference 12). How do these two studies differ methodologically? Why are the incidences different?</p> <p>6. In a paper “Caregiver Depression and Early Child Development: A Mixed-Methods Study From Rural China” by A. Yue et al, Frontiers in Psychology, 2018, the authors find high levels of depression of elderly women in rural communities when they are giving care to their grandchildren (and typically their son and daughter in law are living and working outside of the community). If the authors have this information (who is co-resident in the home – children / grandchildren), I would like to see this since it could be a very important factor/correlate.</p>
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<b>REVIEWER</b>	Dr Frances N. Adiukwu MBBS, FWACP Department of Neuropsychiatry University of Port Harcourt Teaching Hospital, Nigeria
<b>REVIEW RETURNED</b>	10-Apr-2019

<b>GENERAL COMMENTS</b>	<p>General comments</p> <p>The manuscript has some typos that need to be addressed. Before using an abbreviation, the full meaning should be stated first. The writing style of the author is difficult to follow and understand and requires editing.</p> <p>Specific comments</p> <p>The methods section is difficult to understand and will not allow for a wide readership. The section on participants should be re-written and clarified.</p> <p>Result- The sentence incidence of depression should be changed to the incidence of depressive symptoms.</p> <p>Discussion - the first paragraph is a repetition of the results section and not necessary.</p> <p>Page 15, line 17 and 18 should be removed as sleep disorder is not a core symptom of depression. The paragraph on self-perceived health status requires re-writing as studies cited are not properly critiqued.</p> <p>Conclusion - rewrite the last sentence</p>
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### VERSION 1 – AUTHOR RESPONSE

Responses to Reviewer #1's comments:

Reviewer: 1

Reviewer Name: Scott Rozelle

Institution and Country: Stanford University, USA

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

This is a simple but important paper that uses CHARLS, a national representative data set of elderly in China, to examine depression among urban and rural individuals over the age of 45 years old. The paper finds high rates of depression—especially among women and rural individuals. There are also a number of correlates of depression that are identified.

While generally high quality, there are some comments and suggestions (many that have to do with writing more clearly / or explaining things more clearly) that may make the paper even stronger.

Response: Thank you for the encouraging comments, Dr. Rozelle.

1. Throughout the paper the authors refer to different waves of the survey and this gets confusing. I believe in the methods section that they need to define the different waves and then use one and only one name per wave. Now they use language such as: Depressive Symptom in 2 years ... Depressive Symptom in 4 years ... Depressive symptoms in four years of follow up. These are confusing. I actually do not know what they mean.

Response: Thank you for the comment and suggestion. The CHARLS uses a similar study design and sampling methods as the Health and Retirement Study (HRS) in the US. The baseline survey (wave 1) was conducted from Jun 2011 to March 2012 among a nationally representative sample of middle-aged and older Chinese adults. The CHARLS follows participants every two years. The first follow-up survey (wave 2) was carried out in 2013, and the second follow-up survey (wave 3) was done in 2015. We've now revised the method section and described wave 1 as baseline survey, wave 2 as the first follow-up survey, and wave 3 as the second follow-up survey.

2. On page 12 in the section on Incidence of Depressive Symptoms, there is a long paragraph that describes the way that incidence is calculated. Why is this done? Why not simple weighted average shares/ratios? This needs more explanation to allow the reader to follow the logic of the authors.

Response: Thank you for the comment. The CHARLS used a four-stage, stratified, cluster probability sampling design<sup>4</sup>, therefore, sampling design should be considered when estimating the national incidence of depressive symptoms in this population. We were previously criticized for not providing detailed information on how sampling design was handled in our analyses. So, we've used a long paragraph describing it. We have now described it more briefly as below:

"Incidence of depressive symptoms. The incidence of depressive symptoms was analyzed taking into account the complex survey design and nonresponse rate in both estimates and the corresponding standard errors (SEs). Participants were categorized into 5-year age groups. SAS PROC SURVEYFREQ procedure was used to obtain the overall and gender specific incidence of depression among all the participants and by the 5-year age groups. In addition, overall and gender-specific depression incidence was estimated by rural and urban areas. We estimated the incidence of four outcomes of depressive symptoms: having depressive symptoms in the first follow-up survey (2013-2014); having depressive symptoms in the second follow-up survey (2015-2016); ever having depressive symptoms in the first or the second follow-up survey; and consistently having depressive symptoms in both follow-up surveys."

3. I would like to see the authors re-run their analysis with simple OLS rather than more complicated multivariate logistic analysis and put the results in an appendix and tell the reader if there are any differences. This will help with transparency.

Response: Thank you for the comment. We've now re-run the analysis with simple OLS and provided the following table.

Table. Raw and Multi-variate Adjusted Associations of covariates with the occurrence of ever depression in 4 years

Variables	Multi-Variate Adjusted		Raw Association	
	OR (95% CI)	P	OR (95% CI)	P
Age, per year older	0.99 (0.98-0.99)	0.001	0.99 (0.99-1.00)	0.59
Male vs. Female	0.60 (0.51-0.71)	<.0001	0.51 (0.46-0.56)	<.0001
Education level				
No formal education or illiterate	ref.	<.0001	Ref.	<.0001
Some primary school	1.06 (0.90-1.25)		0.93 (0.80-1.08)	
Finished primary school	0.83 (0.71-0.97)		0.67 (0.57-0.77)	
Junior high school or above	0.71 (0.61-0.84)		0.48 (0.42-0.55)	
Rural vs. Urban	1.61 (1.38-1.88)	<.0001	1.72 (1.50-1.96)	<.0001
Not married vs Married	1.25 (1.04-1.51)	0.02	1.28 (1.08-1.51)	0.004
Smoking status				
Non-smokers	ref.		Ref.	
Current smokers	1.02 (0.86-1.20)	0.03	0.51 (0.41-0.62)	<.0001
Former smokers	0.75 (0.59-0.96)		0.68 (0.60-0.76)	
Drinking status				
Never drinkers	Ref.		Ref.	
Former drinkers	1.02 (0.80-1.30)	0.15	0.84 (0.67-1.04)	<.0001
Occasional drinkers	0.79 (0.59-1.06)		0.59 (0.45-0.78)	
Regular drinkers	0.85 (0.71-1.01)		0.59 (0.51-0.68)	
BMI, per 1 kg/m <sup>2</sup> increase	0.99 (0.98-1.01)	0.20	0.99 (0.98-1.00)	0.14
Self-perceived health status				
Excellent	0.36 (0.25-0.52)	<.0001	0.28 (0.20-0.39)	<.0001
Very good	0.36 (0.29-0.45)		0.28 (0.23-0.35)	
Good	0.53 (0.44-0.63)		0.45 (0.38-0.53)	
Fair	0.61 (0.52-0.73)		0.56 (0.48-0.66)	
Poor	ref.		Ref.	
Sleep duration, per hour longer	0.89 (0.87-0.92)	<.0001	0.88 (0.85-0.90)	<.0001
Hypertension (Y vs. N)	1.07 (0.95-1.21)	0.25	1.07 (0.96-1.18)	0.22
Dyslipidemia (Y vs. N)	0.85 (0.69-1.04)	0.12	0.91 (0.76-1.09)	0.29
Diabetes (Y vs. N)	1.19 (1.00-1.42)	0.04	1.11 (0.95-2.30)	0.19
Cancer (Y vs. N)	0.92 (0.48-1.77)	0.80	1.17 (0.65-2.12)	0.61
Chronic Lung Disease (Y vs. N)	1.18 (0.97-1.44)	0.10	1.33 (1.12-1.58)	0.001
Chronic Liver Disease (Y vs. N)	0.90 (0.67-1.22)	0.51	1.04 (0.79-1.37)	0.81
Heart Disease (Y vs. N)	1.06 (0.88-1.28)	0.54	1.27 (1.08-1.49)	0.004
Stroke (Y vs. N)	0.88 (0.56-1.39)	0.59	1.12 (0.75-1.66)	0.58
Chronic Kidney Disease (Y vs. N)	1.32 (1.04-1.67)	0.02	1.45 (1.16-1.80)	0.001
Chronic Digestive Disorders (Y vs. N)	1.15 (1.01-1.31)	0.04	1.43 (1.26-1.61)	<.0001
Psychological Disorders (Y vs. N)	1.00 (0.53-1.89)	0.99	1.44 (0.81-2.56)	0.22
Dementia (Y vs. N)	1.31 (0.72-2.38)	0.37	1.15 (0.67-1.97)	0.62
Arthritis (Y vs. N)	1.43 (1.28-1.61)	<.0001	1.72 (1.54-1.91)	<.0001
Asthma (Y vs. N)	1.25 (0.90-1.75)	0.19	1.43 (1.06-1.91)	0.02

4. In the table that shows the simple incidence of depression (Table 2), I would like to see p-value on

differences between some of the key groupings that are analyzed in the results section of the paper. The authors report differences, yet we do not know if these are statistically significant differences.

Response: Thank you for the suggestion. We've now provided p values for the comparisons of depressive symptoms incidences by location of residence ( $p < 0.0001$ ) and gender ( $p < 0.0001$ ) in the results section. Please refer to page 13.

5. I am confused about the sentence at the bottom of page 4 that compares the results of this paper with those of Li et al. (reference 12). How do these two studies differ methodologically? Why are the incidences different?

Response: Thank you for the comment. Li and colleagues estimated the prevalence of depressive symptoms using baseline data of the CHARLS. Their data provided a burden of depressive symptoms in this population. The current study focused on the incidence of depressive symptoms in 4 years follow-up. We retrieved all participants free of depressive symptoms at baseline and traced the occurrence of depressive symptoms in 4 years follow-up and estimated the incidence of depressive symptoms. Our data reflected the speed of occurring new cases of depressive symptoms and examined risk factors for the condition.

6. In a paper "Caregiver Depression and Early Child Development: A Mixed-Methods Study From Rural China" by A. Yue et al, *Frontiers in Psychology*, 2018, the authors find high levels of depression of elderly women in rural communities when they are giving care to their grandchildren (and typically their son and daughter in law are living and working outside of the community). If the authors have this information (who is co-resident in the home – children / grandchildren), I would like to see this since it could be a very important factor/correlate.

Response: Thank you for the suggestion. Helping children take care of grandchildren is very common in China. However, the CHARLS only collected information on the participants' children and siblings. Therefore, we could not examine findings reported by Yue and colleagues. We agree with reviewer that this is an important factor. The CHARLS is an ongoing study. I would suggest the reviewer to contact the principal investigator of the CHARLS to add questionnaires in future surveys.

Responses to reviewer #2's comments:

Reviewer: 2

Reviewer Name: Dr Frances N. Adiukwu

Institution and Country: MBBS, FWACP, Department of Neuropsychiatry, University of Port Harcourt Teaching Hospital, Nigeria

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

General comments

The manuscript has some typos that need to be addressed. Before using an abbreviation, the full meaning should be stated first. The writing style of the author is difficult to follow and understand and requires editing.

Response: Thank you for the comments. A native English speaker has now read through the manuscript and edit the text.

Specific comments

The methods section is difficult to understand and will not allow for a wide readership. The section on participants should be re-written and clarified.

Response: Thank you for the comment. We've followed the journal's guideline and divided the methods section into: study design, study participants, measurement of major outcome, measurement of risk factors to be assessed, covariates, and statistical analyses.

We've revised the study participants section to clearly describe how the study participants were selected.

Result- The sentence incidence of depression should be changed to the incidence of depressive symptoms.

Response: Thank you for the comment. We've changed the "incidence of depression" into "incidence of depressive symptoms" throughout the manuscript.

Discussion - the first paragraph is a repetition of the results section and not necessary.

Response: Thank you for the comment. We've followed the journal's guideline and summarizes major findings in the first paragraph of the discussion section.

Page 15, line 17 and 18 should be removed as sleep disorder is not a core symptom of depression. The paragraph on self-perceived health status requires re-writing as studies cited are not properly critiqued.

Response: Thank you for the comments. Sleep disorder has been described as a core symptom of depression in many publications<sup>5 6</sup>. Recently, sleep disorder is regarded as a comorbid disorder<sup>7 8</sup>, and therapies targeting insomnia lead to improvement of depression<sup>9-11</sup>. We've revise it as follows:

"Sleep disorder has been described as a core symptom of depression in many publications<sup>5 6</sup>. Recently, sleep disorder is regarded as a comorbid disorder<sup>7 8</sup>, and therapies targeting insomnia lead to improvement of depression<sup>9-11</sup>."

In terms of the discussion on self-perceived health, we've now added more recent publications as references to support our findings. In addition, we've added the following discussion:

"Finally, individuals with depressive disorders were more likely to report poor self-perceived health<sup>12 13</sup>. Therefore, there might be a bi-directional relationship between depressive symptoms and self-perceived health. Future studies examining the bi-directional relationship are warranted."

Conclusion - rewrite the last sentence

Response: thank you for the suggestion. We've now rewritten the last sentence as follows:

"These findings also help to identify individuals at higher risk for depressive symptoms, such as individuals with chronic kidney disease, diabetes, arthritis, women and residents living in rural areas, so that early interventions can be implemented to prevent depressive symptoms."

References:

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13. Alarcão V, Madeira T, Peixoto-Plácido C, et al. Gender differences in psychosocial determinants of self-perceived health among Portuguese older adults in nursing homes. *Aging Ment Health* 2018:1-8. doi: 10.1080/13607863.2018.1471583 [published Online First: 2018/05/23]

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Scott Rozelle Stanford University USA
<b>REVIEW RETURNED</b>	26-May-2019

<b>GENERAL COMMENTS</b>	I have read the paper and believe it is almost ready for publication. The authors are addressing an important issue. Specifically, the objective of this paper is to measure the prevalence of depression among the elderly in China—both urban and rural—and to identify
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	<p>correlates of depression. Using data from CHARLS, a nationally representative sample from 28 provinces of China, enumerators measured depressive symptoms using the Epidemiological Studies Depression Scale short form. The results of the authors demonstrate a high rate of depression, above 20%. The incidence was higher in rural areas and women. Several factors, including baseline health conditions, both perceived and actual, were correlated with depressive symptoms.</p> <p>According to my reading of this version (R1) of the paper, the motivation; statement of the objectives; the description of the methods; and the review of the results are all fine. I have no further suggestions.</p> <p>I really only have one set of suggestion for the discussion section of the paper. The authors currently discuss the implications of findings for policy. They have a number of suggestions for trying to improve access of depressed individuals. The focus of the discussion is (rightly so) on trying to improve the livelihood of the elderly who are experiencing depressive symptoms (allowing better diagnosis; and treatment).</p> <p>I hope the authors also can raise another set of issues about the extent to which there are also implication for the high rates of un-diagnosed and un-treated depression for those beyond the depressed themselves. In particular, in the following two papers, it can be seen that in rural China middle-aged and elderly grandparents often are the primary caregivers of infants and toddlers and young children.</p> <ul style="list-style-type: none"> <li>• Yue et al., “Caregiver Depression and Early Childhood Development: A Mixed Methods Study From Rural China.” <i>Frontiers in Psychology</i>. 2018.</li> <li>• Zhang et al., “Effect of Caregiver’s Health on Early Childhood Development Across Different Rural Communities.” <i>International Journal of Environmental Research and Public Health</i>. 2018.</li> </ul> <p>The facts in these papers are fairly clear and, in key respects, consistent with this papers findings. By the time children are 18 months old, about 40% or more of toddlers are being raised by grandmothers. The rate of the grandmothers with symptoms of depression (using similar scales as the authors of this paper) is similar—around 30%. Finally, it is shown that there is a strong negative correlation between the levels of depression of grandmothers and the levels of development (cognition, language, social-emotional, etc.) of the grandchildren in their care. Raising such issues, I believe, will give those trying to use the results of the study to push forward changes in social policies/programs that address the better and more timely diagnosis and treatment of depression more traction. I would like the see the authors address this issue in the revised manuscript.</p>
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<b>REVIEWER</b>	Frances Nkechi Adiukwu University of Port Harcourt Teaching Hospital, Rivers State, Nigeria.
<b>REVIEW RETURNED</b>	03-Jun-2019



<b>GENERAL COMMENTS</b>	This is a much-improved version, it reads better than the original version. However, the author has removed the section on how the sampling was carried out rather than explain in a simplified manner. Explaining would aid the study in being replicable. Kindly summarise your sampling procedure in the methods section. Also for ethical issues which may arise, state how participants with depressive symptoms were referred for treatment, as you made reference to them receiving treatment in your discussion.
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## VERSION 2 – AUTHOR RESPONSE

Response to Reviewer 1:

I really only have one set of suggestion for the discussion section of the paper. The authors currently discuss the implications of findings for policy. They have a number of suggestions for trying to improve access of depressed individuals. The focus of the discussion is (rightly so) on trying to improve the livelihood of the elderly who are experiencing depressive symptoms (allowing better diagnosis; and treatment).

I hope the authors also can raise another set of issues about the extent to which there are also implication for the high rates of un-diagnosed and un-treated depression for those beyond the depressed themselves. In particular, in the following two papers, it can be seen that in rural China middle-aged and elderly grandparents often are the primary caregivers of infants and toddlers and young children.

- Yue et al., “Caregiver Depression and Early Childhood Development: A Mixed Methods Study From Rural China.” *Frontiers in Psychology*. 2018.
- Zhang et al., “Effect of Caregiver’s Health on Early Childhood Development Across Different Rural Communities.” *International Journal of Environmental Research and Public Health*. 2018.

The facts in these papers are fairly clear and, in key respects, consistent with this papers findings. By the time children are 18 months old, about 40% or more of toddlers are being raised by grandmothers. The rate of the grandmothers with symptoms of depression (using similar scales as the authors of this paper) is similar—around 30%. Finally, it is shown that there is a strong negative correlation between the levels of depression of grandmothers and the levels of development (cognition, language, social-emotional, etc.) of the grandchildren in their care. Raising such issues, I believe, will give those trying to use the results of the study to push forward changes in social policies/programs that address the better and more timely diagnosis and treatment of depression more traction. I would like the see the authors address this issue in the revised manuscript.

Response: Thank you for the important suggestions and for providing important references on the topic. We’ve now added the following discussions on implications of the high rates of incident, un-diagnosed, and un-treated depression. Please refer to lines xx on page 15. have raised these issues about the extent to which there are also implication for the high rates of un-diagnosed and un-treated depression for those beyond the depressed themselves. Please referred to the highlighted text on pages 15 and 16 of the revised manuscript:

“The high incidence rate is not only relevant to middle-aged and older Chinese adults; it also has implications for younger generations of the Chinese. Many depressive symptoms cases remained undiagnosed, and even among those who were aware of the condition, very few sought treatments due to cultural stigma 1 2. Middle-aged and elderly grandparents are the primary caregivers of infants, toddlers, and young children in rural China. Depressed caregivers were more likely to show negative

parenting interactions (e.g., limited facial and behavioral affect) with their children, and these interactions were directly relevant for children's development 3 4. A strong negative correlation has been reported between the levels of depression of grandmothers and the levels of developmental outcomes of the grandchildren in their care, including cognitive, language, social-emotional, and motor functions 5 6. Taken together, changes in social policies and intervention programs should be developed to address timely diagnosis and treatment of depression for these people, which will help improve young children's developmental outcomes in rural China."

#### Responses to Reviewer 2:

1. This is a much-improved version. It reads better than the original version. However, the author has removed the section on how the sampling was carried out rather than explain in a simplified manner. Explaining would aid the study in being replicable. Kindly summarize your sampling procedure in the methods section.

Response: Thanks for your comments. We have now added back the following brief summary of sampling process in the methods section. Please refer to the highlighted text on page 8 of the revised manuscript:

"In brief, in the first stage, all counties were grouped by gross domestic product and by urban or rural regions. In the second stage, counties were stratified and sampled using probabilities proportional to size (PPS). Three rural villages and urban neighborhoods were randomly selected as primary sampling units (PSUs) using PPS in each county. In the third stage, all buildings in each PSU were recognized on Google Earth. A sample of 24 households was randomly selected among all households in each PSU. In the final stage, a short screening form was employed to ensure study eligibility in selected households and members of 45 years of age or above were invited to enroll into the study. The response rate for the survey was over 80% (94% in rural areas and 69% in urban areas) 7."

2. Also for ethical issues which may arise, state how participants with depressive symptoms were referred for treatment, as you made reference to them receiving treatment in your discussion.

Response: Thanks for your comments. CESD-10 cannot be used to clinically diagnose depression. However, participants with depressive symptoms based on the CESD-10 were suggested to visit a physician for further evaluation. We've now added the following description in the manuscript. Please refer to the highlighted text on page 9 and 19.

"Participants with abnormal findings, including depressive symptoms were suggested to visit a physician for further clinical evaluation."

"Finally, new patients with chronic kidney disease and diabetes should be screened for depression using the CES-D short form at initial visit. Persons with depressive symptoms (a score of 12 or higher) should then be assessed by a clinician using the structured clinical interview for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Potential participants with serious depressive symptoms should be referred immediately to a mental health professional. Individuals with these two conditions are particularly vulnerable to the deleterious effects of affective symptoms, since symptoms of depression is a known risk factor for noncompliance with medical treatment and adverse health outcomes 8 9".

#### References:

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