PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	COVID-19-related stigma and its influencing factors: a nationwide cross-sectional study during the early stage of the pandemic in China
AUTHORS	Jiang, Tianyu; Zhou, Xudong; Lin, Leesa; Pan, Yanzheng; Zhong, Yuyuan; Wang, Xiaomin; Zhu, Hui

VERSION 1 – REVIEW

REVIEWER	El-Osta, Austen Imperial College London Department of Primary Care and Public Health, Imperial College London
REVIEW RETURNED	06-Feb-2021

GENERAL COMMENTS	This is an interesting study but the authors would benefit from having the manuscript reviewed by a medical writer to more clearly communicate the main findings. It does not currently read as a scholarly manuscript suitable for publication. When measuring health literacy, it would have been more ideal to ask the respondents' to what extent so you agree with the following statements" as opposed to ' do you agree that,…" Table 4 is not clear. For example, why are there four columns of odds ratio with 95% confidence interval (2 for patients & 2 for Wuhan residents). Further, logistic regression is ideal when the outcome of interest is expected to be rare (<10%) event. On occasion when have a common/prevalent (not rare) event as was the case with stigma, then a Poisson regression may be more ideally suited.

REVIEWER	Baldassarre, Antonio University of Florence, Doctoral School in Clinical Sciences
REVIEW RETURNED	10-Feb-2021

GENERAL COMMENTS	Dear Authors, your contribution proposal deals with a criticality that has plagued public health for decades, often underestimated by stakeholders called upon to manage exceptional events such as the ongoing CoViD-19 pandemic. Discrimination and stigma are an atavistic problem, which has its roots in the foundation of some States and which only a purposeful and proactive cultural movement can overturn over the years

	What happened in the near past must be the starting point so that similar episodes no longer occur; but man, unfortunately, has a short memory. Thank you for sharing your contribution proposal, that should be addressed as letter to the editor or narrative review, since it cannot be defined as "original article". I believe you can further improve the elaborate, still a bit raw as a potential interest for both the scientific community and general audience. I tried to give you some suggestions to help you in this very first review phase. - Why not SARS-CoV-2 among keywords? why not i.e. stigma/discrimination, disparities, inequalities? - Please contextualize and deepen the current pandemic scenario when introducing your work; - Please upload the questionnaire ("Additional file 1" as reported in methods - study design and participants). - It's not clear if participants gave an informed consent or not. - Plese report the of ethics commitee approval number. The methodological part must be thoroughly revised, completing it with the administered questionnaire. Discussion's paragraphs can be improved further. You need conclusions, too port in this first attempt. What are the possible repercussions? What suggestions to give to the health policy maker? Define a clear "take home message" from your perspective and address a conclusion section. The alleged identification of "scientific" bases of stigmata characterizing certain groups of population being the first, decisive and irreversible step towards the creation of a sort of "expendable victims", according to one well known pattern from the history of this kind of human affairs. You should also refer toother examples of scientific literature that have completely misled epidemiological findings. Please update these gaps referring to the following non-exhaustive non-mandatory references list: - Irigoyen-Camacho, M.E.; Velazquez-Alva, M.C.; Zepeda-Zepeda, M.A.; Cabrer-Rosales, M.F.; Lazarevich, I.; Castaño-Seiquer, A. Effect of Income Level and Perception of Susceptibility and Severity of COVID-19 on Stay-at-Home Preventive Behavior in a Group of Older Adults in Mexico City. Int. J. Environ. Res. Public Health 2020, 17, 7418 - Baldassarre, A.; Giorgi, G.; Alessio, F.; Lulli, L.G.; Arcangeli, G.; Mucci, N. Stigma and Discrimination (SAD) at the Time of the SARS-CoV-2 Pandemic. Int. J. Environ. Res. Public Health 2020, 17, 6341 - Sarah Dryhurst, Claudia R. Schneider, John Kerr, Alexandra L. J. Freeman, Gabriel Recchia, Anne Marthe van der Bles, David

	Spiegelhalter & Sander van der Linden (2020) Risk perceptions of COVID-19 around the world, Journal of Risk Research, DOI: 10.1080/13669877.2020.1758193 - Wong, B.Y.-M.; Lam, T.-H.; Lai, A.Y.-K.; Wang, M.P.; Ho, S.-Y. Perceived Benefits and Harms of the COVID-19 Pandemic on Family Well-Being and Their Sociodemographic Disparities in Hong Kong: A Cross-Sectional Study. International Journal of Environmental Research and Public Health 2021, 18, 1217 - Weinstein, B.; da Silva, A.R.; Kouzoukas, D.E.; Bose, T.; Kim, G.J.; Correa, P.A.; Pondugula, S.; Lee, Y.; Kim, J.; Carpenter, D.O. Precision Mapping of COVID-19 Vulnerable Locales by Epidemiological and Socioeconomic Risk Factors, Developed Using South Korean Data. International Journal of Environmental Research and Public Health 2021, 18, 604 - Dye, T.D.; Alcantara, L.; Siddiqi, S.; Barbosu, M.; Sharma, S.; Panko, T.; Pressman, E. Risk of COVID-19-related bullying, harassment and stigma among healthcare workers: an analytical cross-sectional global study. BMJ Open 2020, 10, e046620 In the conclusions you should refer to the very recent introduction of vaccines; what would change in this scenario? deal with it, even because CoViD-19 vaccines are now available all over the globe.

REVIEWER	Abdelhafiz, Ahmed Cairo University
REVIEW RETURNED	10-Feb-2021

GENERAL COMMENTS	Thank you for allowing me to review this manuscript. Social stigma is one of the hidden threats of COVID-19, and it might lead to negative impact on the individuals and societies. The manuscript is interesting, well presented and well written, and the language is clear. Kindly find my comments below. General comment: Although the topic of the manuscript is interesting and important, the data are a bit outdated. Data were collected in March 2020 and COVID-19 sitaution has changed a lot during the past months. To overcome this limitation, I suggest that the authors add more insights from recent publications about the topic of stigma. Many documents, original research, reviews and mini-review articles were published about the topic of social stigma as a threat during COVID-19 pandemic. Some of these documents provided recommendations or solutions about how to deal with stigma. Please have a look at them and use them in the discussion. Specific comments Abstract Objectives: Please put the two objectives in one sentence as follows "…the city of Wuhan in China, and to assess the association ….". Participants: You already mentioned that the study was carried out in 31 provinces in China in the setting. You don't have to mention it again here. Conclusion: line 55: You mentioned that "Tailored interventions were encouraged" Please change into the present tense "are encouraged" instead of the past tense.

	Article Summary Page 4, line 12: You describe COVID-19 as an outbreak. Although this was correct in the beginning, but in March 2020, the WHO declared COVID-19 as a pandemic. Page 4, Line 16: You mentioned that “This is a cross-sectional study with an over sample of minorities” This sentence is not clear for me. Do you mean that the majority of participants were young? Please clarify. Introduction It was interesting and useful to start with a brief definition of stigma, to clarify the concept we are dealing with. Methods • Page 6, line 27: You mentioned that "We conducted 30 online face-to-face interviews with respondents" I think it is not right to say "online" and "face to face" together. Face to face usually means in person. • Would you please explain who the ethnic minorities in the context of this work are? • Page 6, line 47: What do you mean by "We conducted over-sampling for ethnic minority groups"? Do you mean that more participants were selected from these groups? Please clarify. • How was sample size calculated? • Please add more data about the informed consent process. • Page 8, line 25: I am not sure that the option "I am afraid of them" is associated with stigma. Maybe of you say "I am afraid of them and avoid them." Was this question used in previous studies? Discussion • Page 10, line 24: You mentioned that "Overall, the prevalence of stigma was low in China during the COVID-19 pandemic". Were there any previous studies about stigma associated with other diseases in China? It would be interesting to compare this prevalence with past studies. • It would also be interesting to look into the recent literature about stigma against Chinese/Asian people in other countries. There were individual incidents, but was there a trend in some countries /communities against them? How did this attitude evolve overtime? • One interesting insight of the manuscript is the negative association between health literacy and stigma. A lot of information has been provided by the media about the disease. I would think: was this "too much" information associated with growth or decline of stigma? Sometimes loading the person with a lot of information causes confusion and unexpected attitude. The authors can conduct a similar study now to ask "After one year of the pandemic, was health literacy associated with decline of stigma?" This is just a suggestion. • You mentioned that provinces with more ethnic minorities had higher levels of stigma towards COVID-19 patients. Why do you think this happened?

REVIEWER	Baron, Marie VITAM: Research Center on Sustainable Health
REVIEW RETURNED	12-Feb-2021

GENERAL COMMENTS	This is an interesting and useful paper. I would like to suggestion a few improvement points before publication.

	- Introduction: the reference 6 refers in the text to stigma and infectious disease, but the reference's title refers to schizophrenia. Could you explain the link? - P 5 : 100-200 families were selected in each province. Did all selected families answer to the survey? If not, could you present the non-response rates and interpret their possible influence on the results? If yes, could you add more details on the recruitment process that explained this successful number? - P6 : you describe an online survey. Was it possible to include families with no internet connexions? Did you provide technological support to ensure the participation of all families? If not, what could be the exclusion of people without an access to internet on the results? - P6 : You used perceived health literacy measures. What are the limitations of using self-reported health literacy levels compared to health literacy evaluations, for example, for your study? - P 7-8 : First, giving clear title to your figures would be very helpful. Second, I find it hard to interpret the three figures in relationship to each other. Using spatial analyses would be very interesting for this study and I strongly suggest that you test the relationships between the cumulative confirmed cases, stigma and region of residence. I would be very interested to see these results. - Discussion: I would like to read more on the hypotheses you have to explain the differences between factors influencing stigma against covid-19 patients versus stigma against Wuhan residents. As you used Wuhan province as a concept to measure areas with a high number of covid-19 cases, I wonder what can be the reasons between these variations.

REVIEWER	Ahmad, Noor Ani Institute for Public Health, National Institutes of Health, Ministry of Health Malaysia
REVIEW RETURNED	15-Feb-2021

GENERAL COMMENTS	Manuscript ID bmjopen-2021-048983 Title: "COVID-19-related stigma and its influencing factors: a nationwide cross-sectional study in China." The authors should highlight that this study was conducted in the early phase of epidemic; first two weeks of March 2020, which might influence the findings. The title and objectives should highlight this. The study should be more informative if the authors can repeat the study at later stage and compare the stigma status over time. Limitations: should discuss limitations of web-based survey. Should also mention level of internet penetration at the chosen provinces. References: please update the references to those less than 10 years

VERSION 1 – AUTHOR RESPONSE

Reviewer #1:
Comments to the Author:
Comment 1: This is an interesting study but the authors would benefit from having the manuscript reviewed by a medical writer to more clearly communicate the main findings. It does not currently read as a scholarly manuscript suitable for publication.
Response: We went through the manuscript carefully and revised accordingly. We also invited a native English speaker to review and revise the article to improve its readability.

Comment 2: When measuring health literacy, it would have been more ideal to ask the respondents "to what extent so you agree with the following statements" as opposed to "do you agree that…"
Response: The confusion might come from a translation issue. We have revised the expression in accordance with your comments (Methods, page 6, line 22).

Comment 3: Table 4 is not clear. For example, why are there four columns of odds ratio with 95% confidence interval (2 for patients & 2 for Wuhan residents).
Response: We agree that the current display of results would cause misunderstanding. Thus, we have changed the four columns into two columns with two models. Model 1 is a Logistic regression analysis without considering the health literacy. While Model 2 includes the health literacy thus to see the possible impact of health literacy on stigmatizing attitudes. We also added footnotes and endnotes to the table to make it clear for the reader (page 22, Table 4).

Comment 4: Further, logistic regression is ideal when the outcome of interest is expected to be rare (<10%) event. On occasion when have a common/prevalent (not rare) event as was the case with stigma, then a Poisson regression may be more ideally suited.
Response: We agree that Logistic regression is ideal when the outcome of interest is expected to be rare (<10%) event, and the proportion of stigma was low in our survey (<10%). We thus chose to use Logistic regression. We also reviewed the literature to confirm that using Logistic regression was suitable since the outcome was rare (<10%) event.[1,2]
References:
1. Zocchetti C, Consonni D, Bertazzi PA. Estimation of prevalence rate ratios from cross-sectional data. Int J Epidemiol. 1995;24(5):1064-1067.
2. Zou G. A modified poisson regression approach to prospective studies with binary data. Am J Epidemiol. 2004;159(7):702-706.

Reviewer #2:
Comments to the Author:
Dear Authors,

your contribution proposal deals with a criticality that has plagued public health for decades, often underestimated by stakeholders called upon to manage exceptional events such as the ongoing CoViD-19 pandemic.
Discrimination and stigma are an atavistic problem, which has its roots in the foundation of some States and which only a purposeful and proactive cultural movement can overturn over the years What happened in the near past must be the starting point so that similar episodes no longer occur; but man, unfortunately, has a short memory.

Thank you for sharing your contribution proposal, that should be addressed as letter to the editor or narrative review, since it cannot be defined as "original article".

I believe you can further improve the elaborate, still a bit raw as a potential interest for both the scientific community and general audience. I tried to give you some suggestions to help you in this very first review phase.
Comment 1: Why not SARS-CoV-2 among keywords? why not i.e. stigma/discrimination, disparities, inequalities?
Response: We agree that these are really important keywords. Unfortunately, these keywords are not in the list of keywords provided by the submission system and cannot be added.

Comment 2: Please contextualize and deepen the current pandemic scenario when introducing your work;
Response: In the first paragraph of the methods part (page 5, line 5-8), we added information about the current pandemic scenario in China and worldwide to help readers understand the research background more clearly. The added content was shown as below:
The World Health Organization (WHO) declared COVID-19 as a pandemic in March 2020, and our study was conducted between 1 March and 16 March, 2020. As of 16 March, 2020, there were more than 80,000 confirmed cases in China and more than 100,000 cases globally, and during this time people in China were under strict social-distancing policies.

Comment 3: Please upload the questionnaire ("Additional file 1" as reported in methods - study design and participants).
Response: We have uploaded the questionnaire as a supplementary file accordingly.

Comment 4: It's not clear if participants gave an informed consent or not.
Response: Before completing the questionnaire, respondents were informed in the consent statement that this was an anonymous and voluntary survey. We have added this sentence to the methods part (page 6, line 4-5).

Comment 5: Please report the of ethics committee approval number.
Response: This study was approved by the Ethics Committee of the School of Public Health, Zhejiang University (No. ZGL202002-3). We have added the ethical approval code in the methods part accordingly (page 6, line 7).

Comment 6: The methodological part must be thoroughly revised, completing it with the administered questionnaire.
Response: We have thoroughly revised the method section to make this paper more readable (Methods, page 5-7).

Comment 7: Discussion's paragraphs can be improved further.

You need conclusions, too port in this first attempt. What are the possible repercussions? What suggestions to give to the health policy maker? Define a clear "take home message" from your perspective and address a conclusion section.

The alleged identification of "scientific" bases of stigmata characterizing certain groups of population being the first, decisive and irreversible step towards the creation of a sort of "expendable victims", according to one well known pattern from the history of this kind of human affairs.
You should also refer toother examples of scientific literature that have completely misled epidemiological findings.

Please update these gaps referring to the following non-exhaustive non-mandatory references list:

- Irigoyen-Camacho, M.E.; Velazquez-Alva, M.C.; Zepeda-Zepeda, M.A.; Cabrer-Rosales, M.F.; Lazarevich, I.; Castaño-Seiquer, A. Effect of Income Level and Perception of Susceptibility and Severity of COVID-19 on Stay-at-Home Preventive Behavior in a Group of Older Adults in Mexico City. Int. J. Environ. Res. Public Health 2020, 17, 7418

- Baldassarre, A.; Giorgi, G.; Alessio, F.; Lulli, L.G.; Arcangeli, G.; Mucci, N. Stigma and Discrimination (SAD) at the Time of the SARS-CoV-2 Pandemic. Int. J. Environ. Res. Public Health 2020, 17, 6341

- Sarah Dryhurst, Claudia R. Schneider, John Kerr, Alexandra L. J. Freeman, Gabriel Recchia, Anne Marthe van der Bles, David Spiegelhalter & Sander van der Linden (2020) Risk perceptions of COVID-19 around the world, Journal of Risk Research, DOI: 10.1080/13669877.2020.1758193

- Wong, B.Y.-M.; Lam, T.-H.; Lai, A.Y.-K.; Wang, M.P.; Ho, S.-Y. Perceived Benefits and Harms of the COVID-19 Pandemic on Family Well-Being and Their Sociodemographic Disparities in Hong Kong: A Cross-Sectional Study. International Journal of Environmental Research and Public Health 2021, 18, 1217

- Weinstein, B.; da Silva, A.R.; Kouzoukas, D.E.; Bose, T.; Kim, G.J.; Correa, P.A.; Pondugula, S.; Lee, Y.; Kim, J.; Carpenter, D.O. Precision Mapping of COVID-19 Vulnerable Locales by Epidemiological and Socioeconomic Risk Factors, Developed Using South Korean Data. International Journal of Environmental Research and Public Health 2021, 18, 604

- Dye, T.D.; Alcantara, L.; Siddiqi, S.; Barbosu, M.; Sharma, S.; Panko, T.; Pressman, E. Risk of COVID-19-related bullying, harassment and stigma among healthcare workers: an analytical cross-sectional global study. BMJ Open 2020, 10, e046620
Response: The references you provided were valuable and provided us with many new insights for discussion. Benefiting from your comments, we have added the following revisions to the discussion part.

The possible consequences of stigma were discussed in discussion part and was shown as below:
Page 9, line 16-21: Historically, infectious diseases have long been associated with stigma. During the early stage of the COVID-19 pandemic, potentially deadly conditions, the lack of effective treatments, and rumors increased the risk of stigmatization. The stigma associated with COVID-19 threatens the physical and mental health of COVID-19 patients and residents of Wuhan. In the long run, stigmatization also damages the cultural fabric of society and undermines efforts to control pandemics, creating an atmosphere of fear and distrust.

Suggestions were provided to health policy makers in discussion part and was shown as below:
Page 10, line 3-6: COVID-19-related stigma is not unique to China, and has been reported in the United States, Australia, Nepal and other countries. These facts should remind health policy makers to attach more importance to community-based stigma reduction interventions and campaigns.

The possible causes of the influencing factors of stigma were further discussed:
Page 11, line 19-26: The elderly were more likely to progress to severe disease after infection or suffer complications from COVID-19 than younger adults, and had higher perceived susceptibility and perceived severity during the pandemic, which might explain why the elderly were more likely to hold stigmatizing attitudes. The majority of ethnic minorities in China live in less developed mountainous inland or border districts in the western region, and possess relatively low levels of education and income, which have been identified as negative influencing factors for stigma in previous studies and may partially explain their higher levels of stigmatization.

A clear "take home message" was added in the Conclusion part and was shown as below:
Page 12, line 23-28: Those who had low health literacy, who lived in areas with a large number of COVID-19 cases, and who were ethnic minorities were more likely to stigmatize others in the early stage of the pandemic. Although a COVID-19 vaccine is available globally, it will still take time to achieve herd immunity. Before COVID-19 can be controlled globally, tailored interventions are encouraged to improve health literacy and consequently to reduce public COVID-19-related stigma at both the individual and community levels.

Additionally, we have gone through the whole discussion and made some amendments based on your comments.

Comment 8: In the conclusions you should refer to the very recent introduction of vaccines; what would change in this scenario? deal with it, even because CoViD-19 vaccines are now available all over the globe.
Response: We have added discussion about the very recent introduction of vaccines (Conclusion, page 12, line 25-28) and the added content was shown as below:
Although a COVID-19 vaccine is available globally, it will still take time to achieve herd immunity. Before COVID-19 can be controlled globally, tailored interventions are encouraged to improve health literacy and consequently to reduce public COVID-19-related stigma at both the individual and community levels.

Reviewer #3:
Comments to the Author:
Thank you for allowing me to review this manuscript. Social stigma is one of the hidden threats of COVID-19, and it might lead to negative impact on the individuals and societies. The manuscript is interesting, well presented and well written, and the language is clear. Kindly find my comments below.

General comment: Although the topic of the manuscript is interesting and important, the data are a bit outdated. Data were collected in March 2020 and COVID-19 sitaution has changed a lot during the past months. To overcome this limitation, I suggest that the authors add more insights from recent publications about the topic of stigma. Many documents, original research, reviews and mini-review articles were published about the topic of social stigma as a threat during COVID-19 pandemic. Some of these documents provided recommendations or solutions about how to deal with stigma. Please have a look at them and use them in the discussion.
Response: Thank you for your helpful comments. In the discussion part, based on recent publications about the topic of stigma, we made a further comparison of the stigma prevalence (page 9, line 21-28), further discussed the nature of stigma and its relationship with knowledge/literacy (page 10, line 8-11), described the geographic distribution of stigma during the COVID-19 pandemic (page 11, line 1-3), discussed the possible impact of risk perception (page11, line 7-11), and deeply analyzed the influence of sociodemographic factors (page 11, line 17-26). We also provided targeted suggestions to health policy makers (page 10, line 4-6). Additionally, we have gone through the whole discussion and made some amendments based on your comments.
Specific comments
Comment 1: Objectives: Please put the two objectives in one sentence as follows "…the city of Wuhan in China, and to assess the association ….".
Response: It has been modified accordingly in the Objectives part of abstract (page 2, line 3).

Comment 2: Participants: You already mentioned that the study was carried out in 31 provinces in China in the setting. You don't have to mention it again here.
Response: We have changed accordingly in the Participants part of abstract (page 2, line 8).

Comment 3: Conclusion: line 55: You mentioned that “Tailored interventions were encouraged” Please change into the present tense “are encouraged” instead of the past tense.
Response: It has been modified accordingly (Abstract, page 2, line 25).

Comment 4: Page 4, line 12: You describe COVID-19 as an outbreak. Although this was correct in the beginning, but in March 2020, the WHO declared COVID-19 as a pandemic.
Response: It has been modified as a pandemic (Introduction, page 5, line 5) and elsewhere in the whole manuscript.

Comment 5: Page 4, Line 16: You mentioned that “This is a cross-sectional study with an over sample of minorities” This sentence is not clear for me. Do you mean that the majority of participants were young? Please clarify.
Response: This sentence is intended to express that we set up a target sample for ethnic minorities residents and ethnic minorities were over-sampled in this survey to examine the relationship between stigma and ethnicity since the previous study showed ethnicity was an influencing factor of stigma.[1] We have replaced minorities to ethnic minorities (page 3, line 6).
Reference:

1. Wong LP. Prevalence and factors associated with HIV/AIDS-related stigma and discriminatory attitudes: a cross-sectional nationwide study. Prev Med. 2013;57 Suppl:S60-S63.

Comment 6: Page 6, line 27: You mentioned that "We conducted 30 online face-to-face interviews with respondents" I think it is not right to say "online" and "face to face" together. Face to face usually means in person.
Response: We have replaced the “face to face” with the “one to one” (Methods, page 5, line 16).

Comment 7: Would you please explain who the ethnic minorities in the context of this work are?
Response: There are 55 different ethnic minorities (e.g., Zhuang, Man, Hui, Miao, Uyghur, Tujia, Yi, Mongo, Tibetan, Buyei etc.) in China. Our study covered people from 28 different ethnic minorities. Most of them are Tibetan (122), Yi (121), Uyghur (106), Hui (103), Miao (60), and Mongo (55).

Comment 8: Page 6, line 47: What do you mean by "We conducted over-sampling for ethnic minority groups"? Do you mean that more participants were selected from these groups? Please clarify.
Response: We set up a target sample for ethnic minorities residents in order to examine the relationship between stigma and ethnicity since the previous study showed ethnicity was ainfluencing factor of stigma.[1]
Reference:

1. Wong LP. Prevalence and factors associated with HIV/AIDS-related stigma and discriminatory attitudes: a cross-sectional nationwide study. Prev Med. 2013;57 Suppl:S60-S63.

Comment 9: How was sample size calculated?
Response: Sample size calculation was added to the Methods section (page 5, line 28; page 6, line 1-4) and was shown as below.
A sample size of 3,062 was estimated based on a prevalence estimate of 50%, the ±2% margin of error and upward adjusted by 20% considering potential non-response. We set up a target sample for ethnic minorities residents and over-sampled respondents who lived in Wuhan, as it was the center of the pandemic. We intentionally balanced respondents from urban and rural areas while conducting this survey.

Comment 10: Please add more data about the informed consent process.

Response: Thanks for the note. We have added the informed consent process accordingly in the methods part (page 6, line 4-5) and the revision was shown as below:
Before completing the questionnaire, respondents were informed in the consent statement that this was an anonymous and voluntary survey.

Comment 11: Page 8, line 25: I am not sure that the option "I am afraid of them" is associated with stigma. Maybe of you say "I am afraid of them and avoid them." Was this question used in previous studies?
Response: Yes, the question was adopted from a previous study.[1] We agree and have changed the statement to “I am afraid of them and avoid them.”
Reference:

1. Datiko DG, Jerene D, Suarez P. Stigma matters in ending tuberculosis: Nationwide survey of stigma in Ethiopia. BMC Public Health. 2020;20(1):190.

Comment 12: Page 10, line 24: You mentioned that "Overall, the prevalence of stigma was low in China during the COVID-19 pandemic". Were there any previous studies about stigma associated with other diseases in China? It would be interesting to compare this prevalence with past studies.
Response: We compared the prevalence of stigma with the previous studies in the discussion part (page 9, line 21-28)and was shown as below:
Previous studies identified COVID-19-related public stigma as more prevalent and severe when compared with our findings. According to a global survey involving 173 countries, nearly a third of participants believed that people talked badly or gossiped about other people who were thought to associated with COVID-19, and 21.9% of participants believed people who had COVID-19 were not respected by the community.[1] An online survey in February 2020 in China also showed that about half of participants reported they would avoid people from Hubei and 16.9% would even try to expel them from their communities.[2]
References:

1. Dye TD, Alcantara L, Siddiqi S, et al. Risk of COVID-19-related bullying, harassment and stigma among healthcare workers: an analytical cross-sectional global study. BMJ Open. 2020;10(12):e046620.
2. He J, He L, Zhou W, et al. Discrimination and Social Exclusion in the Outbreak of COVID-19. Int J Environ Res Public Health. 2020;17(8):2933.

Comment 13: It would also be interesting to look into the recent literature about stigma against Chinese/Asian people in other countries. There were individual incidents, but was there a trend in some countries /communities against them? How did this attitude evolve overtime?
Response: Thank you for the insightful comment. Evidence based on the recent literature suggested that there was a rapidly increasing trend of stigmatization against Asians during the COVID-19 pandemic.[1,2] Between March and December 2020, the organization Stop Asian American and Pacific Islander Hate, which launched in response to the growing sentiment, recorded nearly 3,000 reports of anti-Asian hate incidents nationwide. The New York City Police Department also reported a 1,900% increase in anti-Asian hate crimes in 2020.[3] This trend reminds health policy makers to attach more importance to community-based stigma reduction interventions and campaigns.
References:

1. Chen JA, Zhang E, Liu CH. Potential Impact of COVID-19-Related Racial Discrimination on the Health of Asian Americans. Am J Public Health. 2020;110(11):1624-1627.
2. Dye TD, Alcantara L, Siddiqi S, et al. Risk of COVID-19-related bullying, harassment and stigma among healthcare workers: an analytical cross-sectional global study. BMJ Open. 2020;10(12):e046620.
3. ABC News. Available: https://abcnews.go.com/US/scapegoated-asians-asian-americans-speak-spate-violence/story?id=75956385

Comment 14: One interesting insight of the manuscript is the negative association between health literacy and stigma. A lot of information has been provided by the media about the disease. I would think: was this "too much" information associated with growth or decline of stigma? Sometimes loading the person with a lot of information causes confusion and unexpected attitude. The authors can conduct a similar study now to ask "After one year of the pandemic, was health literacy associated with decline of stigma?" This is just a suggestion.
Response: Thank you for your valuable suggestion. We agree with your comments that the media has provided a lot of information and sometimes loading the person with a lot of information causes confusion and unexpected attitude. Take stigma on HIV/AIDS as an example, previous studies on HIV/AIDS stigma revealed that people who were well informed about HIV/AIDS were more likely to accurately assess the threat posed by the virus and engage in preventive behaviors.[1] Informing the public and enabling them to gain the information that is necessary for action have therefore remained a major prevention goal. In addition, a noticeable phenomenon was that information provided by the media may widen the gap between urban and rural residents.[2] We agree that further research deserves to be done.
References:

1. Bekalu MA, Eggermont S. Media use and HIV/AIDS knowledge: a knowledge gap perspective. Health Promot Int. 2014;29(4):739-750.
2. Pantelic M, Shenderovich Y, Cluver L, et al. Predictors of internalised HIV-related stigma: a systematic review of studies in sub-Saharan Africa. Health Psychol Rev. 2015;9(4):469-490.

Comment 15: You mentioned that provinces with more ethnic minorities had higher levels of stigma towards COVID-19 patients. Why do you think this happened?
Response: The majority of ethnic minorities in China live in the less developed mountainous inland or border districts in the western region. Their education, income, health services utilization, and health outcomes remain poorer than its Han counterparts (91.5% of the overall Chinese population, non-minority).[1,2] Previous researchers have argued that discrepancies amongst the social determinants (e.g., education, income, race/ethnicity) would cause inequities in the accessing, processing, and utilization of risk communication messages during epidemics.[3-5] This disadvantage may lead to a higher perception of risk among ethnic minorities, and partly explain why they were more likely to hold stigmatizing attitudes towards COVID-19 patients in our study. Previous studies have also identified ethnic minority was an influencing factor of stigma, which was consistent with our findings.[6,7]
References:

1. Zhang S, Lo EC, Liu J, et al. A review of the dental caries status of ethnic minority children in China. J Immigr Minor Health. 2015;17(1):285-297.
2. Gary FA. Stigma: barrier to mental health care among ethnic minorities. Issues Ment Health Nurs. 2005 Dec;26(10):979-99.
3. Huang Y, Shallcross D, Pi L, et al. Ethnicity and maternal and child health outcomes and service coverage in western China: a systematic review and meta-analysis. The Lancet Global Health 2018; 6(1): e39-e56.
4. Liu X, Gao W, Yan H. Measuring and decomposing the inequality of maternal health services utilization in western rural China. BMC Health Serv Res 2014; 14: 102.
5. Castro Campos B, Ren Y, Petrick M. The impact of education on income inequality between ethnic minorities and Han in China. China Economic Review 2016; 41: 253-67 PubMed .
6. Wong LP. Prevalence and factors associated with HIV/AIDS-related stigma and discriminatory attitudes: a cross-sectional nationwide study. Prev Med. 2013;57 Suppl:S60-S63.
7. Peluso Ede T, Blay SL. Public stigma in relation to individuals with depression. J Affect Disord. 2009;115(1-2):201-206.

Reviewer #4:
Comments to the Author:
This is an interesting and useful paper. I would like to suggestion a few improvement points before publication.
Comment 1: Introduction: the reference 6 refers in the text to stigma and infectious disease, but the reference's title refers to schizophrenia. Could you explain the link?
Response: Thank you very much for pointing out the misquote. We replaced a review of infectious diseases as a reference accordingly (Introduction, page 3, line 16).

Comment 2: P 5: 100-200 families were selected in each province. Did all selected families answer to the survey? If not, could you present the non-response rates and interpret their possible influence on the results? If yes, could you add more details on the recruitment process that explained this successful number?
Response: The study response rate was 94.7% and was added to the results part (page 7, line 17). Unfortunately, we were unable to investigate the situation of non-responders. According to the feedback of investigators, most of the reasons for non-response were too busy. We have added it to the limitations (page 12, line 7-11).

Comment 3: P6: you describe an online survey. Was it possible to include families with no internet connexions? Did you provide technological support to ensure the participation of all families? If not, what could be the exclusion of people without an access to internet on the results?
Response: Families with no internet connexions were not included in this survey. We could not ensure all families to participate this survey due to social distancing policies during the pandemic. This online survey may result in selection bias. However, China's Internet penetration rate was 70.4% as of December 2020, and most people in China had access to the Internet via smartphones.[1] We added this to the limitations in the discussion part (page 12, line 7-11) and was shown as below.
Second, this is an online survey, and people who did not have access to the Internet were not included, which may result in selection bias. However, as of December 2020, China's Internet penetration rate was 70.4%, and most people in China had access to the Internet via smartphones.[1]
Reference:
1. China Internet Network Information Center. Statistical report on the development of the Internet in China, 2021. Available: https:// http://www.cnnic.net.cn/

Comment 4: P6: You used perceived health literacy measures. What are the limitations of using self-reported health literacy levels compared to health literacy evaluations, for example, for your study?
Response: We used self-reported health literacy, which may be overreported due to social desirability,[1] and may thus lead to an underestimation of the impact of health literacy on stigma. We have added this as a limitation in the discussion part (page 12, line 11-13) and was shown as below.
Third, health literacy and stigmatizing attitudes rely on self-reporting, and may thus lead to an underestimation of the impact of health literacy on stigma.[1]
Reference:
1. Latkin CA, Edwards C, Davey-Rothwell MA, et al. The relationship between social desirability bias and self-reports of health, substance use, and social network factors among urban substance users in Baltimore, Maryland. Addict Behav. 2017;73:133-136.

Comment 5: P 7-8: First, giving clear title to your figures would be very helpful. Second, I find it hard to interpret the three figures in relationship to each other. Using spatial analyses would be very interesting for this study and I strongly suggest that you test the relationships between the cumulative confirmed cases, stigma and region of residence. I would be very interested to see these results.
Response: The titles of figures have been added in the end of the main manuscript (page 18, line 2-8). Due to the small number of COVID-19 cases in each province, we divided provinces into four

groups based on the cumulative number of COVID-19 cases, and conducted Logistic regression to test the relationship between regions with different cumulative confirmed cases and stigma. Our result showed that compared with people living in low case areas, people living in low-medium case areas and high case areas were 1.74 and 2.03 times more likely to stigmatize COVID-19 patients, respectively (page 9, line 1-3).

Comment 6: Discussion: I would like to read more on the hypotheses you have to explain the differences between factors influencing stigma against covid-19 patients versus stigma against Wuhan residents. As you used Wuhan province as a concept to measure areas with a high number of covid-19 cases, I wonder what can be the reasons between these variations.
Response: We supplemented the discussion on factors influencing stigma (page 11, line 17-26), and explained the differences between factors influencing stigma against covid-19 patients versus stigma against Wuhan residents (page 11, line 11-14). As of March 1, 2020, Hubei Province had a total of 67,103 confirmed COVID-19 cases, of which 49,315 were in Wuhan. Thus, Wuhan was classified as an area with high cases in our study. The added content was shown as below:
In our study, people living in areas severely affected by the COVID-19 pandemic were at higher risk of social interaction with potential COVID-19 patients. Thus, they might have higher risk perceptions, expect to have less social interaction with potential COVID-19 patients, and therefore may hold higher levels of stigma. Interestingly, there was no significant regional differences in attitudes towards residents of Wuhan. A possible reason was that the public perceived the risk posed by COVID-19 patients to be higher than that posed by residents of Wuhan.

Reviewer #5:
Authors should highlight that this study was conducted in the early phase of epidemic; first two weeks of March 2020, which might influence the findings. The study should be more informative if the authors can repeat the study at later stage and compare the stigma status over time.

Please see attached comments
Comment 1: The authors should highlight that this study was conducted in the early phase of epidemic; first two weeks of March 2020, which might influence the findings. The title and objectives should highlight this.
Response: Thank you for your helpful comments. We have changed the title to “COVID-19-related stigma and its influencing factors: a nationwide cross-sectional study during the early stage of the pandemic in China”. We also highlighted the survey was conducted during March 2020, the early stage of the pandemic in the objectives section (page 2, line 4). In the methods part (page 5, line 5-8), we made a detailed introduction to the survey time and the pandemic situation, and added content was shown as below.
The World Health Organization (WHO) declared COVID-19 as a pandemic in March 2020, and our study was conducted between 1 March and 16 March, 2020. As of 16 March, 2020, there were more than 80,000 confirmed cases in China and more than 100,000 cases globally, and during this time people in China were under strict social-distancing policies.

Comment 2: The study should be more informative if the authors can repeat the study at later stage and compare the stigma status over time.
Response: Thank you for your valuable suggestion. We agree with your comment that further comparative studies will enrich our findings.

Comment 3: Limitations: should discuss limitations of web-based survey. Should also mention level of internet penetration at the chosen provinces.
Response: The limitation of web-based survey and the level of Internet penetration in China was discussed in the discussion part (page 12, line 7-11). The added content was shown as below:

Second, this is an online survey, and people who did not have access to the Internet were not included, which may result in selection bias. However, as of December 2020, China's Internet penetration rate was 70.4%, and most people in China had access to the Internet via smartphones.[1]
Reference:

1. China Internet Network Information Center. Statistical report on the development of the Internet in China, 2021. Available: https:// http://www.cnnic.net.cn/

Comment 4: References: please update the references to those less than 10 years
Response: The references were updated accordingly.

VERSION 2 – REVIEW

REVIEWER	Baldassarre, Antonio University of Florence, Doctoral School in Clinical Sciences
REVIEW RETURNED	04-Apr-2021

GENERAL COMMENTS	Dear Authors, conclusions results still poor. You have to expand this section by explaining the "tailored interventions" you cite, and how to stakeholder, health policy makers should be involved in managing this issue. Thanks for your contribution,

VERSION 2 – AUTHOR RESPONSE

Reviewer #2:
Comments to the Author:
Dear Authors,
Conclusions results are still poor. You have to expand this section by explaining the "tailored interventions" you cite, and how to stakeholder, health policy makers should be involved in managing this issue.
Thanks for your contribution.

Response: We have detailed the specific measures of tailored intervention by providing recommendations for stakeholders and health policy makers. Please kindly refer to page 12, line 26-28 and page 13, line 1-6 that we have added.
We recommend joint actions of all sectors of our society, including but not limited to governments, health institutions, and public figures, such as athletes, communicators and social influencers to reduce the COVID-19-related stigmatization. Health policy makers should include early prevention and elimination of stigma into emergency preparedness plans for infectious diseases. Community-based stigma reduction interventions targeted the ethnic minorities and those lived near the epidemic center are encouraged to support the most stigmatized groups. In addition, information campaigns to offer a better access and easy understandable messages thus to increase public health literacy of infectious diseases by medical authorities and the media are recommended.