

Response Letter

Dear Dr. editor, Dr. Reviewers, and the Company Editor-in-Chief, Dr. Ma,

Thank you for your letter and comments on our manuscript titled 'Time series analysis-based seasonal autoregressive fractionally integrated moving average to estimate hepatitis B and C epidemics in China' (Manuscript NO.: 87364). These comments helped us improve our manuscript, and provided important guidance for future research. We have addressed the comments raised by the reviewers and editor to the best of our abilities. The amendments are highlighted with yellow color in the revised manuscript and the revised manuscript has been re-submitted for your consideration. Besides, we have revised the text to meet the style requirements of *World Journal of Gastroenterology* and also hoped this to meet your requirements for a publication. Point by point responses to the Company Editor-in-Chief's, the editor's and the reviewers' comments are listed below this letter.

We hope that the revised version of the manuscript is now acceptable for publication in your journal.

I look forward to hearing from you soon.

With best wishes,

Yongbin Wang

Professor

Corresponding author

We would like to express our sincere thanks to the editor and reviewers for the constructive and positive comments.

Replies to Reviewer #1

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: No special comment.

Response: Thanks very much for your suggestion. To further improve the clarity and readability of our revised manuscript, we have used the English language editing services for language usage, spelling, and grammar. The edited version and certificate of English editing certificate were also submitted in the related attachments and we hoped to meet the language requirements of World Journal of Gastroenterology at this time.

Replies to Reviewer #2

Comments to the manuscript: Time series analysis-based seasonal autoregressive fractionally integrated moving average to estimate and control hepatitis B and C epidemics in China. The present study made by Wang YB *et al*, aim to evaluate the usefulness of SARFIMA in monitoring and containing HB and HC epidemics (projection into 2030) in mainland China; and to assess the forecasting potential of paradigm seasonal autoregressive fractionally integrated moving average (SARFIMA) and comparing the effectiveness with seasonal autoregressive integrated moving average (SARIMA).

1. Title:

It is advisable to adjust the title of this research: omitting the word "control"; Since the scope of this research only reaches the comparison of the two prediction methods, and the prediction of hepatitis B and C in China for the year 2030.

Response: Thanks very much for your suggestion. Based on this suggestion, we have removed the 'control' from the title. The title has changed to "Time series analysis-based seasonal autoregressive fractionally integrated moving average to estimate hepatitis B and C epidemics in China". Besides, we also adjust some statements in the whole text of the revised version.

2. Abstract:

The abstract is clear, and adequately describes the state of the art of the subject of study and is consistent with the title of the study.

Response: Thanks very much for your positive comments.

3. Background:

The introduction is adequate and allows a proper understanding of the problem, and the first-degree hypotheses.

Comments

This research is of practical importance due to the high prevalence and incidence of Hepatitis B (HB) and hepatitis C (HC) not only in China, but in various parts of the world. Making accurate predictions will help develop better strategies to reduce not only this infectious problem, but also its relationship with liver cirrhosis, liver cancer, and mortality related to viral hepatitis.

Response: Thanks very much for your positive comments.

4. Discussion

The results support the hypothesis that the SARFIMA method as a more comprehensive approach for capturing the epidemic dynamics of HB and HC compared to SARIMA. With this study, the

researchers demonstrated that unlike the global downward trend in the incidence of HB and HC, in the Chinese population a general increase was observed at an average rate of 0.44% for HB and 8.91% for HC per year, is consistent with previous studies in Guangxi. Although it would be interesting if the researchers explained a little more about all the factors associated with the behavior of these two infections (HB and HC). For example, commenting a little more about all the variables analyzed (since the authors described that the SAFIRMA method is useful in the analysis of a greater number of variables); It would be of interest if the authors describe how the following variables can affect or influence the observed results: a) the age of the affected population, b) the nutritional status of the population, c) the comorbidities (diabetes, hypertension, immunological problems, among many others), d) the characteristics of the water consumed daily, e) the hygiene habits, f) the habits or cultural patterns (infection risk) in the period of spring celebrations, and g) immunological resistance due to the genetic characteristics of the Chinese population, among others.

Response: Thanks very much for your suggestion. Based on this suggestion, we have added the effect of the age of the affected population and the habits or cultural patterns (infection risk) in the period of spring celebrations on the observed results. As we can only obtain the monthly data during 2004-2019 related to the age of the affected population (<https://www.phsciencedata.cn/Share/>), So we used these data to estimate the effect of the age of the affected population on the observed results. These results have been added in **L325-330 and L347-348** in the revised version: “Moreover, two sensitivity analyses were conducted to examine the influence of the age of the affected population and the cultural patterns during the spring season on the predictive quality of SARFIMA. These analyses indicated that SARFIMA consistently produced lower forecasting error rates compared to SARIMA (Supplementary Tables 5 and 6). This reinforces the robustness of the SARFIMA (**L347-348**); “Importantly, the forecasting robustness was confirmed by our further sensitivity analyses (Supplementary Tables 5 and 6)”. The resulting results and details can be found below:

Supplementary Table 5 Comparison of the forecasting ability under the seasonal autoregressive integrated moving average and the seasonal autoregressive fractionally

integrated moving average model constructed using the data from different age groups between January 2004 and December 2019.

Metrics	Hepatitis B		Hepatitis C	
	SARIMA	SARFIMA	SARIMA	SARFIMA
0-14 years old*				
MAD	125.336	65.350	35.972	35.940
MAPE	0.200	0.105	0.348	0.347
RMSE	143.401	84.209	43.361	43.284
MER	0.190	0.099	0.282	0.282
RMSPE	0.235	0.135	0.467	0.466
15-64 years old*				
MAD	5143.208	4383.085	866.012	571.380
MAPE	0.072	0.060	0.064	0.043
RMSE	5874.019	5450.755	1056.119	781.632
MER	7.802	6.649	6.789	4.479
RMSPE	0.082	0.072	0.079	0.060
65 and above years old*				
MAD	1798.493	1653.961	697.902	650.415
MAPE	0.157	0.142	0.162	0.151
RMSE	1897.415	1797.900	757.843	707.928
MER	2.728	2.509	5.471	5.099
RMSPE	0.164	0.150	0.172	0.160

* In Hepatitis B forecasting, the best SARIMA models were SARIMA(3,1,0)(0,1,2)₁₂ for the 0-14 years old, SARIMA(0,1,1)(2,1,1)₁₂ for the 15-64 years old, and SARIMA(2,1,1)(2,1,0)₁₂ for the 65 and above years old; the best SARFIMA models were SARFIMA(3,-0.232,0)(0,0.048,2)₁₂ for 0-14 years old, SARFIMA(0,0.484,1)(2,-0.185,1)₁₂ for 15-64 years old, and SARFIMA(2,-0.093,1)(2,-0.437,0)₁₂ for the 65 and above years old. In Hepatitis C forecasting, the best SARIMA models were SARIMA(1,1,1)(2,0,0)₁₂ for the 0-14 years old, SARIMA(3,1,0)(2,1,0)₁₂ for the 15-64 years old, and SARIMA(1,1,0)(2,0,2)₁₂ for the 65 and

above years old; the best SARFIMA models were SARFIMA(1,-0.33,0)(2,0,0)₁₂ for 0-14 years old, SARFIMA(3,-0.142,0)(2,-0.203,0)₁₂ for 15-64 years old, and SARFIMA(1,0,1)(2,-0.072,2)₁₂ for the 65 and above years old. SARIMA: Seasonal autoregressive integrated moving average; SARFIMA: Seasonal autoregressive fractionally integrated moving average; MAD: Mean absolute deviation; MAPE: Mean absolute percentage error; RMSE: Root mean square error; MER: Mean error rate; RMSPE: Root mean square percentage error.

Supplementary Table 6 Comparison of the forecasting ability under the seasonal autoregressive integrated moving average and the seasonal autoregressive fractionally integrated moving average

Metrics	Hepatitis B		Hepatitis C	
	SARIMA	SARFIMA	SARIMA	SARFIMA
	(0,1,1)(2,0,2) ₁₂	(0,0.499,1)(2,0.392,2) ₁₂	(0,1,1)(2,0,0) ₁₂	(1,0,1)(2,0.365,0) ₁₂
MAD	14780.282	14578.232	3282.314	3223.797
MAPE	0.177	0.174	0.2035	0.2034
RMSE	20172.797	19011.714	4055.280	3994.377
MER	0.145	0.143	0.174	0.171
RMSPE	0.277	0.268	0.284	0.289

Note: here the SARIMA and SARFIMA were developed by considering the habits or cultural patterns (infection risk) in the period of spring celebrations (the spring celebrations fall within January and February in China per year, thus a new variable was created, which was coded as “1” in January and February per year, while which was coded as “0” in other months per year). SARIMA: Seasonal autoregressive integrated moving average; SARFIMA: Seasonal autoregressive fractionally integrated moving average; MAD: Mean absolute deviation; MAPE: Mean absolute percentage error; RMSE: Root mean square error; MER: Mean error rate; RMSPE: Root mean square percentage error.

Besides, because we cannot obtain the data pertaining to the nutritional status of the population, comorbidities such as diabetes and hypertension, the specifics of daily water consumption, and immunological resistance related to the genetic traits of the Chinese population,

we are unable to further describe how the factors above can affect the observed results. But, we have added this in our limitations in **L445-450 in the revised version**: “Fifth, due to the lack of available data pertaining to the nutritional status of the population, comorbidities such as diabetes and hypertension, the specifics of daily water consumption, and immunological resistance related to the genetic traits of the Chinese population, we are unable to provide a more detailed analysis of how these factors may impact the observed results (L445-450)”

5. In Table 1, it is important to explain the meaning of the acronyms used at the bottom of the table

Response: Thanks very much for your suggestion. We have added the meaning of the acronyms used at the bottom of the table, and we also check all the table and make a modification.

Replies to Science editor:

The manuscript has been peer-reviewed, and it is ready for the first decision.

Language Quality: Grade A (Priority publishing)

Scientific Quality: Grade A (Excellent)

Response: Thanks very much for your positive comments. Besides, we have returned our revised to further polish the language of our paper. The edited version and certificate of English editing certificate were also submitted in the related attachments. Also, we make a modification of the whole text based on the Guidelines for revising the content, Format for Manuscript Revision, Requirements for Article Highlights, and Common issues in revised manuscript.

Replies to Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office’s comments and

the Criteria for Manuscript Revision by Authors. Before final acceptance,

1. uniform presentation should be used for figures showing the same or similar contents; for example, “Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...”. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.

Response: Thanks very much for your suggestions. We have checked the whole text, and major changes were made according to your suggestions including the text, all tables, all figures, and Supplementary material. Besides, we organized all figures into a single PowerPoint file. These changes can be found in our revised manuscript.

2. Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response: Thanks very much for your suggestions. All these contents have been checked and made modifications according to your suggestion.

3. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is ‘original’, the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT):
Copyright ©The Author(s) 2023.

Response: Thanks very much for your suggestions. All figures are original in our paper, we have provided the copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2023.

4. Before final acceptance, when revising the manuscript, the author must supplement and

improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Response: Thanks very much for your suggestions. We can ensure that we have supplemented and improved the highlights of the latest cutting-edge research results based on the RCA database.

The screenshot displays the Reference Citation Analysis (RCA) website interface. At the top, there is a navigation bar with the logo 'Reference Citation Analysis™' and buttons for 'Login', 'Scholar Register', 'Business Register', and 'Subscribe'. Below the navigation bar is a search bar with the text 'SARFIMA' and buttons for 'Find an Article' and 'Find an Author'. A secondary navigation bar contains links: 'Find an Article (54038453)', 'Find a Category (123)', 'Find a Journal (6103)', 'Find a Scholar (3835)', 'Find an Academic Assistant (13)', 'Find an Article PDF (4527479)', 'Today's Articles (3746)', and 'Subscriber (48749)'. The main content area is divided into two columns. The left column has a 'Download' button and a 'Total Articles' section showing 3 articles from Reference Citation Analysis, with options for 'Article PDFs (1)' and 'Cited by > 0 (3)'. Below this is a 'Searched Name' section with 'SARFIMA' and a 'Ranked By' section with radio buttons for 'Impact Index Per Article' (selected) and 'Citation(s) in RCA'. The right column is titled 'Citation Analysis' and contains a table with 3 rows of search results. Each row includes a number, the article title, authors, journal information, and various links like 'Impact Index Per Article', 'Reference Citation Analysis', 'What about the content of this article?', 'Affiliation(s)', 'Abstract', 'Key Words', 'Track Full Text', 'Download PDF', 'Figures', 'Journal Information', 'Subscribe', 'Scholar Register', 'Received', 'Accepted', and 'Indexed'.

Number	Citation Analysis
1	Qi C, Zhang D, Zhu Y, Liu L, Li C, Wang Z, Li X. SARFIMA model prediction for infectious diseases: application to hemorrhagic fever with renal syndrome and comparing with SARIMA. <i>BMC Med Res Methodol</i> 2020;20:243. [PMID: 32993517] [PMCID: PMC7526348] [DOI: 10.1186/s12874-020-01130-8] [Citation(s) in RCA: 7] [Impact Index Per Article: 2.3] [Reference Citation Analysis] [What about the content of this article? (0)] [Affiliation(s)] [Abstract] [Key Words] [Track Full Text] [Download PDF] [Figures] [Journal Information] [Subscribe] [Scholar Register] [Received: 01/28/2020] [Accepted: 09/23/2020] [Indexed: 11/24/2022] Open
2	Peerajit W, Areepong Y, Sukparungsee S. Explicit analytical solutions for ARL of CUSUM chart for a long-memory SARFIMA model. <i>COMMUN STAT-SIMUL C</i> 2017. [DOI: 10.1080/03610918.2017.1408821] [Citation(s) in RCA: 1] [Impact Index Per Article: 0.2] [Reference Citation Analysis] [What about the content of this article? (0)] [Affiliation(s)] [Track Full Text] [Journal Information] [Subscribe] [Scholar Register] [Indexed: 10/18/2022]
3	Egrioglu E, Aladag CH, Kadilar C. The CSS and The Two-Stage Methods for Parameter Estimation in SARFIMA Models. <i>Journal of Probability and Statistics</i> 2011;2011:1-11. [DOI: 10.1155/2011/691058] [Citation(s) in RCA: 1] [Impact Index Per Article: 0.1] [Reference Citation Analysis] [What about the content of this article? (0)] [Abstract] [Track Full Text] [Journal Information] [Subscribe] [Scholar Register] [Indexed: 11/18/2022] Open

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Answering editor-in-chief's comments

Response Letter

Dear Dr. editor, and the editor-in-chief's comments, Dr. Isakov,

Thank you for your letter and comments on our manuscript titled 'Time series analysis-based seasonal autoregressive fractionally integrated moving average to estimate hepatitis B and C epidemics in China' (Manuscript NO: 87364). These comments helped us improve our manuscript, and provided important guidance for future research. We have addressed the comments raised by the editor-in-chief to the best of our abilities. The amendments are highlighted with yellow color in the revised manuscript and the revised manuscript has been re-submitted for your consideration. Besides, we have revised the text to meet the style requirements of *World Journal of Gastroenterology* and also hoped this to meet your requirements for a publication. Point by point responses to the Editor-in-Chief's comments are listed below this letter.

We hope that the revised version of the manuscript is now acceptable for publication in your journal.

I look forward to hearing from you soon.

With best wishes,

Yongbin Wang

Professor

Corresponding author

We would like to express our sincere thanks to the editor and reviewers for the constructive and positive comments.

Replies to editor-in-chief

JOURNAL EDITOR-IN-CHIEF (ASSOCIATE EDITOR) COMMENTS TO AUTHORS This is the nice study and manuscript is solid and well prepared. However, discussion is weak and needs corrections and additions.

1. Authors nicely confirm that SAFRIMA provide better prediction than SARIMA, but tell nothing why this kind of prediction is needed. For HCV as well as HBV epidemiology is much more important to know the incidence in high risk groups than in blood donors or healthy population as the high-risk groups are the main drivers for the new infection cases.

Response: Thanks very much for your suggestion. Based on this suggestion, have added the related contexts in the revised version: “These findings provide further validation for the effectiveness of SARFIMA as a promising alternative in monitoring the spread of HB and HC. Moreover, the application of SARFIMA can superbly contribute to guiding the intensity and type of public health measures. For example, if the model clearly showed an upsurge in the midst of receding HB and HC epidemics, it would suggest the effectiveness of measures currently in place. Instead, if the SARFIMA predicted a decline despite increasing HB and HC epidemics, the need for further or optimized measures should be heightened. These practical and actionable insights hold great promise for SARFIMA in monitoring and controlling HB and HC epidemics **in page 13 of the revised version**”, “enabling it an invaluable tool for monitoring HB and HC epidemics, contributing to more informed decision-making and improved understanding of complex temporal dynamics. Considering that time series analysis is a crucial aspect of forecasting that combines various factors and the comprehensive effects of uncertain variables into a time variable, which is cost-effective and widely applicable in practice^[25], promoting the adoption of SARFIMA can contribute to the improved accuracy and reliability of modelling and forecasting other infectious diseases **in page 14 of the revised version**”, “Therefore, comprehensive measures should be taken,

such as expanding the scope of adult HB vaccination, a breakthrough in vaccination for HC, preventing mother-to-child transmission, investigating high-risk factors, implementing standardized antiviral treatment in rural areas, and enhancing health education and promotion **in page 18 of the revised version”**

2. Any prediction is useless if it does not reveal or indicate the point and tools for actions to overcome or change predicted trends. Authors need to deeply discuss it in the manuscript discussion section

Response: Thanks very much for your suggestion. Based on this suggestion, have added the related contexts in the revised version: “Therefore, addressing these challenges requires a comprehensive approach that encompasses prevention, diagnosis, and treatment^[2,4]. First, efforts should be focused on expanding the reach of the neonatal HB vaccination program to ensure that all infants are protected from HBV infection^[2,4]. Additionally, targeted vaccination campaigns should be implemented to reach vulnerable populations, such as women of reproductive age, in order to reduce the risk of mother-to-child transmission^[3]. Second, it is imperative to improve the diagnostic rate of both HBV and HCV infections in China. This can be achieved through increased awareness and education among healthcare professionals, as well as the general population, regarding the importance of early detection and screening^[2,4]. Furthermore, the establishment of screening programs in high-risk areas and the provision of affordable and accessible diagnostic tests can significantly contribute to improving the diagnostic rate. Lastly, it is crucial to strengthen the healthcare infrastructure and expand access to antiviral therapies for both HB and HC^[2,4]. This can be achieved by training healthcare professionals in the latest treatment guidelines and protocols, as well as ensuring the availability and affordability of antiviral drugs. Additionally, efforts should be made to reduce the stigma associated with these diseases, as this can act as a barrier to seeking medical help and receiving appropriate treatment^[2,4] **in page 16 of the revised version”**

3. Some authors explanations of seasonal increase in incidence of HBV and HCV by overeating and poor sleeping during festive period are naive and non-scientific, it is more appropriate to

propose that during this period the people behaviour is changing to realize the transmission of HCV/HBV (unprotected sexual contacts, IDU etc.) with subsequent increase in demand of testing as the people are more aware to check their status after the festive.

Response: Thanks very much for your positive comments: “In China, although the primary mode of HB and HC transmission has shifted from drug use to sexual transmission, injecting drugs and engaging in unprotected high-risk sexual activities following drug use are common practices^[38]. People's behavior is evolving to recognize the potential transmission risks of HCV/HBV, such as unprotected sexual contacts and IDU^[38]. This shift is resulting in a growing demand for testing, as individuals are becoming more conscious of the need to check their status after festive events, leading to an increase in patients during this period **in page 16 of the revised version**”

4. Prediction models which evaluated by authors can be used for better information background for the change the prevention and treatment policy of HBV and HCV, therefore authors need to greatly rewrite the discussion section to show the importance of this prediction tools for such changes in other countries focusing for barriers and problems of HCV elimination and PИM control. I add the manuscript with some of my remarks inline of the text of discussion.

Response: Thanks very much for your suggestion. Based on this suggestion, have added the related contexts in the revised version: “These findings provide further validation for the effectiveness of SARFIMA as a promising alternative in monitoring the spread of HB and HC. Moreover, the application of SARFIMA can superbly contribute to guiding the intensity and type of public health measures. For example, if the model clearly showed an upsurge in the midst of receding HB and HC epidemics, it would suggest the effectiveness of measures currently in place. Instead, if the SARFIMA predicted a decline despite increasing HB and HC epidemics, the need for further or optimized measures should be heightened. These practical and actionable insights hold great promise for SARFIMA in monitoring and controlling HB and HC epidemics **in page 13 of the revised version**”; “enabling it an invaluable tool for monitoring HB and HC epidemics, contributing to more informed decision-making and improved understanding of complex temporal dynamics. Considering that time series analysis is a crucial aspect of forecasting that combines

various factors and the comprehensive effects of uncertain variables into a time variable, which is cost-effective and widely applicable in practice^[25], promoting the adoption of SARFIMA can contribute to the improved accuracy and reliability of modelling and forecasting other infectious diseases **in page 14 of the revised version**”, “Therefore, addressing these challenges requires a comprehensive approach that encompasses prevention, diagnosis, and treatment^[2,4]. First, efforts should be focused on expanding the reach of the neonatal HB vaccination program to ensure that all infants are protected from HBV infection^[2,4]. Additionally, targeted vaccination campaigns should be implemented to reach vulnerable populations, such as women of reproductive age, in order to reduce the risk of mother-to-child transmission^[3]. Second, it is imperative to improve the diagnostic rate of both HBV and HCV infections in China. This can be achieved through increased awareness and education among healthcare professionals, as well as the general population, regarding the importance of early detection and screening^[2,4]. Furthermore, the establishment of screening programs in high-risk areas and the provision of affordable and accessible diagnostic tests can significantly contribute to improving the diagnostic rate. Lastly, it is crucial to strengthen the healthcare infrastructure and expand access to antiviral therapies for both HB and HC^[2,4]. This can be achieved by training healthcare professionals in the latest treatment guidelines and protocols, as well as ensuring the availability and affordability of antiviral drugs. Additionally, efforts should be made to reduce the stigma associated with these diseases, as this can act as a barrier to seeking medical help and receiving appropriate treatment^[2,4] **n page 16 of the revised version**”, “Therefore, comprehensive measures should be taken, such as expanding the scope of adult HB vaccination, a breakthrough in vaccination for HC, preventing mother-to-child transmission, investigating high-risk factors, implementing standardized antiviral treatment in rural areas, and enhancing health education and promotion **in page 18 of the revised version**”

Besides, to further improve the clarity and readability of our revised manuscript, we have used the English language editing services for language usage, spelling, and grammar. The edited version and certificate of English editing certificate were also submitted in the related attachments and we hoped to meet the language requirements of World Journal of Gastroenterology at this time.