PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Predicting the local COVID-19 outbreak around the world with	
	meteorological conditions: a model-based qualitative study	
AUTHORS	Chen, Biqing; Liang, Hao; Yuan, Xiaomin; Hu, Yingying; Xu, Miao;	
	Zhao, Yating; Zhang, Binfen; Tian, Fang; Zhu, Xuejun	

VERSION 1 – REVIEW

REVIEWER	Aleš Urban
	Institute of Atmospheric Physics of the Czech Academy of
	Sciences
REVIEW RETURNED	14-Jul-2020
	· ·
GENERAL COMMENTS	Thanks to the authors for this interesting manuscript, investigating the effect of meteorological conditions on the outbreak of COVID- 19 around the world. The focus of the manuscript is especially important and of the highest interest. Findings of the study are also important and interesting and deserve to be published quickly. However, several steps of the study are not clearly explained, which makes the whole manuscript a little bit confusing. Therefore, following issues need to be revised before acceptance of the manuscript.
	 It is not clear, which data were used for which analysis. Material and methods text suggests that the analysis was carried out on data from all countries, however, a caption of Fig 1 as well as text in the supplementary material suggest, that the short and long term model was calibrated using Wuhan data only and then tested on data from other countries. Although this is specified in individual figures, this needs to be clarified in the main manuscript, otherwise the results are very confusing. The authors used the visibility parameter to represent the number of droplets (amount of water) in the air. Although I eventually understood this choice, this should be justified clearly in methods. Moreover, did authors consider using of absolute humidity rather than visibility". It took me a while to realize, why the authors talk about "visibility". In general, the choice of the weather parameters should be better justified. I miss more detailed information about the statistical models, their outputs, the choices that led to use of these exact models and formulas. E.g. authors state that the weather on days 3-7 was correlated best with the incidence of COVID (page 8), but they do not provide any evidence of this. Although I can agree that the relationship seems to be best according to Figure 1, any comparable quantification of the relationships is necessary. Similarly, authors present a resulting fit of the short-term and long-term complex models, but they do not specify what kind of

consider the use of generalized additive models instead of predetermined quadratic and linear functions? 5) I do not understand the meaning of multiplicative factor "alfa" and a site-related constant "beta" in short/long term model.
Except of this, several specific points need to be clarified:
Page 6, Lines 2-4: Please clarify this sentence. Although I understand, "five time delays" might be a bit confusing?
Page 6, line 21: See above. Please explain the use of these variables.
Page 7, line 4-5: How do you know this? Just by visual checking of the plot?
Page 10, lines 18-20: Does this agree with other countries? Do you have any information?
Page 11, line 21-22. What is the difference between values in Fig. 3F and 3A-E. I do not see any. Page 12, line 18-20. Have the authors checked if there is any study investigating this behaviour for influenza?
Page 13, lines 2-3: Please explain better the role of visibility. That we are talking about the absolute air humidity (i.e. amount of water in the air) rather than "visibility".
Page 13, lines 5-7: I do not understand the use of the multiplicative factor. How did you choose the constant? Is it a model intercept?
Page 13, lines 10-11: Where are these different prediction- observation correlation patterns shown.
Page 14, lines 13-19: More information about how you defined these models and their output parameters is needed.
Supplementary Material – Statistical modelling: this should be in the main text. But still more details are needed. Does this mean that you basically tested model from Wuhan in other countries and it worked quite well in some "controlled" countries?
Supplementary results: "In order to reduce the potential contamination of modelling by this outlier, we substituted the counts on that day by four, that was 13,436/4=3,359, which was still the largest number but not deviated from the dataset too much." How did you get these numbers?
"the average temperature ranged -23.54°C ~ 22.85°C" are you talking about Chinese data, Italian data or all data now? Please provide more detailed information about which data were used for which country, what time span, in which analysis etc. This is very confusing throughout the manuscript.
Limitation: Although there is a chapter "Strengths and limitation of the study" in this manuscript, I have not found any discussion about limitations of the study.

Conclusion: Please move the last paragraph of the manuscript to Conclusion and/or highlight in any other way, where are the main conclusions of the study.

REVIEWER	Rathin Adhikari Centre for Theoretical Physics, Jamia Millia Islamia (Central University), New Delhi- 110025, INDIA
REVIEW RETURNED	16-Jul-2020

2) For long term model the basic relationship presented in this work in page 11, is as follows:
New Case Count = (0:14T 2 + 0:93T + 100)Extant Case Count (2)
Around T 300C the expression inside the bracket in equation (2) vanishes. As is positive, this expression is negative at temperature higher than that. But in countries like India, Iran,
Pakistan with average temperature around 300C or higher than that, the number of new cases have neither approached zero or have decreased.
In fact, the expression inside bracket in (2) is larger near 00 C to 70C temperature. So normally based on this long term model, one would expect, then maximum rise in new cases around that range of temperature. Even if we change the value of for di erent countries, this feature will remain. In many places there is signi cant rise at much above that temperature. Authors should clarify these.
3) Apart from these issues, there seem to be apparent contradiction of the two models in the following sense: In short term model, checking graphically one can see that the new case count is mainly controlled by relative humidity irrespective of temperature and with the increase in humidity the magnitude (mentioning magnitude as there is negative sign!) of new case count increases. But relative humidity, which is playing so much signi cant role in short term model, is totally absent in long term model in which instead of relative humidity only temperature as meteorological variable is playing the role. Authors should explain how this apparent contradiction in these two models, may be reconciled.
4) In Figure 3, in all the plots, the errors seem to be not independent in nature, there is heteroscedastic feature in it and the error variance changes. As for example, in Figure 3 F, with higher counts, errors have increased. So author should mention clearly what are the required criteria for errors in their analysis and justify how these required criteria of errors have been ful lled while analysing errors (say evaluating con dence level, p values etc.) for di erent cases.
5) This is kind of a suggestion. In di erent places considered by authors, the population density is di erent, total population is di erent and this may be expected that the the number of new COVID-19 cases could be related with this. As for example, we have seen signi cant number of cases in New York city in USA or New Delhi in India where population density and the population are large. In this work r value has been shown to be di erent for di erent countries. Author may explore whether this variation in r could be due to population density. However, there could be various other reasons some of which have been mentioned by authors.
Authors should particularly clarify points 1 to 3 related to the validity of the models in general and point 4 related to the error

analysis of these models. Due to lack of clarity, the manuscript in
its present form, is not recommended for publication.

VERSION 1 – AUTHOR RESPONSE

"Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name

Aleš Urban

Institution and Country

Institute of Atmospheric Physics of the Czech Academy of Sciences

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

None declared.

Please leave your comments for the authors below

Thanks to the authors for this interesting manuscript, investigating the effect of meteorological conditions on the outbreak of COVID-19 around the world. The focus of the manuscript is especially important and of the highest interest. Findings of the study are also important and interesting and deserve to be published quickly. However, several steps of the study are not clearly explained, which makes the whole manuscript a little bit confusing. Therefore, following issues need to be revised before acceptance of the manuscript.

1) It is not clear, which data were used for which analysis. Material and methods text suggests that the analysis was carried out on data from all countries, however, a caption of Fig 1 as well as text in the supplementary material suggest, that the short and long term model was calibrated using Wuhan data only and then tested on data from other countries. Although this is specified in individual figures, this needs to be clarified in the main manuscript, otherwise the results are very confusing. "

Response: Thanks for these positive opinions and suggestions. We have modified the manuscript's method and results sections to clarify the detailed datasets and corresponding analyses (revised manuscript with track: Lines 136-162, 180-183, 190-191, 207-212, 215-219, 226-228, 236-237, 307-308). The relationship of each meteorological variable with epidemic data and time delay effect was investigated using Wuhan data. The single-factor modeling, final short-term and long-term models was fitted with the discovery data (Chinese top outbreak cities including Wuhan), and tested on data from Italian cities and other countries.

"2) The authors used the visibility parameter to represent the number of droplets (amount of water) in the air. Although I eventually understood this choice, this should be justified clearly in methods. Moreover, did authors consider using of absolute humidity rather than visibility. It took me a while to realize, why the authors talk about "visibility". In general, the choice of the weather parameters should be better justified."

Response: Thanks for this suggestion. We have included both visibility and humidity in the analyses, while humidity was in the form of relative humidity. These two parameters are different from each other. The choice of weather parameters was based on recommendations from one atmospheric scientist and consideration of complete data availability. In fact, we have considered absolute humidity at the beginning. Both absolute humidity and relative humidity are derived from dew point and air temperature, and they both describes the amount of water vapor in the area. Furthermore, the associations with epidemic data for absolute humidity was similar to those for relative humidity in the current study. Considering the public acceptability (relative humidity is typically referred to on weather reports), we finally used relative humidity rather than absolute humidity. On the other hand, visibility is a measure of how far one can observe. The factors influencing visibility include not only the amount of droplets in the air (which is generally reflected by humidity), but also the amount and distribution of particles other than water droplets, such as dust and air pollutants. In fact, haze caused by air pollution impacts visibility much more. Virus can not only adhere to droplets but also cling to various solid particles such as dust and air pollutants. Thus, the visibility parameter is important, and distinct from humidity parameter. Furthermore, the association pattern of visibility (the left panel of the following figure) with COVID-19 outbreak differed from that of absolute humidity (the right panel of the following figure). We have mentioned about the reason to choose visibility in the introduction section (revised manuscript with track: Line 78). Nevertheless, the elaboration might be not clear and insufficient. We have added explanations about the choice of the weather parameters in the method section (revised manuscript with track: Lines 113-118).



"3) I miss more detailed information about the statistical models, their outputs, the choices that led to use of these exact models and formulas. E.g. authors state that the weather on days 3-7 was correlated best with the incidence of COVID (page 8), but they do not provide any evidence of this. Although I can agree that the relationship seems to be best according to Figure 1, any comparable quantification of the relationships is necessary."

Response: Thanks the reviewer for advices. We have added details about the statistical models, their outputs (estimations and model fitness statistics), the choices that led to use of these exact models and formulas in the revised manuscript (revised manuscript with track: Lines 136-162, 180-196, 215-

220, 232-246, 305-312), supplementary results (supplementary materials: Lines 47-83) and tables (Table S1, S2, S3).

"4) Similarly, authors present a resulting fit of the short-term and long-term complex models, but they do not specify what kind of regression model they used. In this regard – did the authors consider the use of generalized additive models instead of predetermined quadratic and linear functions? "

Response: We used non-linear least square method implemented in R for model regression. Whether to use quadratic or linear function was determined by non-linear least square modeling with each one meteorological variable in the Wuhan dataset. The results only suggested visibility as linearly correlated with epidemic data. Then, the exact parameters for the quadratic and linear functions were determined by non-linear least square modeling with each one meteorological variable in the discovery dataset. Only the constants in the composed model were fitted again. We have considered generalized additive models before (results in R listed below), but the regression statistics was worse than non-linear models. We have specified the models in the method section (revised manuscript with track: Lines 136-138, 141-143, 146-158) and the supplementary results (supplementary materials: Lines 59-81).

Coefficients:

	Estimate S	Std. Error t value Pr(> t)
(Intercept)	118.5530	63.4981 1.867 0.06220.
т	0.9550	1.1227 0.851 0.39518
RH	-40.8721	75.9289 -0.538 0.59050
SPD	-0.5916	2.7036 -0.219 0.82683
VSB	-7.2749	2.4028 -3.028 0.00253 **

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Table. Model fitting statistics comparing generalized additive model and non-linear leas	t
square model, with the discovery dataset	

model	logLik	AIC	BIC	deviance
GAM	-6648	13308	13337	49001216
NLS	-6648	13300	13309	48989771

Note: The generalized additive model (GAM) is: confirmed new case counts = T+RH+SPD+VSB, with coefficients and constants needed to be estimated. The short-term model in the current study (NLS) is: $-0.11 \times T^2 + 1.40 \times T - 576 \times RH^2 + 904 \times RH - 0.27 \times SPD^2 + 2.29 \times SPD - 7.02 \times VSB$, with constants needed to be estimated.

"5) I do not understand the meaning of multiplicative factor "alfa" and a site-related constant "beta" in short/long term model." **Response:** Although we got estimated values for these two factors through model fitting, when used these two models for exact values prediction, sometimes we found overestimation or underestimation of epidemic data but the predicted values correlated well with the observed values. It seemed that the overall coefficient for extant confirmed cases changed with sites. The Q-Q plot better illustrates this shift in predicted values from observed values. We supposed that it was due to some site-related confounders, such as isolation policy and sunlight radiation. Because we derived these two models with Chinese data, the constant coefficients (so-called multiplicative factor) could vary for other countries with different isolation policies.

"Except of this, several specific points need to be clarified:

Page 6, Lines 2-4: Please clarify this sentence. Although I understand, "five time delays" might be a bit confusing?"

Response: Thank you for advice. We have changed the expression to "five time point's delay of virus infection" in the revised manuscript (revised manuscript with track: Lines 92-93).

"Page 6, line 21: See above. Please explain the use of these variables."

Response: We have added explanations about the choice of these four variables in the revised manuscript (revised manuscript with track: Lines 113-118).

"Page 7, line 4-5: How do you know this? Just by visual checking of the plot?"

Response: We got the results by comparing model fitness statistics (estimated standard error of the residuals, the log-likelihood, Akaike's Information Criterion, Bayesian Information Criterion) and Spearman's correlation coefficient between the real values and the predicted values by the predisposed model, in combination with visual check of Loess regression interpolation curves and common knowledge of coronavirus transmission. The part of results has been largely revised (revised manuscript with track: Lines 180-196).

"Page 10, lines 18-20: Does this agree with other countries? Do you have any information?"

Response: We could not obtain detailed information about the usage, duration, generalization, and popularity of shelter hospitals in other countries. Thus, we are not sure about the generalization of this explanation.

"Page 11, line 21-22. What is the difference between values in Fig. 3F and 3A-E. I do not see any."

Response: Fig 3F illustrated the prediction performance for long-term model. Fig 3A-E illustrated the prediction performance for short-term model. These two models are different, though they share some

parameters, temperature and extant case count. It is possible that these two models derived similar Q-Q plot patterns, as Q-Q plots reflect the deviation of predicted values from observed values and the two models both had good prediction performance. Nevertheless, we have to admit that there is some mistake in data usage for long-term model prediction. We have corrected it in the revised manuscript (Fig 3F).

"Page 12, line 18-20. Have the authors checked if there is any study investigating this behaviour for influenza?"

Response: Yes, there are several studies investigating humidity and influenza virus transmission, and they suggested that influenza virus outbreaks correlate closely with decreases in humidity in the temperate regions. We have added references talking about this in the revised manuscript (revised manuscript with track: Line 335).

"Page 13, lines 2-3: Please explain better the role of visibility. That we are talking about the absolute air humidity (i.e. amount of water in the air) rather than "visibility"."

Response: We have explained about the definition of visibility before in the response letter. What we meant is indeed visibility (i.e. amount of particles such as dust and air pollutants), rather than absolute air humidity. We have added more explanations about the role of visibility in the revised manuscript (revised manuscript with track: Lines 342-344).

"Page 13, lines 5-7: I do not understand the use of the multiplicative factor. How did you choose the constant? Is it a model intercept?"

Response: We found that there was overestimation or underestimation if only multiply the extant confirmed case count with weather coefficient, thus, we added a multiplicative constant coefficient to make the predicted values more closer to the observed values. It is not a model intercept. This constant was derived from non-linear least square modeling in the discovery dataset. However, we found that the fitted value only suitable for Chinese dataset, there was still overestimation when applied to other countries. We supposed that this constant might reflect some site-specific factors such as isolation policy. Thus, this constant determination requires regression with some known data for a certain site.

"Page 13, lines 10-11: Where are these different prediction-observation correlation patterns shown."

Response: These patterns are shown in Fig. 3, and text discussing about this issue is in the result section--- "Different modes of viral transmission illustrated by the model". Fig 3A-E are patterns about the short-term model, while Fig 3F shows all the patterns about the long-term model. We have modified Fig 3F to show the five correlation patterns.

"Page 14, lines 13-19: More information about how you defined these models and their output parameters is needed."

Response: As mentioned above, we have added details about models and their outputs in the result section, mainly the first three paragraphs, and supplementary materials. Model outputs are listed in supplementary tables and results.

"Supplementary Material – Statistical modeling: this should be in the main text. But still more details are needed. Does this mean that you basically tested model from Wuhan in other countries and it worked quite well in some "controlled" countries? "

Response: Thank you for advice. We have moved this part to the main text and added more details in this part (revised manuscript with track: Lines 136-162). We tested models from China top-outbreak cities and it work well in most countries in the northern hemisphere. Statistics are listed in the result section---" Different modes of viral transmission illustrated by the model".

"Supplementary results: "In order to reduce the potential contamination of modeling by this outlier, we substituted the counts on that day by four, that was 13,436/4=3,359, which was still the largest number but not deviated from the dataset too much." How did you get these numbers?"

Response: The number of newly confirmed cases on February 13, 2020, reached over four times larger than that on any other dates, while the weather condition did not change too much. Thus, we supposed that it was due to abrupt large supplement of virus test kits or data correction on that day. Previously we intended to reduce the effect of this odd number on regression, so we substituted the counts on that day by four, just to keep data on this date highest but not too odd. Nevertheless, we discarded data on this date in the revised manuscript (supplementary materials: Lines 38-41).

""the average temperature ranged -23.54°C ~ 22.85°C" are you talking about Chinese data, Italian data or all data now? Please provide more detailed information about which data were used for which country, what time span, in which analysis etc. This is very confusing throughout the manuscript."

Response: Yes, we are talking about the Chinese data, or so-called discovery data here. We have mentioned the dataset referred to in this sentence (supplementary materials: Line 43).

"Limitation: Although there is a chapter "Strengths and limitation of the study" in this manuscript, I have not found any discussion about limitations of the study."

Response: Thanks for pointing it out. We have added several limitations in the discussion section (revised manuscript with track: Lines 377-396) and added several points of limitations in the "Strengths and limitation of the study".

"Conclusion: Please move the last paragraph of the manuscript to Conclusion and/or highlight in any other way, where are the main conclusions of the study."

Response: Thank you for your suggestion. We have moved the last paragraph to Conclusion section in the revised manuscript (revised manuscript with track: Line 397).

"Please see more comments in the reviewed pdf file (attached)."

Response: Thank you for such useful comments. We have responded to each comment below.

Page 2, Line 17: " why visibility?"

Response: Visibility reflects the amount and distribution of particles, such as dust and air pollutants, in the air, while humidity reflects the amount of water droplets. Virus could also cling to these solid particles. We have explained in detail about the choice of visibility before in the response letter (Point 2).

Page 5, Line 18-19: " is it relevant for a scientific paper? "

Response: This is predictions from a traditional Chinese medicine theory. We have deleted this sentence in the revised manuscript (revised manuscript with track: Lines 83-84).

Page 6, Line 2: "which areas? were did you get the data. More information is needed. "

Response: We have mentioned details about these areas in the first paragraph in the method section (revised manuscript with track: Lines 105-111) and in the supplementary method previously. These areas included 428 Chinese cities and areas, of which 42 were tested for models, other countries with high COVID-19 incidence in February, namely, United States, United Kingdom, Germany, France, Italy, Spain, Iran, Korea, Japan, countries in the southern atmosphere, e.g., Australia and South Africa, and tropical countries India, Thailand, and Singapore. For Italy, province-level data were collected. We have added information about tested areas in the revised manuscript (revised manuscript with track: Lines 91-92).

Page 8, Line 22: "please consider using meter per second."

Response: Thank you for your suggestion. We have changed the unit to meter per second.

Page 9, Line 5: "what kind of model? Where did you run the model? What software was used? what about GAM?"

Response: It is a non-linear model, with four meteorological variables added together as a coefficient to multiply with the number of extant confirmed cases. The function assumed for temperature, relative humidity, and wind speed is quadric, while that for visibility is linear. We separately ran model regression with each meteorological variable in the discovery dataset (Chinese top-affected cities) to determine the exact coefficient parameters, using the non-linear least square (nls) package implemented in R. Then, a combined model with each single-factor regressed function added together as a weather coefficient was fitted to determine the constant coefficient that was multiplied with the weather coefficient and the number of extant confirmed cases. We have added details about modeling in the result section and the supplementary result section in the revised manuscript. We have considered GAM before, however, the regression statistics was not better than non-linear model (see response above).

Page 9, Line 17-19: "Not clear. Please explain better."

Response: The multiplicative factor is a constant coefficient to adjust the impact of weather coefficient on epidemic spread, which might be site-specific (such as related to isolation policy). See response above. We have added more explanations for this constant in the revised manuscript (revised manuscript with track: Lines 247-261).

Page 11, Line 18: " input model formula"

Response: We added the input formula in the supplementary results (supplementary materials: Lines 59-81).

Page 11, Line 21-22: " seems to be same as previous model?"

Response: The long-term model only includes temperature measured 14 days ago as a weather coefficient, while the previous short-term model includes all four variables measured 3~7 days ago. It is possible for the two model to look similar, since they are both good prediction models, but the statistics were different.

Page 13, Line 8-9: " did you measure these isolation steps anyhow?"

Response: Sorry, we did not measure these isolation steps as we could not obtain enough information depicting detailed isolation steps in these countries. This is worthy of future research.

Page 20, Fig 1: " is this for Wuhan or all cities?"

Response: As we stated in the figure legend, this figure is for Wuhan dataset.

Page 21 & 22, Fig 2 & Fig 3:

Response: We have revised the figure legends to be more clear and accurate.

Page 25, Line 6: " time span? more information about cities and stations should be provided"

Response: The time span for all datasets was from January 20 to April 9. While the beginning date for each site was the date the first COVID-19 case was confirmed and reported. The list of cities or countries with epidemic data was obtained from an online website DXY-COVID-19-Data (https://github.com/BlankerL/DXY-COVID-19-Data). Information about stations was obtained from the Integrated Surface Database of USA National Centers for Environmental Information. There is a list of cities and stations, which could be shared upon email request.

"Reviewer: 2

Reviewer Name

Rathin Adhikari

Institution and Country Centre for Theoretical Physics, Jamia Millia Islamia (Central University), New Delhi- 110025, INDIA

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

None declared

Please leave your comments for the authors below

Comments for the authors are given in the attached file (Covidchen)

FORMATTING AMENDMENTS (if any)

Required amendments will be listed here; please include these changes in your revised version:"

Response: Thank you for such useful comments. We have responded to each comment below.

"In this work, COVID-19 epidemic data has been modeled with meteorological data related to average temperature, relative humidity, wind speed and visibility. Corresponding models are expected to predict the new COVID-19 case counts, based on the earlier extant confirmed cases. Two models - one short term for predicting new cases in the following three days and another long term for predicting new cases in the following week or month, have been presented. In short term model above-mentioned all four meteorological variables are considered while in long term model only average temperature has been considered as independent variable to estimate number of new cases which is dependent variable. Following points require some clarifications :

1) For short term model the basic relationship presented in this work in page 9, is as follows:

New Case Count = $(-0.13 \times T^2 + 1.45 \times T - 608 \times RH^2 + 974 \times RH - 0.23 \times SPD^2 + 0.89 \times SPD - 0.23 \times SPD^2 + 0.89 \times SPD^2 +$

 $7.45 \times VSB - 200) \times \alpha \times Extant Case Count (1)$

In the above relationship, it may be checked that for short term model relationship in equation (1), the expression inside the bracket is negative for a wide range of temperature (T) from -10°C to 40°C and relative humidity (RH) from 0% to 90% with any moderate values of wind velocity (SPD in miles/hr)

and visibility (VSB in statute miles). Author should explain why new case count is coming as negative (because α is mentioned as some positive value). If one takes care of the sign then this will probably indicate the decrease in number of cases. But then, for higher relative humidity although the magnitude of the expression inside the bracket increases but with negative sign, if it is interpreted as decrease in number of cases, then there is contradiction in the statement, made in page 12 line number 46, suggesting more spreading of COVID-19 with higher relative humidity."

Response: Thank you for your summary and comments. First, we have to admit that we have mixed up the units for relative humidity in the submitted manuscript. The note after this equation was inaccurate. Here in the equation (1), the RH value ranges 0~1, not 0~100. Thus, when relative humidity ranges 0.3~0.98 (which is the range of relative humidity values in the current datasets), temperature ranges -10°C~30°C, wind speed ranges 0~10 miles/hr, visibility less than 10, the expression inside the bracket could be positive at most conditions. In fact, the predicted values derive from this equation were generally positive as shown in Fig 3. Nevertheless, we have modified this short-term model because of removal of one outlier data according to another reviewer's suggestion. The new equation is as follows:

New Case Count = $(-0.11 \times T^2 + 1.40 \times T - 0.058 \times RH^2 + 9.04 \times RH - 1.36 \times SPD^2 + 5.12 \times SPD - 0.058 \times RH^2 + 0.04 \times RH - 0.058 \times RH^2 + 0.04 \times RH^2 +$

 $7.02 \times VSB - 126.66) \times 0.001 \times Existing Confirmed Case Count (3)$

where T is temperature in °C, RH is relative humidity in percentage (ranges 0~100), SPD is wind speed in m/s, VSB is visibility in statute miles.

We calculated predicted daily new case counts using this equation (3) for our datasets (over 1890 days of records) covering the world, mainly temporal areas, and only 0.1% predicted values were negative. According to this equation, the daily new cases would increase the most when temperature was 6°C, relative humidity was 78%, wind speed was 2 m/s, and visibility was low. In fact, the best suitable condition was what Wuhan city looked like in the first two months of 2020. This model was derived using Chinese datasets, mainly in the first three months of 2020, thus, this model might be more suitable for predicting the outbreak in the spring in temporal areas, as shown in Fig 3. In fact, with relative humidity ranging 0~100%, the expression about RH is always positive, and it reached the extremum at 78%, in accordance with more spreading of COVID-19 with higher relative humidity.

"2) For long term model the basic relationship presented in this work in page 11, is as follows:

new case count = $(-0.14 \times T^2 + 0.93 \times T + 100) \times \beta \times$ Extant Case Count (2)

Around T ~ 30°C the expression inside the bracket in equation (2) vanishes. As β is positive, this expression is negative at temperature higher than that. But in countries like India, Iran, Pakistan with average temperature around 30°C or higher than that, the number of new cases have neither approached zero or have decreased.

In fact, the expression inside bracket in (2) is larger near 0°C to 7°C temperature. So normally based on this long term model, one would expect, then maximum rise in new cases around that range of temperature. Even if we change the value of β for different countries, this feature will remain. In many places there is significant rise at much above that temperature. Authors should clarify these."

Response: Yes, we agree with the reviewer that this long-term model is improper for predictions with high temperature although we have modified this model with new dataset. The new long-term model is as follows (4):

new case count = $(-0.10 \times T^2 + 1.11 \times T + 46.42) \times \beta \times \text{Existing Confirmed Case Count (4)}$

We agree with the reviewer that the value of β is related with site-specific constant confounding factors, such as isolation policy, but unrelated with weather. According to the equation (4), when temperature is higher than 28°C, the predicted new case count would be negative. We calculated predicted daily new case counts using this equation (4) for our datasets, most discordant values (those negative predictions) were from tropic areas. Although negative predictions were less than 5% in the current datasets, this might be because most studied areas in our study were temporal areas. This model was derived using Chinese datasets, mainly in the first three months of 2020, thus, this model might be more suitable for predicting the outbreak in the spring in temporal areas. We admit that this model is imperfect, and might be not suitable for areas with high temperature (e.g., tropic areas).

Another explanation for the inaccurate prediction in areas with high temperature could be that SARS-CoV-2 transmission in these areas was mainly not influenced by weather, but in another direct way. In temporal areas with cool weather, the virus could stay in the air with good viability for a long time, causing indirect infections when uninfected people enter this place. On the other hand, in tropical areas with hot weather, infection may be mainly through direct face-to-face contact or crowd gathering in a small area. Under that situation, the virus could not stay in the air for a long time, but the environment is enough for infection due to crowded people.

We have added discussion about this limitation of model application in the revised manuscript (revised manuscript with track: Lines 377-385).

"3) Apart from these issues, there seem to be apparent contradiction of the two models in the following sense: In short term model, checking graphically one can see that the new case count is mainly controlled by relative humidity irrespective of temperature and with the increase in humidity the magnitude (mentioning magnitude as there is negative sign!) of new case count increases. But relative humidity, which is playing so much significant role in short term model, is totally absent in long term model in which instead of relative humidity only temperature as meteorological variable is playing the role. Authors should explain how this apparent contradiction in these two models, may be reconciled."

Response: Parameters for the long-term model were chosen only based on data availability in a long time scale, not based on the magnitude of influence for a factor. We agree that relative humidity play a most significant role in short term model (but with positive sign, see explanations above). However, the main reason we did not include relative humidity in long-term model was not due to its unimportance, but because of its generally unavailability in weather forecasts. On the contrast, average temperature in the future couple of days is usually easily available from weather forecasts. This is the main reason that drive us to include only temperature in the long-term model. Besides, in the Wuhan dataset, the daily new case count was correlated more with temperature rather than with relative humidity. It talks about data correlation, which is actually the influence on variance, not the influence on magnitude.

"4) In Figure 3, in all the plots, the errors seem to be not independent in nature, there is heteroscedastic feature in it and the error variance changes. As for example, in Figure 3F, with higher counts, errors have increased. So author should mention clearly what are the required criteria for errors in their analysis and justify how these required criteria of errors have been fulfilled while analysing errors (say evaluating confidence level, p values etc.) for different cases."

Response: Thank the reviewer for suggestions. You have pointed out an interesting phenomenon. The figure 3 plots the predicted values by our models against the observed real data. Yes, it seems that the prediction performance drops with the increase in new case count, suggesting that the prediction model might be inaccurate and not suitable for large new case count. We are not clear about the reason. It might be due to that there was less points with large new case count, thus, the error variance became large. We have discussed about this issue in the discussion section of the revised manuscript (revised manuscript with track: Lines 385-389). We did not provide criteria for errors in our analysis, but listed the p-value for each correlation analysis for different cases (revised manuscript with track: Lines 272, 281-282, 290-291, 296-297, 301-302). For most countries, the *p*-values of Spearman's correlation between prediction and observation were less than 0.001. Only the correlation *p*-value for Korea was 0.002, that for Thailand was 0.001, and that for South Africa was 0.08. It indicates that the prediction performance correlated with the observed data significantly well.

"5) This is kind of a suggestion. In different places considered by authors, the population density is different, total population is different and this may be expected that the number of new COVID-19 cases could be related with this. As for example, we have seen significant number of cases in New York city in USA or New Delhi in India where population density and the population are large. In this work r value has been shown to be different for different countries. Author may explore whether this variation in r could be due to population density. However, there could be various other reasons some of which have been mentioned by authors.

Authors should particularly clarify points 1 to 3 related to the validity of the models in general and point 4 related to the error analysis of these models. Due to lack of clarity, the manuscript in its present form, is not recommended for publication."

Response: Thanks for such nice advice. Population density could be one confounding factor that interfere the effect of weather. As we have discussed before, when people are crowded, the virus may spread in a more efficient way, that is directly from person to person, without being mediated by the environment. We have added this in the discussion section of the revised manuscript (revised manuscript with track: Lines 350-351). However, it is difficult for us to explore whether this variation in r could be due to population density, as our datasets about other countries could only collect nation-level data, while population density varies dramatically in one country. We suspect that isolation is one more important factor since isolation could dramatically reduce the possibility of crowd gathering and person to person contact, which would reduce the impact of population density. In fact, it is what happened in Wuhan.

	Aleš Urban Institute of Atmospheric Physics
	21-Aug-2020
GENERAL COMMENTS	 Thanks to the authors for their conscientious revisions. The comprehensibility of the manuscript is now much better. I have only few more minor comments. 1) Some new parts of Results, where decisions in methodology are justified might fit better to Methods. Please doublecheck this aspect.

VERSION 2 – REVIEW

2) Discussion: Lines 302, 306: "Second, it seems that the
prediction performance drops with the increase in new case count,
suggesting that the prediction model might become inaccurate and
not suitable for very large new case count. This could be due to
that there was less data points with large new case count.
Therefore, the model's prediction performance would be better
with more data points, especially the large case count points." -
Can this be explained by a kind of threshold of cases above which
the transmission is simply not dependent on weather anymore (for
example in US). In general, I would expect that the weather may
play the key role by the time of the epidemic outbreak, while other
(socio-economic) factors are more important later.
3) Discussion, lines 400–403: Perhaps another and the main
limitation is a general lack of data and cases. Although we have
global pandemic, data for two months are just not enough to
provide any robust results. This is nothing against your results, but
a general aspect of time-series studies.

REVIEWER	Rathin Adhikari Centre for Theoretical Physics Jamia Millia Islamia (Central University) New Delhi-110025 INDIA
REVIEW RETURNED	06-Sep-2020

2) For long term model, upto about 280C, COVID cases are coming as positive then it vanishes and after that becomes negative. This model is not expected to be valid at temper-ature higher than that and so not valid for countries having COVID with temperature higher
than 280C. But in reality, this model may not work even at somewhat lower temperature than 280C. However, authors have mentioned this as the limitations in the revised version. Apart from that choice of di erent multiplicative factors like and for di erent places, seems to be some drawbacks of these two models and may be considered as limitations.
3) This is related to point 4 in the earlier report related to errors. Authors have mentioned that they have provided only p values but no criteria for errors. However, while calculating p
values using any software program, some distribution of errors are assumed, as for example normal distribution, t-distribution etc. Depending on the validity of such distributions, the calculation of p can only be justi ed. Suppose in that software program, normal distribution has been considered for errors, then one is required to check whether such distribution is valid for the errors in their analysis. Otherwise, the calculated p value will not be correct.
In fact, in this paper, for errors with heteroscedastic feature where the variance changes, the assumption of normal distribution will not be correct. Due to that, the calculation of p values could be wrong. So author should mention the assumption of the error distribution in calculating p values and check whether it is valid in their analysis.
Authors should take care of all these three points - particularly point 1 and 3. As it stands, short term model has serious problem of giving negative number of cases over the wide range of variations of all independent meteorological variables, covering all possible weather throughout world including Wuhan. Authors have decided models based on p values but calculation of p values are not expected to be correct for the reasons discussed above. Due to these two main problems, the manuscript in its present form, is not recommended for publication.

VERSION 2 – AUTHOR RESPONSE

" Reviewer(s)' Comments to Author: Reviewer: 1 Reviewer Name Aleš Urban Institution and Country Institute of Atmospheric Physics Please state any competing interests or state 'None declared': 'None declared' Please leave your comments for the authors below Thanks to the authors for their conscientious revisions. The comprehensibility of the manuscript is now much better. I have only few more minor comments.

1) Some new parts of Results, where decisions in methodology are justified might fit better to Methods. Please doublecheck this aspect."

Response: Thanks for these positive opinions and suggestions. We have moved the part of methodology in the result section to the method section (revised manuscript with track: Lines 118-122, 126-127, 130-133, 139-143, 146, 165-166, 173, 187-189, 198-199).

" 2) Discussion: Lines 392–396: "Second, it seems that the prediction performance drops with the increase in new case count, suggesting that the prediction model might become inaccurate and not suitable for very large new case count. This could be due to that there was less data points with large new case count. Therefore, the model's prediction performance would be better with more data points, especially the large case count points." – Can this be explained by a kind of threshold of cases above which the transmission is simply not dependent on weather anymore (for example in US). In general, I would expect that the weather may play the key role by the time of the epidemic outbreak, while other (socio-economic) factors are more important later."

Response: Thanks for this suggestion. We agree with the reviewer that the influence of weather is not constant at any time or any place. This explanation by the reviewer could be one reason for the increasing prediction errors with the increase of new case count. We have added this explanation in the discussion as the reviewer suggested (revised manuscript with track: Lines 343-346).

" 3) Discussion, lines 400–403: Perhaps another and the main limitation is a general lack of data and cases. Although we have global pandemic, data for two months are just not enough to provide any robust results. This is nothing against your results, but a general aspect of time-series studies."

Response: Thanks the reviewer for advices. I have to first explain a bit about the reason of lacking data and cases. In fact, we began data collection and analysis early in March, and published our drafted manuscript in the preprint server medrxiv.org on March 16th. However, the formal manuscript submission lasts a long time and we did not update the data after the mid-April. Nevertheless, we have added this point as a main limitation in the discussion section as suggested by the reviewer (revised manuscript with track: Lines 352-354).

" Reviewer: 2 Reviewer Name Rathin Adhikari Institution and Country Centre for Theoretical Physics Jamia Millia Islamia (Central University) New Delhi-110025 INDIA Please state any competing interests or state 'None declared': None declared Please leave your comments for the authors below: In the revised version, authors have modified the basic relation

In the revised version, authors have modified the basic relationship for short term cases by removing some outliers. Also after correcting the units, it seems that the number of COVID cases has become sensitive to both temperature and relative humidity. Earlier short term model was not that much sensitive to temperature. But long term model was depending only on temperature and it was difficult to reconcile these two models. So now two models could be reconciled better and answers to some extent, the question raised in point 3 in earlier report. In this sense, the revised version seems better. However, author should address the following:

1) In this modified relationship for the short term model, the number of COVID cases are still becoming negative for all possible relative humidity (0 to 100) and temperature from -10°C to 40°C, wind speed from a few hundred m/sec to several thousands m/sec and visibility starting from 0 to any

value in statute miles! The range mentioned above covers entire world weather including weather of Wuhan. So it seems in 100% cases, this relationship mentioned in page 10, gives some negative value of number of COVID cases (as both α and existing confirmed case count are positive)! This was mentioned in the earlier report but it seems in the revised version this problem is still there in the short term model."

Response: Thank you for your summary and comments. The equation for short-term model is as follows:

New Case Count = $(-0.11 \times T^2 + 1.40 \times T - 0.058 \times RH^2 + 9.04 \times RH - 1.36 \times SPD^2 + 5.12 \times SPD - 7.02 \times VSB - 126.66) \times 0.001 \times Existing Confirmed Case Count (1)$

where T is temperature in °C, RH is relative humidity in percentage (ranges 0~100), SPD is wind speed in m/s, VSB is visibility in statute miles.

We have calculated predicted daily new case counts using this equation (1) for our datasets (over 1890 days of records) covering the world, mainly temporal areas, and only <u>0.1% predicted values</u> were negative (the smallest value for predicted new case count is -0.17).

For example, taking temperature 3.96 (°C), relative humidity 82.1 (%), wind speed 2.23 (m/s), and visibility 4.02 (statute miles) (which was the real observed weather data for Wuhan on February 1st, 2020), the equation in the bracket = $-0.11 \times 3.96^2 + 1.40 \times 3.96 - 0.058 \times 82.1^2 + 9.04 \times 82.1 - 1.36 \times 2.23^2 + 5.12 \times 2.23 - 7.02 \times 4.02 - 126.66 = 204.8333$, which is obviously positive. Taking the day March 31th, 2020 in New Delhi as another example, when temperature was 22.85 (°C), relative humidity was 66.56 (%), wind speed was 5.62 (m/s), and visibility was 1.66 (statute miles), the equation in the bracket = 166.8118, which is also positive.

In addition, the equation in the bracket is positive when temperature ranges 0~30 (°C), relative humidity ranges 50~100 (%), wind speed 0~6 (m/s), visibility less than 10 (statute miles), which covers conditions for most areas in the studied time period (mainly February and March) (see Figure 2).

"2) For long term model, up to about 28°C, COVID cases are coming as positive then it vanishes and after that becomes negative. This model is not expected to be valid at temperature higher than that and so not valid for countries having COVID with temperature higher than 28°C. But in reality, this model may not work even at somewhat lower temperature than 28°C. However, authors have mentioned this as the limitations in the revised version. Apart from that choice of different multiplicative factors like α and β for different places, seems to be some drawbacks of these two models and may be considered as limitations."

Response: Yes, we agree with the reviewer that this long-term model is improper for predictions for hot weather such as temperature higher than 28°C, and thus not suitable for predicting the outbreak in tropical areas. We have elaborated this issue in the revised discussion section (revised manuscript with track: Lines 335-338).

However, for the studied areas in the current study, which covers mainly temporal areas, this model works not badly. For the replication datasets (15 countries covering the world's temporal zones and several tropical areas) in all, the predicted values was correlated with the observed values with a Spearman's correlation coefficient 0.66. Even for tropical areas under not very hot weather, such as New Delhi in spring 2020 (mainly March), the prediction performed quite well, with the Spearman's correlation coefficient reached 0.95 between the predicted daily new case counts and the observed ones.

"3) This is related to point 4 in the earlier report related to errors. Authors have mentioned that they have provided only p values but no criteria for errors. However, while calculating p values using any software program, some distribution of errors are assumed, as for example normal distribution, t-distribution etc. Depending on the validity of such distributions, the calculation of p can only be justified. Suppose in that software program, normal distribution has been considered for errors, then one is required to check whether such distribution is valid for the errors in their analysis. Otherwise, the calculated p value will not be correct. In fact, in this paper, for errors with heteroscedastic feature where the variance changes, the assumption of normal distribution will not be correct. Due to that, the calculation of p values could be wrong. So author should mention the assumption of the error distribution in calculating p values and check whether it is valid in their analysis.

Authors should take care of all these three points - particularly point 1 and 3. As it stands, short term model has serious problem of giving negative number of cases over the wide range of variations of all independent meteorological variables, covering all possible weather throughout world including Wuhan. Authors have decided models based on p values but calculation of p values are not expected to be correct for the reasons discussed above. Due to these two main problems, the manuscript in its present form, is not recommended for publication."

Response: Thank the reviewer for raising up the issue about errors and p-values. We used R packages to conduct Spearman's correlation analysis to assess the prediction performance of models. Spearman's correlation is non-parametric, thus, it does not assume any distributions of data and homogeneity of variance is not required for this analysis. Instead, Spearman's correlation analysis calculates correlation coefficient, p-value, and standard error based on data ranks. In addition, we focused on the values of correlation coefficient (which reflects the extent of concordance of the predicted values with the observed values) rather than the values of p-value, when investigating the model prediction performance by Spearman's correlation analysis in the manuscript. We did not assess the performance of our models based on p-values at all.

For questions related to point 4 raised in the previous review, we used geom_smooth function in the gglot2 package on the R platform to draw the smoothed fitting curves and 95% confidence intervals in Figure 2 and 3. This function computes the standard error bounds using a t-based approximation for local smooths (the cases for figure 3A, 3B, 3E, 3F), and normal distribution for generalised linear smooths (the cases for figure 2, 3C, 3D). The standard error reflects residual error of the smoothly fitted models, and it did change with different observed case counts, whose reason was unknown. We have mentioned about this issue as a limitation in the discussion section of the manuscript (revised manuscript with track: Lines 341-346). Nevertheless, this standard error bound was plotted automatically and no p-values were provided or assessed.

As to the model comparison and choice of suitable models, we decide the best model based on model fitness statistics, including log-likelihood, Akaike's Information Criterion, Bayesian Information Criterion, deviance, Spearman's correlation coefficient, etc. (Supplementary materials Table S1, S2, S3), but not based on p-values.

VERSION 3 – REVIEW

REVIEWER	Rathin Adhikari
	Centre for Theoretical Physics,
	Jamia Millia Islamia (Central University)
	New Delhi-110025

	INDIA
REVIEW RETURNED	10-Oct-2020
GENERAL COMMENTS	Report on \Predicting the local COVID-19 outbreak around the world with
	meteorological conditions: a model-based qualitative study"
	by Biqing Chen et al
	Manuscript ID bmjopen-2020-041397.R2
	The responses of the authors to my earlier comments made in points 1 and 2 are satis-factory.
	1) In fact, in point 1 in my earlier comment, I have not properly taken care of the change of units, authors have made, for the wind velocity in the later version. Now, as I see, their long term model indicates that for wind velocity from 0 to about 6 m/sec and temperature
	over a wide range of 100 C to 400 C, the COVID-19 pandemic is very unlikely to occur for very low humidity lesser than about 15 %.
	2) However, the response of authors to point 3 in my earlier comment, is not that satisfac-tory. Author should mention (may be near line 130) why they have considered Spearman's correlations in their work. Is there the monotonic correlations are present for the new case counts with temperature, humidity and other parameters ? The other point is that the sig-ni cance test of Spearman's correlation as shown (near line 182 of the paper) does depend on p values and should have in uenced the construction of the model. Authors should make a short comment on this in the paper.
	Authors should take care of particularly the second point. After these minor appropriate modi cations, the paper may be recommended for publication.

VERSION 3 – AUTHOR RESPONSE

"Reviewer(s)' Comments to Author:

Reviewer: 2

Reviewer Name

Rathin Adhikari

Institution and Country

Centre for Theoretical Physics,

Jamia Millia Islamia (Central University)

New Delhi-110025

INDIA

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

None declared

Please leave your comments for the authors below

Please see the attached file covchen2.pdf

The responses of the authors to my earlier comments made in points 1 and 2 are satisfactory.

1) In fact, in point 1 in my earlier comment, I have not properly taken care of the change of units, authors have made, for the wind velocity in the later version. Now, as I see, their long term model indicates that for wind velocity from 0 to about 6 m/sec and temperature over a wide range of -10°C to 40°C, the COVID-19 pandemic is very unlikely to occur for very low humidity lesser than about 15 %."

Response: We thank the reviewer for the positive opinion and understanding. It's true that from real observed data the relative humidity is rarely less than 15%. We would further narrow down the range of the relative humidity between 15% and 100%. Thus, our short-term model would fit for the situations redefined (revised manuscript with track: Lines 209).

"2) However, the response of authors to point 3 in my earlier comment, is not that satisfactory. Author should mention (may be near line 130) why they have considered Spearman's correlations in their work. Is there the monotonic correlations are present for the new case counts with temperature, humidity and other parameters ?"

Response: We thank the reviewer for raising up this question. We considered Spearman's correlations in the work only for readers to obtain a general idea about <u>the contribution of each</u> <u>meteorological factor to the new case counts</u>, which does not related to model construction assumptions. We considered Spearman's correlation test because <u>it is a non-parametric method</u> that does not request linear relationship (revised manuscript with track: Lines 130-134). A monotonic relationship is usually required but not strictly an assumption of Spearman's correlation. We assumed monotonic correlations between the new case counts and meteorological variables in this research. However, monotonic relationship is usually checked visually, and real-world data are rarely ideally monotonic. Nevertheless, we think it does not affect the reliability of the conclusions. For these reasons we chose Spearman's correlation that could tell us about the extent of the contribution of the meteorological factors to COVID-19 epidemiology.

"The other point is that the significance test of Spearman's correlation as shown (near line 182 of the paper) does depend on p values and should have influenced the construction of the model. Authors should make a short comment on this in the paper.

Authors should take care of particularly the second point. After these minor appropriate modifications, the paper may be recommended for publication."

Response: We thank the reviewer for his suggestion. This Spearman's correlation test is unrelated to the model construction. As we mentioned above, we included the Spearman's correlation in our work only to illustrate the contributions of meteorological factors to COVID-19 case counts. It is an independent result. The exact relationship between meteorological factors and COVID-19 case counts, which was related to model construction, was investigated through non-linear modeling. The p-values provided by R program when calling Spearman's correlation test indicate whether the correlation coefficient is significantly unequal to zero, which suggests true correlation exists. As Spearman's correlation is non-parametric, it did not assume distributions. We have also added a short comment on this in the revised manuscript (revised manuscript with track: Lines 134-136).