Response to Reviewer 1 Comments

Thank you very much for giving us an opportunity to revise our manuscript. We appreciate the editor and reviewers very much for their constructive comments and suggestions on our manuscript. We have studied the comments carefully and made corrections. Hope meet with approval.

Point 1
What about the possible collinearity issues in the covariates, most importantly regarding the meteorological variables?

Response 1
We calculated the variance inflation factor (VIF) for all candidate variables to assess the multicollinearity; variables with a VIF less than 5 were selected for inclusion in the model. Table 2 showed the results of the multicollinearity analysis. The VIF values of all variables were less than 5, so it could be considered that there was no multicollinearity between the variables, and all variables were included in the model.

Point 2
Do you consider other risk factors influence the occurrence of this disease? Why do you select just the few factors? What is the relative importance of these variables on HFMD?

Response 2
In fact, many factors may affect the occurrence of HFMD. This study mainly focused on the impact of climate and socio-economic on HFMD. These factors have been mentioned in previous related articles, therefore, we included these factors, and studied the influence of these factors on HFMD in Guangdong province while considering the spatiotemporal variability.

Micro level factors may also influence HFMD transmission, such as personal hygiene, educational background and incomes of children’s parents, living conditions and composition of major pathogens. Future studies will consider the potential impacts of these factors.

Point 3
How many weather stations in each locations? Would you please present the spatial distribution of these stations? How do you collect and spatial interpolate for climatic data?

Response 3
• We updated the meteorological data of the article. The current data is complete data for 2009-2012.
• There were 26 surveillance stations within Guangdong province.
• The meteorological surveillance stations were mapped in Figure 2 of the article.
• All data was obtained from the China Meteorological Data Sharing Service System.
• The monthly county level meteorological variables were calculated using ordinary spatial kriging methods based on the 26 surveillance stations.

Point 4
Do you consider the confounders?
Response 4
Spatial and temporal components were the confounders to be adjusted, which had both effect on the number of reported HFMD cases (dependent variable) and meteorological or socioeconomic variable (explanatory variables).

Point 5
There are some parts of the manuscript that are still confusing as regards the methodology used and its implementation step-by-step.
Response 5
We further elaborated on the method in the article.

Point 6
There are some other spatial-temporal model, such as spatial panel model, et al. Can the author(s) elaborate on their methodology selection?
Response 6
In related research, the most commonly used is the spatiotemporal scan statistic model. However, because the covariates cannot be included, the potential predictors cannot be quantitatively analysed and therefore are not suitable for our research.

The spatial panel model is an extension of the spatial regression model in the temporal dimension. The spatial panel model considers whether there is spatial correlation between dependent variables of adjacent regions and whether there is spatial correlation between the same explanatory variables of adjacent regions, however, it cannot express the trend of space and time separately. In the Bayesian spatiotemporal model used in this study, we extracted the spatiotemporal effect and divided it into three parts (space effect, temporal effect and spatiotemporal interaction effect) to represented the residual caused by latent variables that are not included in the model. This will help us to explain the results more clearly.

Point 7
The discussion and conclusion is one of the most interesting parts of the paper. The authors should highlight better their new contributions of their analysis as compared to the previous literature.
Response 7
We have supplemented our new contributions in the discussion section.

Point 8
Line 159,269, “The spatial distribution of HFMD risk also exhibited explicit spatial heterogeneity”. The spatial heterogeneity should be quantified by statistic index, such as q statistics.
Response 8
We added the q statistic in the article to quantify the heterogeneity of space and time.

Point 9
Line 116, “We assumed that meteorological data did not vary significantly across years”, can the author(s) verify the assumption?
Response 9
According to the reviewers’ suggestions, we later thought that this was an imprecise statement, and then updated the meteorological data of the article. Please refer to Response 3.

Point 10
Line 190: “In previous studies, spatial effects were assumed to be fixed and did not change over time.” Add references.

Response 10
Related references have been added.

Point 11
Table 2, what’s mean of “Range” and “Coefficients”?

Response 11
In the original Table 2, the range refered to the range of values of the covariates, and the coefficient refered to the estimated value of the regression coefficient. Putting these two columns together may make people misunderstanding; we have now divided them into two tables, Tables 1 and 5.

Point 12
Figure 6, what’s mean of “RR values of associated potential predictors.”? What are the exposure and control index?

Response 12
The formula for “estimated RR values of associated potential predictors” is:

\[ \hat{RR}_{pi} = \hat{\beta}_p \times \bar{X}_{(sd)p,i}, \]

\( \hat{\beta}_p \) was the estimated value of the regression coefficient of the \( p \)-th potential predictor and \( \bar{X}_{(sd)p,i} \) was the average of the standardization value of the \( p \)-th potential predictor in the region \( i \). Their product term \( \hat{RR}_{pi} \) represented the relative risk of HFMD caused by potential predictor \( p \) to region \( i \). We added a clearer explanation in the article.