



Global prediction for mpox epidemic

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ABSTRACT

The mpox epidemic had spread worldwide and become an epidemic of international concern. Before the emergence of targeted vaccines and specific drugs, it is necessary to numerically simulate and predict the epidemic. In order to better understand and grasp its transmission situation, and take some countermeasures accordingly when necessary, we predicted and simulated mpox transmission, vaccination and control scenarios using model developed for COVID-19 predictions. The results show that the prediction model can also achieve good results in predicting the mpox epidemic based on modified SEIR model. The total number of people infected with mpox on Dec 31, 2022 reached 83878, while the prediction of the model was 96456 with a relative error of 15%. The United States, Brazil, Spain, France, the United Kingdom and Germany are six countries with serve mpox epidemic. The predictions of their epidemic are 30543, 11191, 7447, 5945, 5606 and 4291 cases respectively, with an average relative error of 20%. If 30% of the population is vaccinated using a vaccine that is 78% effective, the number of infected people will drop by 29%. This shows that the system can be practically applied to the prediction of mpox epidemic and provide corresponding decision-making reference.

1. Introduction

Monkeypox (recently renamed mpox) has infected more than 85,000 people worldwide by April 25, 2023 (GLOBAL.HEALTH, 2022). Furthermore, the mpox epidemic has been declared a global health emergency by the World Health Organization on May 23, 2022 (Nuzzo et al., 2022). Mpox is a zoonotic infectious disease caused by the mpox virus in the genus Orthopoxvirus, which belongs to the same genus as smallpox virus. Typical symptoms include fever, severe headache, swollen lymph nodes, back pain, rash, muscle pain and so on (Wilson et al., 2014). Mpox can be transmitted to humans from rodents, primates and other animals, and also from humans. Mpox virus is spread by direct contact with the body fluids of infected people or with virus-contaminated items such as clothing and bedding. Similar to SARS-CoV-2, it can also be transmitted through highly toxic respiratory droplets. First time when the name of Monkeypox infection was used before 1970 but the virus was described in the Democratic Republic of the Congo until the 1970s. There was also an outbreak of mpox in the United States in 2003. However, unlike before, this mpox outbreak was caused by a variant of the mpox virus. The reason why this outbreak is much larger than before is that the rate of human-to-human transmission has increased significantly (Khan et al., 2022). This has to

arouse people's vigilance.

Studies have demonstrated that the Modified Vaccinia Ankara-Bavaria Nordic (MVA-BN), an attenuated smallpox vaccine can prevent 78% of mpox virus (Bertran et al., 2023; Rimoin et al., 2010), but its acquisition has become more difficult because of the extinction of smallpox in 1980. In addition, there has been no breakthrough in the specific drug for mpox so far (Adler et al., 2022). Therefore, due to the difficulties in development vaccines and specific drugs, non-pharmaceutical interventions are still an important means to fight back the mpox epidemic, similar to it of COVID-19. The mathematical models can provide a reliable scientific basis for various control measures. Moreover, the mathematical model can also analyze many dynamic characteristics of the mpox epidemic, such as infection rate, cure rate, mortality rate, incubation period, etc. Cross-species transmission of mpox virus among different species can also be simulated. This can provide a scientific basis for targeted measures to alleviate the impact of the epidemic on human society.

Khan et al. (2022) constructed a stochastic simulation model of cross-infection between human and other species to simulate the spread of mpox outbreaks in highly disturbed environments (Khan et al., 2022). Peter et al. (2022) constructed a deterministic mathematical model utilizing classical and fractional differential equations, and studied the

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simulation results with various parameter inputs. And the dynamic behavior of the model is investigated to provide a basis for formulating control policies (Peter et al., 2022). In addition, Peter et al. (2021) also analyzed the local and global disease-free and endemic equilibrium asymptotic stability conditions of the mpox epidemic by studying the transmission dynamics of mpox (Peter et al., 2021). Usman and Isa Adamu (2017) added the impact of treatment and vaccine prevention measures to the dynamic model, simulating that under the above intervention measures, the spread of mpox epidemic has been contained (Usman and Isa Adamu, 2017). The above models simulate and analyzes the spread of mpox well, but timely prediction is also urgently needed. Fitting, simulation and dynamic analysis can analyze the transmission characteristics of the mpox epidemic. And it is possible to simulate the suppression effect of different control measures and vaccination programs on the epidemic by changing the parameter input. However, timely and accurate prediction of the epidemic development trend is badly needed when faced with a sudden epidemic. We also should assess its possible impact on the social economy. Then we can adjust the response measures according to the development trend to the epidemic to achieve the best results as possible. Therefore, developing a practical and fast predicting model is also of great importance.

The development of modern weather forecasting technology is very mature. From nowcasting within hours to long-term climate forecasting in units of years has become a reality. Although it still needs many improvements to further increase the accuracy, the prediction methods and parameterization scheme ideas in climate models are still worth learning and being added to epidemic prediction models. For example, the CESM model is the most complete for simulating the entire Earth system in atmospheric science. It is a fully coupled multi-sphere global climate model that can be used for simulations of the Earth's past, present and future climate states (Kay et al., 2015; NCAR, 2023). Moreover, the statistical-dynamic forecasting method in weather numerical forecasting can also serves as reference in epidemic models. On the one hand, the dynamic models are both composed of differential equations, so the dynamical system are relatively similar. On the other hand, there are situations where the historical situation is similar to the current situation. Therefore, it is entirely possible to invert the coefficients of the epidemic model through statistical-dynamic methods, and combine historical coefficients for prediction (Huang et al., 1993; Huang and Yi, 1991). Furthermore, climate models comprise many parameterizations. For example, the parameterization scheme of solar radiation absorption allows the model to simulate more physical processes while being streamlined (Lacis, A., Hansen, J., 1973). We can also introduce the idea of parameterization scheme into the epidemic model.

In this study, we propose to introduce statistical dynamical forecasting methods and the idea of parameterization scheme from atmospheric science to epidemic prediction. First, based on the improved SEIR (susceptible-exposed-infectious-removed) model, a SEIQRDP model (susceptible-exposed-infectious-quarantined-recovered-death-protected) is constructed. Then, we construct corresponding parameterization schemes according to different scenarios in actual situations. Finally, by inputting current data or historical data to invert the coefficients, and then extrapolating the model to predict the development trend of the epidemic. During COVID-19 pandemic, we used the same method to construct GPCP (Global prediction system for COVID-19 pandemic) and GPEP (Global Prediction System for Epidemiological Pandemic) (Huang et al., 2020), and achieved reliable prediction results. Especially in the prediction of local epidemics in China, it provides suggestions of epidemic response for government. After replacing it with mpox epidemic data and corresponding parameterization schemes, we built a mpox epidemic prediction system and achieved reliable prediction results. This demonstrates the generality of this method in epidemic prediction.

2. Method

2.1. Modified SEIR model

To predict the global spread of mpox, we use the modified SEIR model (SEIQRDP) which divides the population into seven categories: susceptible people (S), potentially infected people (E, infected cases in a latent period), infected people (I, infected cases which have not been quarantined), quarantined people (Q, confirmed and quarantined cases), recovered people (R), deaths (D) and insusceptible people (people who take protective measures). The model consists of the following equations:

$$dS(t)/dt = -\beta I(t)S(t)/N - \alpha S(t) \quad (1)$$

$$dE(t)/dt = \beta I(t)S(t)/N - \gamma E(t) \quad (2)$$

$$dI(t)/dt = \gamma E(t) - \delta I(t) \quad (3)$$

$$dQ(t)/dt = \delta I(t) - \lambda(t)Q(t) - \kappa(t)Q(t) \quad (4)$$

$$dR(t)/dt = \lambda(t)Q(t) \quad (5)$$

$$dD(t)/dt = \kappa(t)Q(t) \quad (6)$$

$$dP(t)/dt = \alpha S(t) \quad (7)$$

The total population (N) is equal to the sum of the seven populations at any time.

$$S + P + E + I + Q + R + D = N \quad (8)$$

The coefficients of the model: α , β , γ , δ , λ , and κ represents the rate of protection, the rate of infection, the inverse of the average latent time, the rate at which infected people enter quarantine, the time-dependent recovery rate, and the time-dependent mortality rate, respectively. The model assumes that the total population is a constant, so the birth rate and death rate are not considered. Compared with the traditional SEIR model, this modified model adds P (insusceptible) and Q (quarantined) cases. In reality, people will take self-protection measures because they are aware of the existence of the epidemic, so the possibility of infection may be less (Amer et al., 2023). Moreover, the actual number of infected people is almost impossible to know, while the number of people in quarantine (official quarantine and self-quarantine) is. The number of death is also separated from the number of recoveries to obtain more accurate simulation and prediction result. The modified model can describe more infection processes and describe the spread of the real world in more detail.

2.2. Parameterization schemes

By introducing the idea of parameterization scheme in atmosphere science into epidemic model, it is possible to describe more scenarios of mpox epidemic transmission on the basis of slightly modifying the dynamic system of the model (Guanabara et al., 1978). In this way, repeated modifications to the model dynamic system can be avoided, thereby affecting the stability of the model. In addition, different parameterization schemes can be flexibly selected for prediction and simulation in the face of different situations. The practicability, flexibility and expansibility of the model are greatly improved.

2.2.1. Parameterization scheme of vaccination

Although specific vaccines and drugs against mpox have not been developed, studies have shown that the smallpox vaccine has a high resistance to mpox virus (Bertran et al., 2023; Beutner et al., 2008). Therefore, constructing a vaccine parameterization scheme is favorable for simulating and predicting the mpox epidemic. The schematic diagram of the model is shown in Fig. 2. To be close to reality, we assume

that the protection rate of the vaccine is 78%, so people who have been vaccinated can no longer be infected by mpox virus (Bertran et al., 2023). We assume that vaccinations have been completed at the start of the outbreak. Of course, large-scale vaccination in the real world is impossible to complete in a short period of time, or even unnecessary. And actually, there is no mass vaccination. However, such a simplified assumption can already achieve the simulation effect. Because vaccination will directly divide the susceptible into the protector group, the parameterization scheme constructed is as follows:

$$S(0) = S(0) - Va * S(0) \quad (9)$$

where $S(0)$ represents the initial number of susceptible population, and Va represents the proportion of vaccinated population.

2.2.2. Parameterization scheme of control measures

Although the transmission mode of mpox is different from COVID-19 pandemic, control measures such as reducing human interaction are still one of the effective means to deal with the epidemic. Because the main route of transmission of mpox is still through direct contact between people (Allan-Blitz et al., 2022), constructing a parameterization scheme of control measures like infection rate decay is important to simulate the prevention and control effects of different countermeasures, as shown in Fig. 2b. It is assumed that government departments or people themselves start to take control measures after discovering the epidemic T_0 days. The epidemic infection rate β_0 changes with time and decays with rate. In the real world, in addition to simply considering the effect of prevention and control, it is also necessary to measure according to specific economic conditions. In the face of different epidemics, it is necessary to strike a balance between economic development and epidemic prevention and control (Khadiolkar et al., 2020). The impact of the mpox epidemic on the real world is relatively small, so this is simply an academic study to explore the impact of different control measures on the mpox epidemic. The infection rate variation in the control parameterization scheme is as follows:

$$\beta(t) = \begin{cases} \beta_0, & t \leq T_0 \\ \beta_0 * \text{rate}^t, & t > T_0 \end{cases} \quad (10)$$

where β_0 represents the basic infection rate, rate represents the decay rate of infection rate, T_0 represents the time when control measures begin.

2.3. Inversion method

The data of mpox is obtained from the website: <https://www.mpox.global.health/>. It includes the data of all the countries with mpox outbreaks, and now there are more than 100 countries. By introducing the latest epidemic data in actual time and using the improved least squares method to invert the latest model coefficients, the subsequent epidemic development can be predicted (Huang et al., 2020; Zhao et al., 2022). The operation of the model is mainly divided into two steps: inversion and simulation/prediction. In the inversion step, the acquired actual data is firstly preprocessed to facilitate the inversion calculation of the model. For example, data with cumulative value greater than 20 (given empirically) in each country will be intercepted and the influence of 0 value will be eliminated. Secondly, an initial value is given for each population and coefficient, and then the equations are integrated using the fourth-order Runge-Kutta scheme (Zealand, 1996), so as to obtain a sequence of the number of each population. Then, the least squares calculation is performed on the sequence of infected people (quarantined plus dead plus recovered) obtained by the integration above and the actual sequence of infected people, which will be repeated until the sum of the squared residuals of the two sequences becomes the minimum, so as to obtain the basic coefficient of the inversion. In the simulation/prediction step, an appropriate parameterization scheme is firstly selected according to the needs of the actual scenario. For

example, the control parameterization scheme will be chosen to simulate the control scenario in a certain region. The model is then extrapolated using the inverted coefficients and parameterization schemes to obtain simulation/prediction results.

2.4. Scoring method

In order to objectively evaluate the prediction effect of the model and provide a reference for subsequent model improvement, it is necessary to construct a prediction score. The scoring equation is as follows:

$$PS = 1 - |RE| \quad (11)$$

Where PS represents the scores for predictions in various countries, RE represents the relative error of the cumulative prediction data.

3. Results

The model prediction process is shown in Fig. 1a. First, the input data are collected. After selecting the corresponding parameterization schemes, inversion and prediction are performed. Finally the prediction results are obtained. Through the processing of mpox epidemic data in more than 100 countries around the world, the model obtained the prediction results, as shown in Fig. 3. The model uses 1/2 of the data with cumulative data greater than 20 for the inversion coefficient, and then uses the remaining 1/2 of the data for testing. In September 2022, the trend of the epidemic had already been predicted by the model when the outbreak of mpox was as its peak. For details, please refer to the preprint article and the display website (<http://covid-19.lzu.edu.cn/>) (Zhang et al., 2022). Whether it is the prediction in 2022 or the backtest results in this article, the model has shown reliable prediction results. It is obvious that both the fitting and prediction results are highly consistent with the actual data. This proves that the model can grasp the development trend of the epidemic and present better prediction results. The model can fit the actual data well, although the data of some countries fluctuate greatly, it can still grasp the trend of the epidemic development. Therefore, the model can still conform to the actual epidemic development trend well when extrapolating predictions. However, because this round of mpox epidemic has only one wave, the epidemic curve is unimodal, so it is relatively easy to predict.

In some studies, the transmission of mpox is simulated by giving the coefficient of the mpox epidemic model. In this study, the coefficients are inverted from actual data to obtain coefficients that conform to both

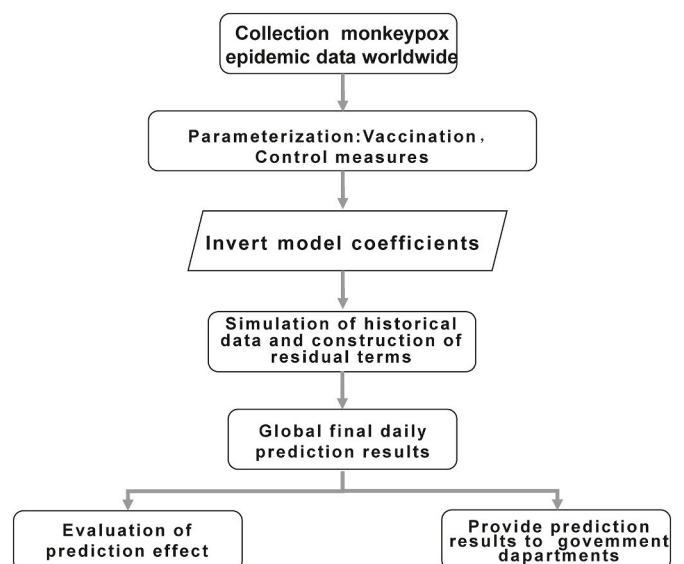


Fig. 1. Flowchart for predicting mpox outbreak.

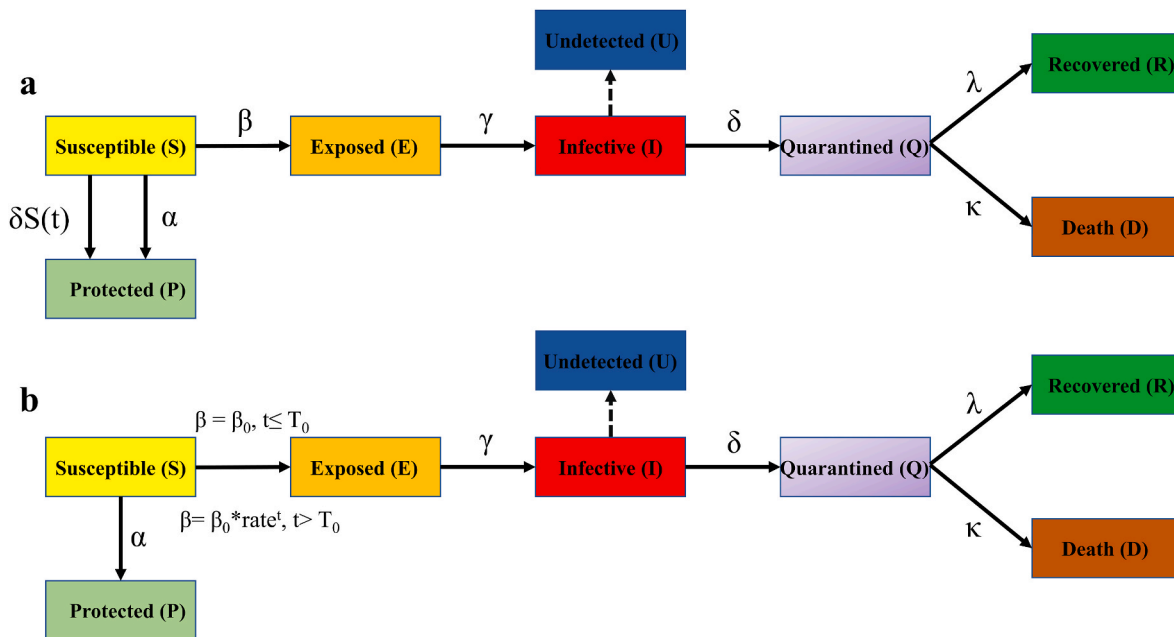


Fig. 2. Schematic diagram of the model, a, the schematic diagram of the vaccine parameterization scheme, b, the schematic diagram of the model of the control parameterization scheme.

the actual data and the dynamic model, as shown in Table 1. According to alpha, the number of people who take self-protection measures is still a minority. The beta only reflects that in this round of the epidemic, although the mpox virus has greatly enhanced its infectivity in the population, it is still far lower than other viruses such as SARS-CoV-2 (Luna et al., 2022). The delta indicates that only a small fraction of the infected population was detected and reported, implying that a large number of mpox patients may not be included in official reports (De Baetselier et al., 2022). If people's self-protection awareness can be enhanced, the contact rate can be reduced, and the detection and isolation of sick cases can be increased, the number of infections will be greatly reduced.

Fig. 4a shows the cumulative predictions to the end of December 2022 for all countries with mpox epidemic. By December 31, 2022, the system predicts that the number of people infected with mpox worldwide will be 96,456. The actual number of infected people was 83,878, and the relative error of the system was 15%. It can be seen from the figure that the mpox epidemic, like COVID-19, has heterogeneity in spatial distribution. In North America, South America, and Europe, the outbreak is significantly more severe than in other parts of the world. Specifically, from Fig. 5a, the prediction of mpox cases in the United States, Brazil, Spain, France, the United Kingdom and Germany all exceed 4000 by the end of December 2022. In particular, the United States and Brazil had more than 10,000 cases. The number of them are 30543, 11191, 7447, 5945, 5606 and 4291 cases respectively, with an average relative error of 20%. This is because those countries vary in culture, lifestyle, population density, control measures, etc. In addition, although the spread of mpox is not very high, it can still spread to the whole world. This shows that while the modern transportation system greatly facilitates human beings to cross spatial locations, it also brings great convenience to the spread of infectious diseases (Balcan et al., 2009; Tatem et al., 2006).

By comparing the actual cumulative data with the predicted cumulative data at the end of 2022, the prediction scores of the model are calculated using the above equation (11). The spatial distribution of scores is shown in Fig. 4b. Corresponding to the results shown in Fig. 3, the prediction scores of most countries in the world are above 90. This reflects that the model has a strong predictive ability for mpox epidemic. In prediction for some countries in Eastern Europe and South America,

the model scores lower, which has a high correlation with actual data collection. For example, in Chile, due to statistical errors, the daily new data has negative value, exerting a great misleading effect on the prediction results.

Mass vaccination could help humans fight the mpox virus, as shown in Fig. 5a, if 20% of people were vaccinated against mpox by the end of the year, it could have reduced cases by about 16%. And if the vaccination ratio was increased to 30%, the number of cases could be reduced by 29%. This suggests that the proportion of vaccinations and the proportion of potential case reductions are not simply linearly related. Although mpox is less contagious than SARS-CoV-2, it still spread to many countries due to a globalized transportation system. In theory, no matter what measures humans take, it was only a matter of time before most countries in the world would be invaded by mpox virus. In reality, countries had taken far fewer measures against mpox than they did against COVID-19. In order to simulate the impact of control measures on the suppression of mpox, we used the above-mentioned parameterization scheme of control measures for simulation. The simulation results show that if the epidemic is intervened in time, the mpox can be greatly suppressed. Although economic costs and other factors must be considered comprehensively in actual implementation, the simulation results also show that the earlier effective interventions are carried out, the more likely it is to greatly reduce the impact of the epidemic. In reality, it is obvious that the implementation of control measures can be more flexible to achieve the optimal choice of epidemic control and economic development (Rowthorn et al., 2009). Therefore, this enlightenment to us is that normalized monitoring of infectious diseases allows us to respond in a timely manner, thereby minimizing losses.

In order to further test the prediction performance of the model, the prediction results of 10 countries with serious mpox epidemics in the world were evaluated, as shown in Fig. 6. Except for the high value of the rmse divided by mean due to the volatility of the data, both PS and CORR are close to 1. Evaluating from the daily average number of daily confirmed cases, the values of the United States, Brazil, and Spain are significantly higher than those of other countries, and the United States is the most serious. Except for France and the United Kingdom whose scores are lower than 0.6, the scores of other countries are close to 1. Most correlations between the predicted sequence and the actual sequence are higher than 0.8. In a word, the model achieved reliable

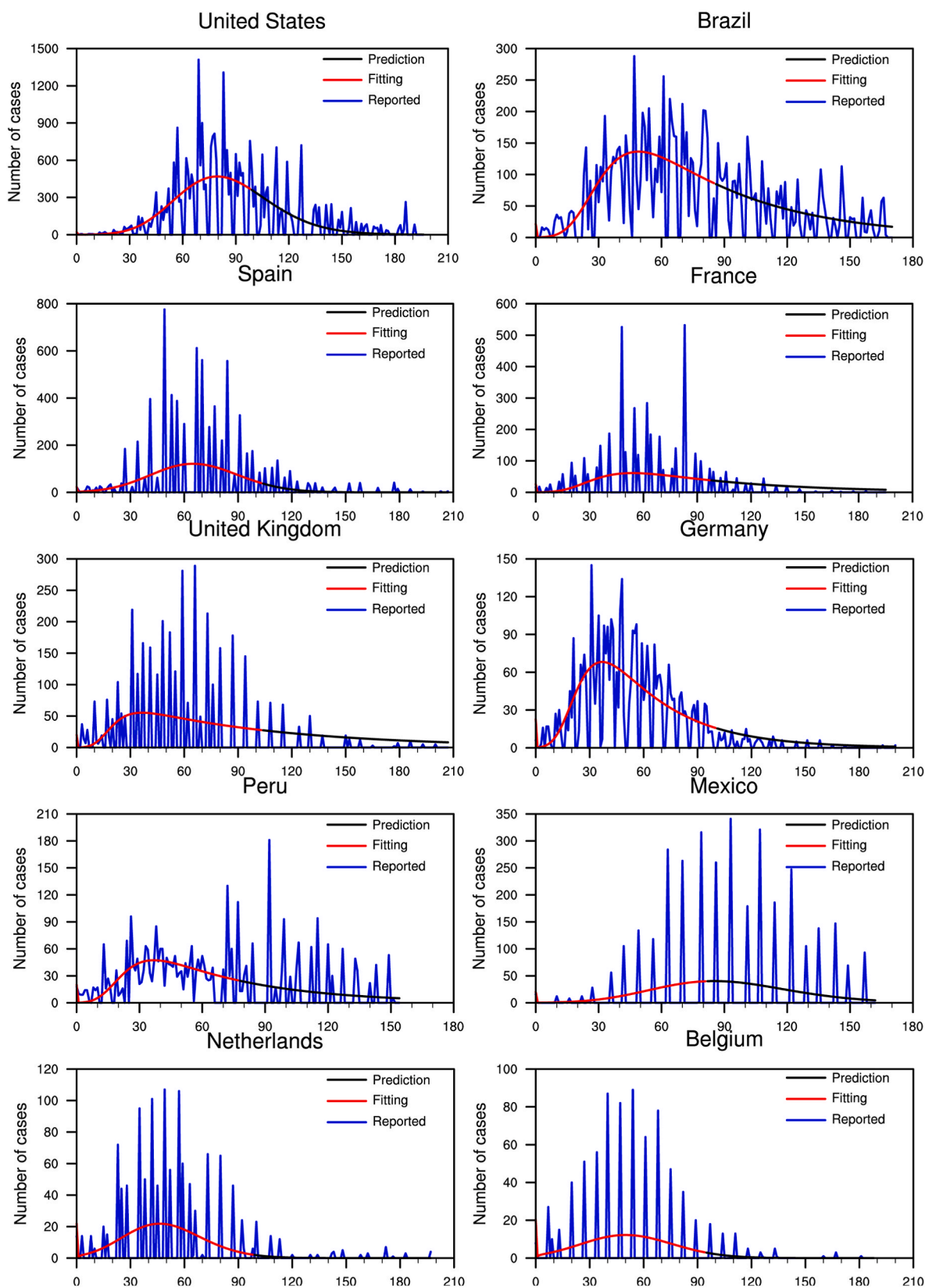


Fig. 3. The fitting, prediction data of the model are compared with the reported data. The blue curve represents the data of reported cases, the red curve represents the fitting data, and the black curve represents the prediction data.

Table 1

The inverted model coefficients of the ten countries with serve mpox epidemic.

Countries	alpha	beta	gamma	delta	lambda	kappa
United States	0.030	0.891	0.125	0.095	0.009	0.009
Brazil	0.116	1.338	1.000	0.005	0.002	0.002
Spain	0.008	0.429	1.000	0.253	0.009	0.009
France	0.067	0.545	1.000	0.016	0.011	0.011
United Kingdom	0.134	1.245	1.000	0.012	0.004	0.004
Germany	0.095	0.801	1.000	0.028	0.005	0.005
Peru	0.106	0.872	1.000	0.021	0.018	0.018
Mexico	0.024	0.556	0.091	0.085	0.009	0.009
Netherlands	0.017	0.312	1.000	0.146	0.003	0.003
Belgium	0.010	0.617	0.255	0.378	0.011	0.011

results in predicting mpox epidemic outbreaks.

Perhaps due to people's experience in fighting against COVID-19 pandemic, people took corresponding protective measures after the large-scale outbreak of mpox. In addition, thanks to the development of the smallpox vaccine, people can be vaccinated against the mpox virus as a targeted manner. Although the smallpox vaccination is only a small minority, this also helped reduce potential mpox virus infection. These factors had led to a downward trend in the current mpox epidemic. However, this may only be the first wave of mpox outbreaks, and

subsequent viruses may variate, or there may be more waves as environmental conditions change. Maybe the mpox epidemic will not come back in the short term, but the risk of its variation and re-infecting humans on a large scale still exists. Regarding the current epidemic situation, it is safer to maintain a cautious attitude.

4. Conclusion

The prediction of mpox epidemic outbreaks can provide meaningful prediction and analysis on the global time and space scale, and offer scientific basis for decision-making of governments around the world. Similar to the various scenarios that emerge in atmosphere science, there were a variety of different scenarios in the epidemic spread such as control situation, unblocking situation, vaccination, drug intervention situation. These situations can be expressed by some simplified parameterization schemes as used in atmospheric science (Kain, 2004). In this way, the model can more accurately describe the actual situation, and then provide more accurate simulation and prediction results.

Based on the global prediction system of the Global Prediction System for Epidemiological Pandemics (GPEP), this study developed a general global prediction system that can be used for the prediction of other infectious diseases such as mpox. According to the actual situation

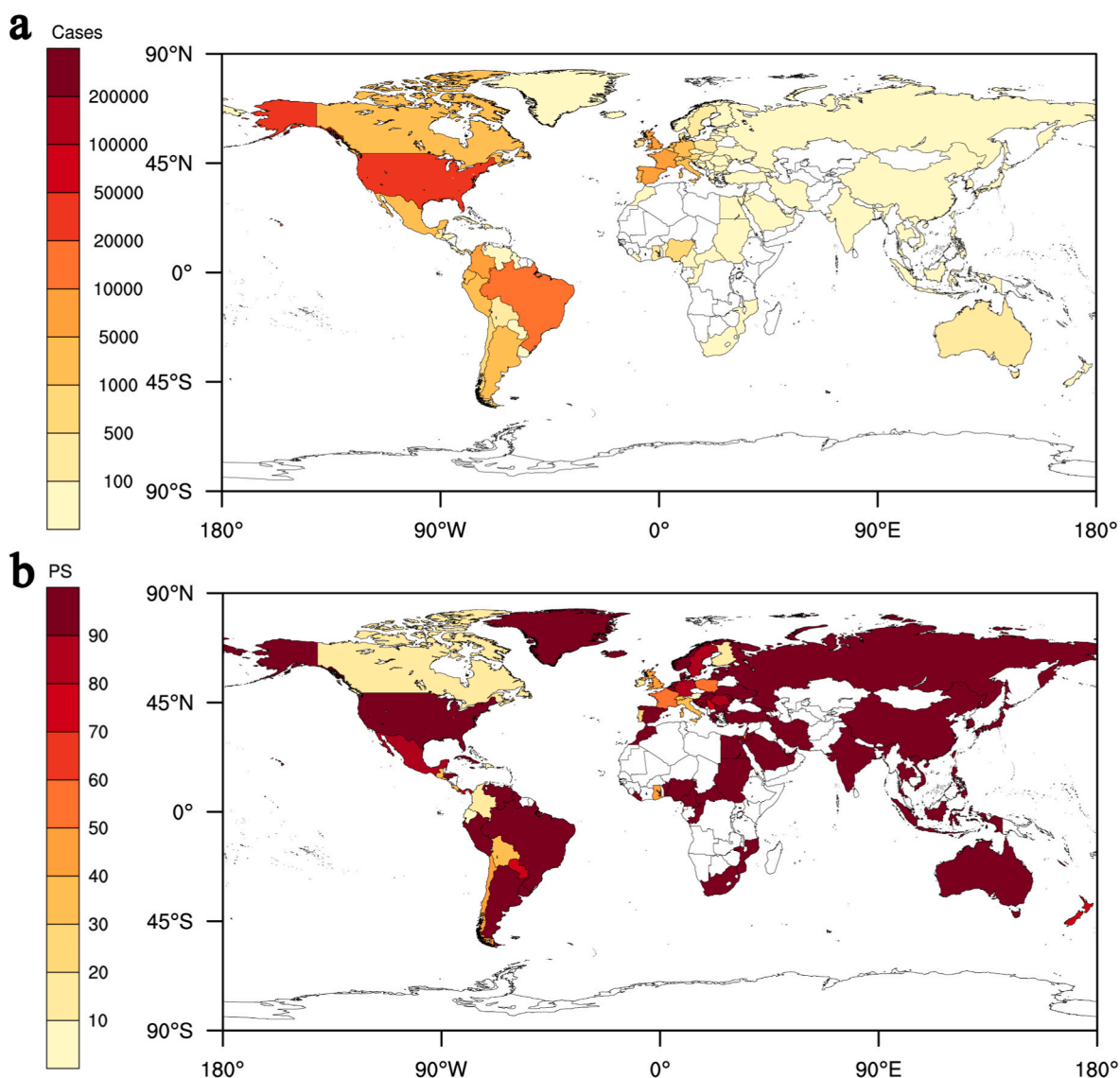


Fig. 4. a, global prediction of cumulative cases of mpox on Dec 31, 2022, b, global prediction score of cumulative cases of mpox on Dec 31, 2022.

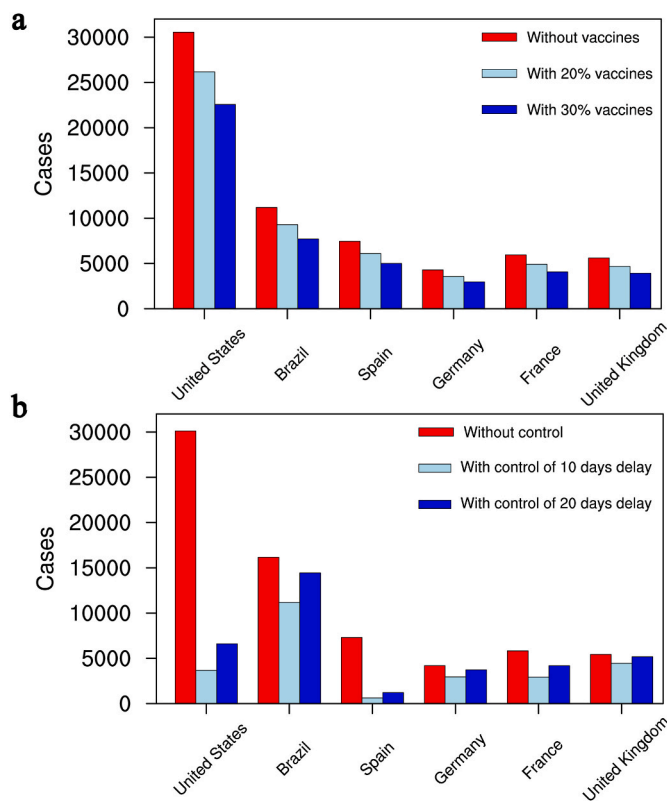


Fig. 5. a, simulated cumulative cases of mpox on Dec 31, 2022 for six countries with or without vaccines. b, simulated cumulative cases of mpox on Dec 31, 2022 for six countries with or without control measures.

of the mpox epidemic, the corresponding parameterization scheme: control parameterization scheme and vaccination parameterization scheme were developed. This system has successfully used part of the epidemic data to predict the mpox epidemic relatively accurately, and describe the development trend of the epidemic in various countries of

the world. The relative error of the prediction of the cumulative number of infected people in the global epidemic at the end of 2022 is 15%. The relative error of the prediction for the six countries with severe epidemic: the United States, Brazil, Spain, France, the United Kingdom and Germany is 20%. The system has been able to actually predict various epidemics based on certain data, and provide certain policy references for relevant government departments. In addition, the impact of different control measures and vaccination programs on the epidemic was simulated using the constructed control parameterization scheme and vaccination parameterization scheme. This provides a certain reference for the actual operation in the future.

5. Discussion

Although some basic predictions can be generated by the current general model, it still needs to be improved. Due to the lack of monitoring means, it is difficult to obtain actual infectious disease data, which directly impact the effect of epidemic simulation and prediction. The current model does not sufficiently describe the objective situation of the spread of infectious diseases because many factors need to be taken into consideration, such as traffic data, human behavior changing data, data of different building types, economic data, etc., so it is still necessary to improve the model (Buckee, 2020).

Finally, further understanding of mpox virus and its transmission mechanism and variation characteristics are needed. In view of the limitations of existing biological and medical technology, people still lack timely and effective vaccines and specific drugs in the face of large-scale emerging infectious diseases. So people's own self-protection is very important. In the prevention of sexually transmitted infectious diseases such as mpox, the prevention methods of developed countries are worthy of reference for most developing countries, such as: helping women improve decision-making about self-protection during sexual activity (Konkle-Parker et al., 2018), using a type of contraceptive that is both a spermicide and a microbicide to prevent sexual transmission of HIV (Uckun & D'Cruz, 1999), and so on. As climate change becomes more and more severe, the habitat of a large number of wildlife may change, potentially leading to more contact with humans, thus creating opportunities for a large number of pathogens to enter the human body

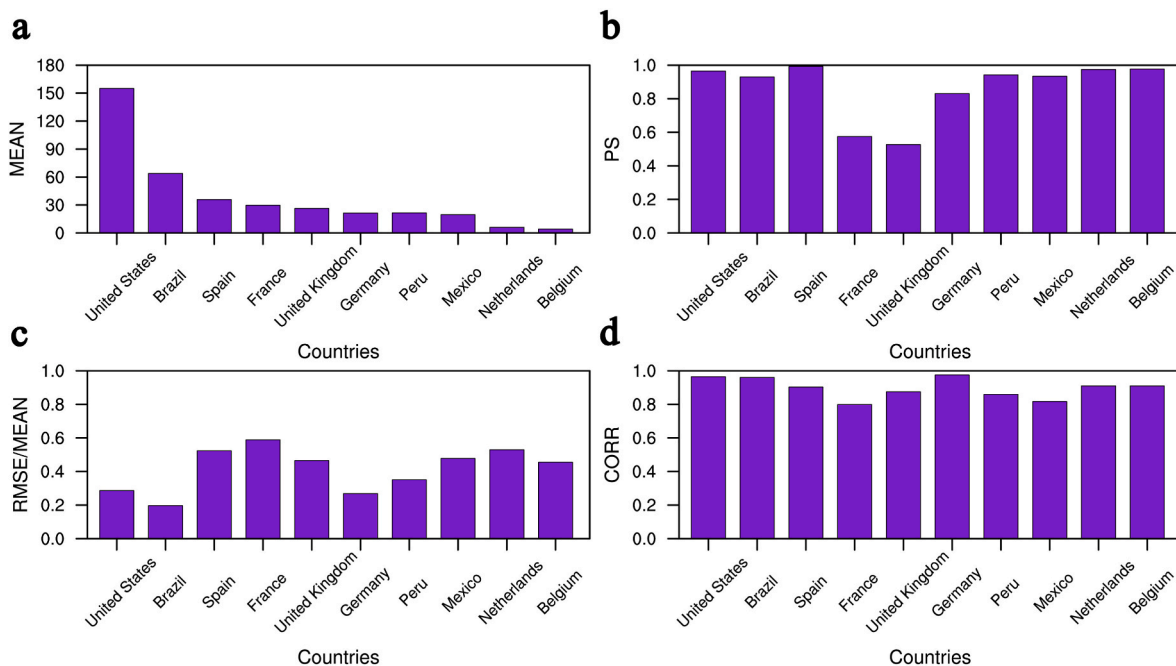


Fig. 6. a, daily average data for ten countries with severe mpox epidemic, b, prediction scores for ten countries with severe mpox epidemic, c, ratio of RMSE to MEAN for ten countries with severe mpox epidemic, d, correlation of prediction and reported data for ten countries with severe mpox epidemic.

(Altizer et al., 2013). If humans are simply struggling to cope with a large-scale outbreak that has already occurred, and ignore the strengthening of monitoring research on pathogen spillover at the source, we may pay a very heavy price. Moreover, the risk of 58% zoonotic disease has increased (Mora et al., 2022), and the development of general epidemic dynamic models is also an extremely important method to quickly respond to various potential large-scale infectious diseases in the future.

Credit author statement

Li Zhang analyzed the data, wrote the code, wrote the initial manuscript edition, joined in the discussion, and finalized the manuscript; Jianping Huang developed the core idea, participated in the data analysis and writing of the initial version of the manuscript, supervised the research, and edited and reviewed the final version of the manuscript; Wei Yan, Yingjie Zhao, Danfeng Wang, Bin Chen participated in data collection, developed the methodologies, wrote the code and participated in the writing of the early versions of the manuscript. All authors have read and consent to the final version of the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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