ANNALS OF MEDICINE
2022, VOL. 54, NO. 1, 941–952
https://doi.org/10.1080/07853890.2022.2060522

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ORIGINAL ARTICLE

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Comparison of health-oriented cross-regional allocation strategies for the COVID-19 vaccine: a mathematical modelling study

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ABSTRACT

Background: Controlling the epidemic spread and establishing the immune barrier in a short time through accurate vaccine demand prediction and optimised vaccine allocation strategy are still urgent problems to be solved under the condition of frequent virus mutations.
Methods: A cross-regional Susceptible-Exposed-Infected-Removed dynamic model was used for scenario simulation to systematically elaborate and compare the effects of different cross-regional vaccine allocation strategies on the future development of the epidemic in regions with different population sizes, prevention and control capabilities, and initial risk levels. Furthermore, the trajectory of the cross-regional vaccine allocation strategy, calculated using a particle swarm optimisation algorithm, was compared with the trajectories of other strategies.
Results: By visualising the final effect of the particle swarm optimisation vaccine allocation strategy, this study revealed the important role of prevention and control (including the level of social distancing control, the speed of tracking and isolating exposed and infected individuals, and the initial frequency of mask-wearing) in determining the allocation of vaccine resources. Most importantly, it supported the idea of prioritising control in regions with a large population and low initial risk level, which broke the general view that high initial risk needs to be given priority and proposed that outbreak risk should be firstly considered instead.
Conclusions: This is the first study to use a particle swarm optimisation algorithm to study the cross-regional allocation of COVID-19 vaccines. These data provide a theoretical basis for countries and regions to develop more targeted and sustainable vaccination strategies.

ARTICLE HISTORY
Received 29 October 2021
Revised 7 February 2022
Accepted 25 March 2022

KEYWORDS
Vaccine allocation strategies; mathematical modelling; COVID-19; particle swarm optimisation

KEY MESSAGE

- The innovative combination of particle swarm optimisation and cross-regional SEIR model to simulate the pandemic trajectory and predict the vaccine demand helped to speed up and stabilise the construction of the immune barrier, especially faced with new virus mutations.
- We proposed that priority should be given to regions where it is possible to prevent more infections rather than regions where it is at high initial risk, thus regional outbreak risk should be considered when making vaccine allocation decisions.
- An optimal health-oriented strategy for vaccine allocation in the COVID-19 pandemic is determined considering both pharmaceutical and non-pharmaceutical policy interventions, including speed of isolation, degree of social distancing control, and frequency of mask-wearing.

1. Introduction

Faced with the increasing reported COVID-19 infections [1] and severe situation of the epidemic prevention and control, the production and allocation of safe and effective vaccines has become an accepted global strategy for the long-term control of COVID-19 [2], which is prior to non-pharmaceutical interventions because the adoption of non-pharmaceutical interventions is unsustainable and may cause countries with insufficient economic benefits and social safety nets to suffer aggravate social and economic inequality [3–5]. Although the collaborative efforts of researchers globally have increased the scale and speed of vaccine development [6,7], a shortage of vaccines in the initial stage of vaccination is inevitable because of the high demand and the requirement for at least two doses of most COVID-19 vaccines [8]. Moreover, frequent virus mutations [9] also call for the immediate establishment

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Supplemental data for this article can be accessed here.

Table 1. Health-oriented vaccine allocation strategies.

No.	Allocation strategy	Weight to allocate vaccine resources in each region
1	Report-based	Cumulative number of confirmed cases
2	Report-pop-based	Total number of confirmed cases as a proportion of the regional population
3	Infect-based	Cumulative number of confirmed and suspected cases
4	Report-pop-calibrated	Cumulative number of confirmed cases calibrated to the regional population size
5	New-infect	Number of new suspected and confirmed cases
6	New-infect-pop-based	Number of new suspected and confirmed cases as a proportion of the regional population
7	New-infect-pop-calibrated	Cumulative number of new suspected and confirmed cases calibrated by the regional population size
8	Particle swarm	Particle swarm optimisation with the objective of minimising the total number of confirmed cases
9	Imported-based	Cumulative number of imported cases
10	Death-based	Cumulative number of deaths
11	Pop-based	Total population
12	Average	Equal allocation

of population immunity. Therefore, an effective strategy to reduce the spread of the epidemic, especially the new strains, through the optimal allocation of various vaccine resources has become a globally urgent issue.

The Susceptible-Exposed-Infected-Removed (SEIR) model, which is one of the most used models of infectious disease dynamics in recent studies, has been integrated with genetic algorithms to predict the trajectory of the epidemic and determine the optimal strategy for COVID-19 vaccination [10,11]. However, due to the limitations of population size, it is difficult for genetic algorithms to efficiently optimise thousands of parameters. In contrast, in continuous parameter-solving problems, particle swarm optimisation algorithms usually converge faster and can optimise thousands of parameters within 20 iterations [12]. Therefore, this study creatively combined a particle swarm algorithm with an SEIR model to determine the optimal vaccine allocation strategy and acquire optimal allocation ideas at a theoretical level. In addition, from the perspective of the SEIR model itself, merely considering a single non-pharmaceutical measure cannot effectively represent the level of prevention and control capabilities, which leads to a biased prediction of the spread of the epidemic and the demand for vaccines [13]. In this study, we systematically incorporated non-pharmaceutical interventions in the three dimensions of isolation speed, degree of social distancing control, and mask-wearing frequency into the SEIR model to decrease bias in the predictions and simulations.

In addition to accurately forecast vaccine demand, the choice of an effective vaccine allocation strategy is the basis for sufficient vaccine supply and the most direct means to protect the susceptible population [14] and reduce the risk of virus mutations [15]. Existing studies have extensively explored and discussed COVID-19 vaccine allocation strategies in terms of age structure, ethical framework, and other vaccine allocation optimisation factors [16–19]. However, under the condition of the highly infectious characteristics of SARS-CoV-2, an immunisation strategy based on reducing transmission has not been highly valued by scholars, despite it being an indispensable part of reducing the overall burden of disease in previous allocation strategies for influenza vaccines and the RTS,S malaria vaccine [20,21]. Incorporating correlations between the spread of the epidemic in different regions into the model from a spatial dimension to identify health-oriented vaccine allocation strategies is a high priority in the context of the current pandemic [22]. Therefore, this study used a cross-regional SEIR model that considered the interactions of epidemic evolution in different regions to explore epidemic prevention and control effects that the health-oriented vaccine allocation strategies could produce.

Overall, this study innovatively integrated particle swarm optimisation into the cross-regional SEIR model simulation and compared the effects of epidemic prevention and control by applying different health-oriented vaccine allocation strategies under the influence of non-pharmaceutical interventions of different intensities in each region. Our study provided a theoretical analysis framework and model for optimising vaccine allocation for future highly infectious global health crises. From a practical perspective, we proposed specific and feasible cross-regional vaccine allocation strategies which may be applicable to all regions of the world, especially those countries and regions with a low level of vaccine development and shortage of vaccine resources, to reduce the spread of the virus and deal with the risk of virus mutations.

2. Methods

2.1. Trajectory predictions and scenario simulations

Considering that the optimal cross-regional vaccine allocation strategy calculated using a particle swarm optimisation algorithm has a certain "black box"

Table 2. Description of scenarios with different population sizes, prevention and control capabilities and initial number of infections.

Scenarios	No.	Population size	Prevention and control ability	Initial infection number
Two-region Scenarios	A1	Small	High	Low
	A2	Large	Low	High
	B1	Small	Low	High
	B2	Large	High	Low
	C1	Small	Low	Low
	C2	Large	High	High
	D1	Small	High	High
	D2	Large	Low	Low
Eight-region Scenarios	E1	Small	High	Low
	E2	Large	Low	High
	E3	Small	High	High
	E4	Large	Low	Low
	E5	Small	Low	Low
	E6	Large	High	High
	E7	Small	Low	High
	E8	Large	High	Low
Random-region Scenarios	–	Random	Random	Random

Note. High prevention and control ability means that (a) every resident has an average of 2 days in the social distancing control state and does not have contact with outsiders; (b) all patients within the incubation period or with symptomatic infection who have not been hospitalised have a 40% probability of being tracked and will be isolated after 5 days on average and (c) the initial frequency of mask wearing is 50%. Low prevention and control ability means that (a) each resident has only 1 day of social distancing control and does not have contact with outsiders; (b) all patients in the incubation period or with symptomatic infection who have not been hospitalised have a 20% probability of being tracked and will be isolated after 7 days on average and (c) the initial frequency of mask wearing is 30%. Small and large population sizes were defined as 2 million and 10 million, respectively. The low and high numbers of initial infections were defined as 10 and 50, respectively.

attribute, it is difficult to extract stable rules, form strategies, and apply them to the real-world scenario. Therefore, our study proposed 11 vaccine allocation strategies with clear operability as alternatives, as shown in Table 1. The daily allocation weight was based on factors such as the population, the total number of confirmed cases, the rate of increase in the number of confirmed cases, the total number of deaths, confirmed cases as a percentage of the total population, and the total number of imported cases into each region.

The settings of scenario simulations are shown in Table 2. We first simulated a model of two regions with different populations, prevention and control capabilities, and initial numbers of infections, to test the effectiveness of different allocation strategies under different regional infection conditions and, simultaneously, to test the effectiveness of the allocation strategy in different scenarios. In the two-region scenario, the initial daily vaccine supply was 0.1% of the total population of the two regions, with a daily increase of 0.005%.

To further clarify the risk levels and vaccine demand in the eight regions, we developed an eight-region model and applied 12 allocation strategies to this model. We focussed on the vaccine allocation strategy of the particle swarm algorithm to investigate how it allocated vaccines among the eight regions to minimise the cumulative number of confirmed cases. Through the allocation strategy of the particle swarm algorithm, the risk level of each of the eight regions and the priority of allocation were roughly inferred.

Finally, to test the average effectiveness and stability of the different allocation strategies in the different scenarios evaluated, we used random numbers to generate 30 random scenarios. In these random scenarios, there were eight regions where the parameters were randomly allocated. By calculating the multiples of the number of final confirmed cases for the 11 strategies relative to the number of final confirmed cases from the particle swarm algorithm, the effectiveness and stability of the 11 algorithms, excluding the particle swarm algorithm, were recorded.

2.2. Model structure

Since combining the infectious disease dynamics model with vaccine allocation strategies and the particle swarm algorithm is a complex and abstract process, we provided a flowchart of the infectious disease dynamics model (Figure 1) and showed details of the model construction, the particle swarm algorithm, and relevant mathematical formulations in the Supplementary Material. Based on the transmission characteristics of the COVID-19 epidemics and related intervention policies, this study made several improvements based on the traditional SEIR model. Firstly, we further distinguished the exposed and infected individuals as “Non-infectious Exposed Individuals,” “Infectious Exposed Individuals,” “Symptomatic

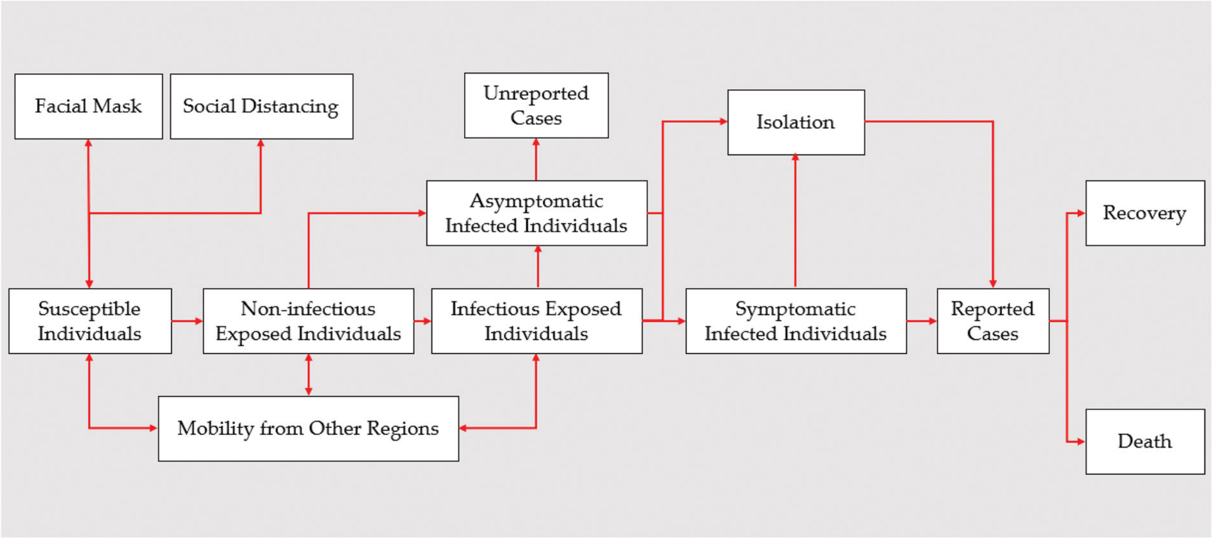

Figure 1. Structure of Infectious Diseases Dynamic Model.

Infected Individuals" and "Asymptomatic Infected Individuals". Secondly, we integrated human mobility and non-pharmacological interventions into the model, including isolation measures, mask-wearing, and social distance control. Finally, based on the construction of infectious disease dynamics model, we applied 12 vaccine allocation strategies including particle swarm algorithms by setting up above combinations of the scenarios for simulation, with a view to obtaining ideas and rules for optimal allocation. The model building and running, trajectories analysis, and visualisation were done in R version 3.7.5.

3. Results

3.1. Results of the two-region scenario

Figure 2 shows the changes in the total number of confirmed cases overtime after 12 vaccine allocation strategies were adopted using the two-region scenario. As shown in Figures 2-A-1 and 2-A-2, the intelligent allocation strategy 8, based on a machine learning particle swarm algorithm, provided the most protection and minimised the number of confirmed cases. It is worth noting that Strategies 2 and 6 increased the amount of vaccine allocated to region A1, which had strong prevention and control capabilities and a small population, rather than region A2, which had weak prevention and control capabilities but a larger population. We also observed that Strategies 1, 3, and 5, which only considered the epidemic situation, gave greater weight to regions with a higher initial number of infections; thus, resources were allocated to region C1, which had a high initial number of cases and high prevention and control capabilities. Scenario D showed similar results to scenario A, while the particle swarm algorithm (Strategy 8) still showed the best performance. Furthermore, due to poor prevention and control capabilities in densely populated regions in this scenario, Strategies 4 and 7, which favoured large-population regions, also achieved results second only to those of Strategy 8.

Figure 3 shows the number of vaccine resource allocations over time for the 12 vaccine allocation strategies in the two-region scenario. We focussed on analysing the basis of the particle swarm algorithm to allocate vaccine resources between two regions in different scenarios. Specifically, as shown in Figures 3-A-Particle-Swarm-1 and 3-A-Particle-Swarm-2, the particle swarm algorithm allocated more vaccine resources to the riskiest region, A-2, and realised the optimal allocation of resources. In Scenario C, based on the results of the particle swarm algorithm, more resources were allocated to region C-1, which had low prevention and control capabilities. In Scenario D (Figures 3D-Particle-Swarm-1 and 3 D-Particle-Swarm-2), although region D-1 had a high initial infection rate, the particle swarm algorithm allocated more resources to region D-2, possibly because region D-2 had low prevention and control capabilities. Therefore, prevention and control capacities are key factors in determining the allocation of vaccine resources.

3.2. Results of the eight-region scenario

Figure 4 shows the trajectory of the epidemic after adopting the 12 vaccine allocation strategies in the eight-region scenario. As seen in Figure 4-Final Total Cases and Figure 4-Total Cases, Strategy 8, which was

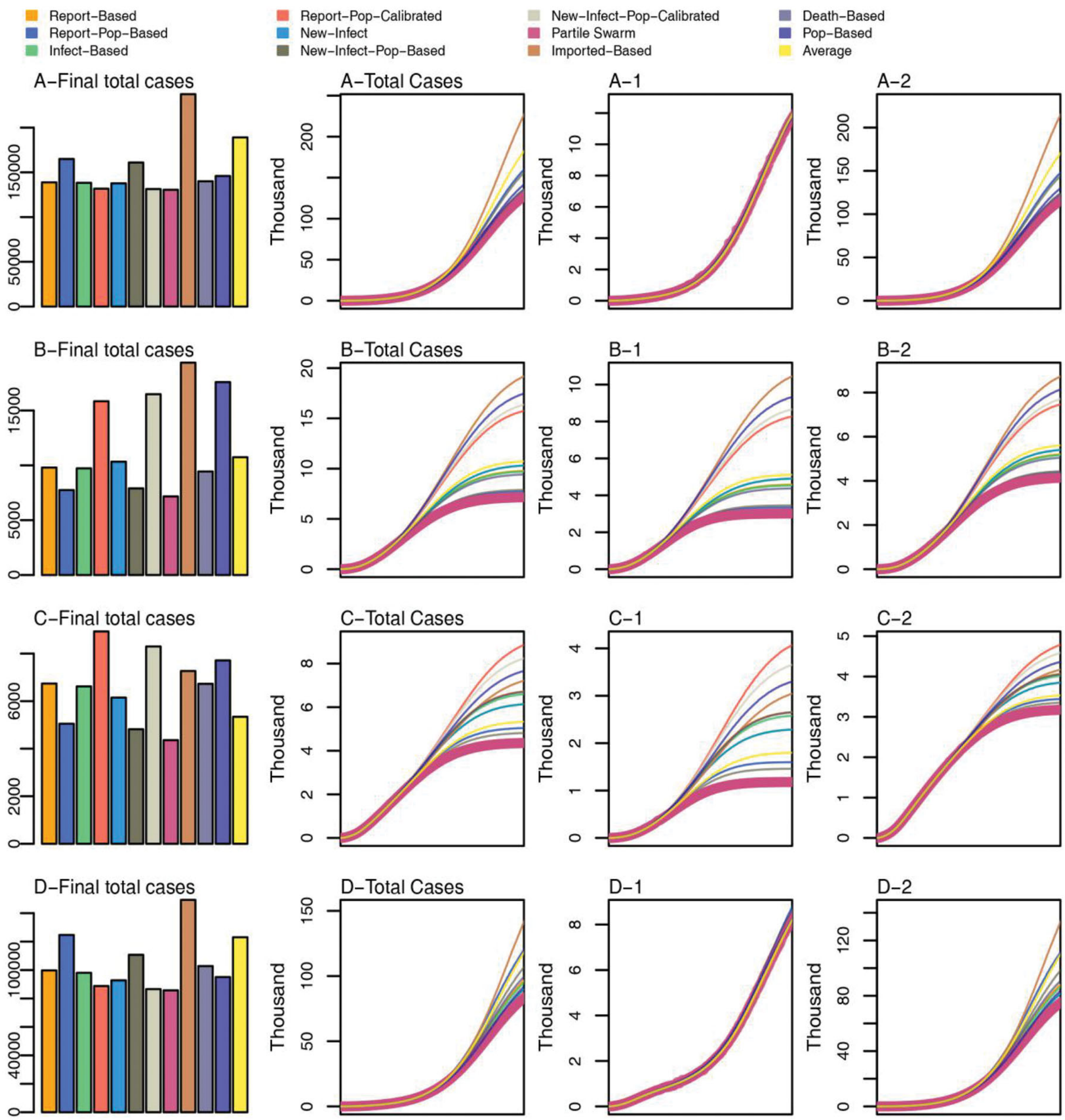

Figure 2. Total number of confirmed cases in the two-region model with 12 vaccine allocation strategies.

based on the particle swarm algorithm, controlled the development of the epidemic in all regions at the earliest time point and gave the smoothest trajectory of the number of confirmed cases. It is worth mentioning that, due to the lack of focus on small-population regions in Strategies 4 and 7, resource mismatches occurred in regions E5 and E7, resulting in poor performance. Strategies 2 and 6 resulted in resource mismatches that occurred in small-population but low-prevention regions. Strategies 1, 3, 5, and 10, which allocated vaccine resources based only on the trend of epidemic development, performed similarly in all regions. The worst-performing strategy was Strategy 9, which allocated vaccine resources according to the number of externally imported cases. This strategy performed worst in every region except region E7.

Figure 5 shows the variation in the number of vaccine resources allocated using the particle swarm algorithm, which analysed the demand for vaccine resources among eight different regions over time. Intuitively, region E2, the riskiest region, received the greatest resource allocation. However, although regions E6 and E8 both had large populations and high prevention and control capabilities, the particle swarm algorithm initially allocated more resources to region E8, which had fewer initial infection cases. For small-population regions (regions E1, E3, E5, and E7), the allocation strategy of the particle swarm algorithm

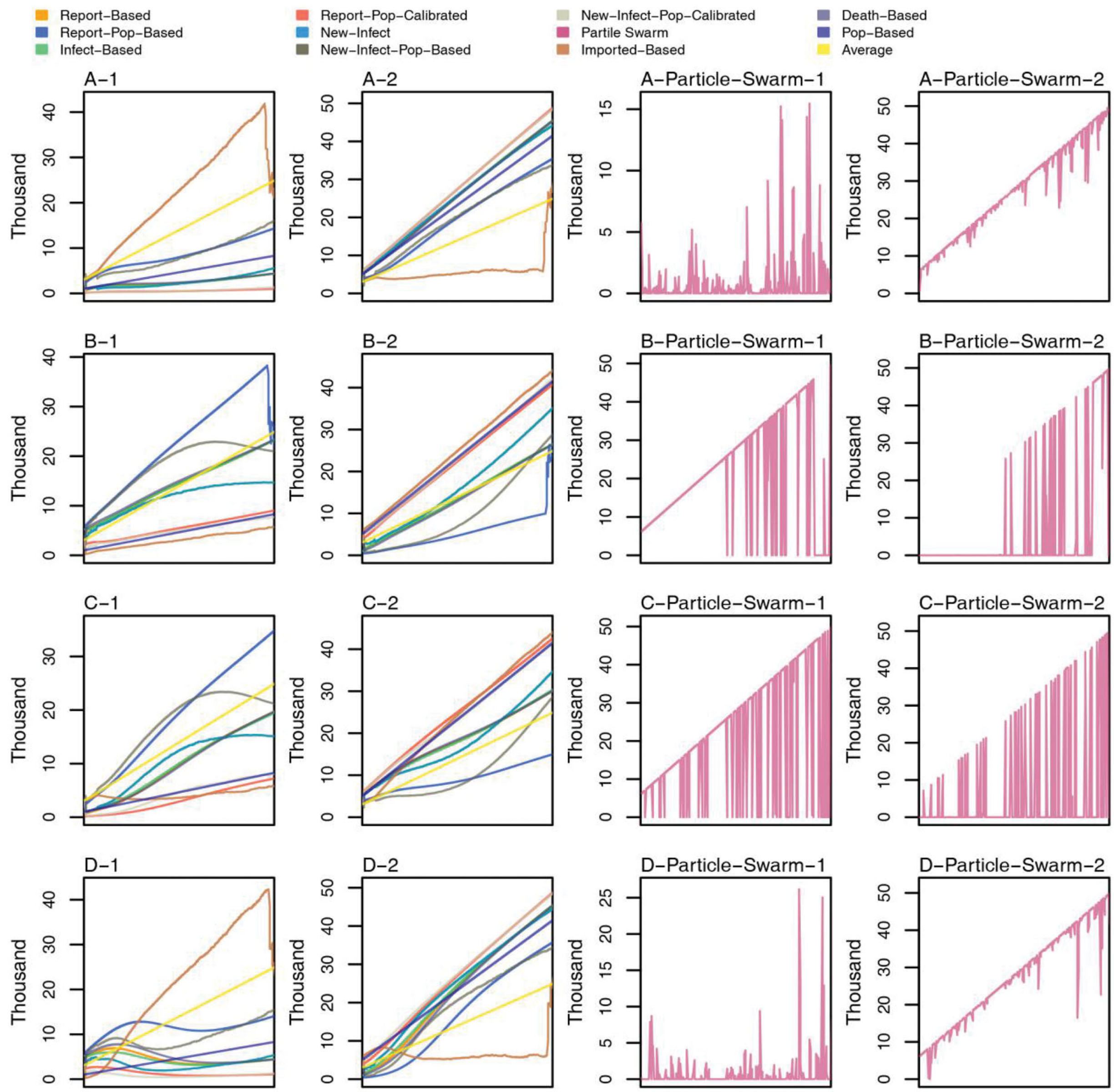

Figure 3. Vaccine allocation quantity of 12 vaccine allocation strategies in the two-region model.

was to not allocate any vaccine most of the time but to allocate vaccine resources at several key time points.

3.3. Results of the random-region scenario

Figure 6 shows a box plot of the final confirmed case multiples of the 11 allocation strategies relative to the vaccine allocation strategy of the particle swarm algorithm in 30 random scenarios. A higher average number of multiples indicated a lower level of protection by the allocation strategy. A wider 95% confidence interval of the multiples indicated less stability of the allocation strategy. Figure 6 shows that Strategy 5 was the most stable (the narrowest 95% confidence interval) and the most effective (the lowest average) strategy. Furthermore, under the condition of not knowing the regional population, prevention and control capacity, or the initial number of cases, the data showed that Strategies 9, 11, and 12 should not be adopted.

4. Discussion

In addition to incorporating the traditional health-oriented vaccine allocation strategy based on population size or epidemic development into the SEIR model, our study used the particle swarm optimisation algorithm to simulate the minimisation of the total number of confirmed cases, and the optimisation of

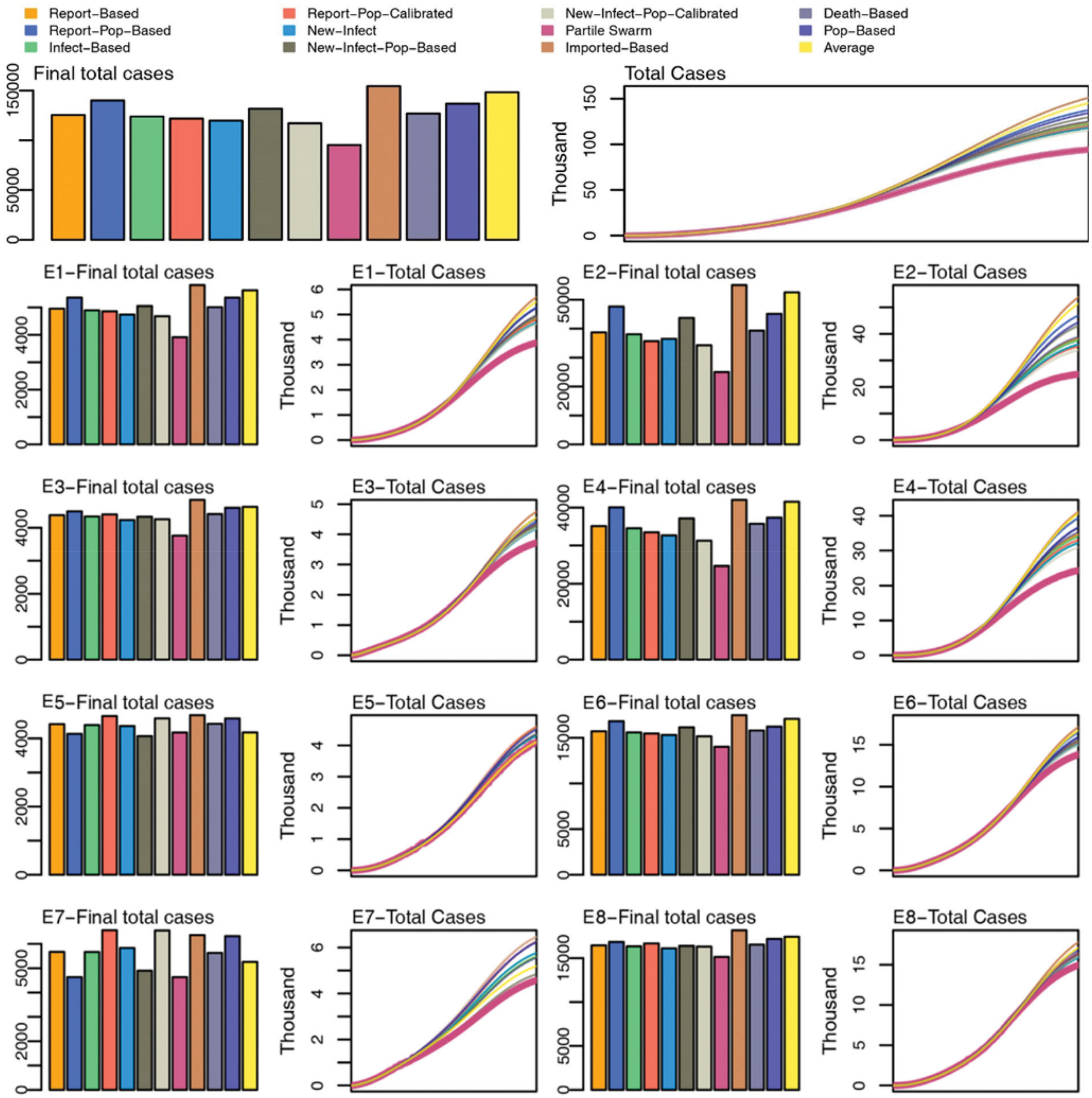

Figure 4. Trajectory of confirmed cases after adopting the 12 vaccine allocation strategies in the eight-region model.

vaccine allocation was obtained by comparing the particle swarm optimisation algorithm and other allocation strategies. We provided evidence that the vaccine allocation strategy based on the particle swarm optimisation algorithm (Strategy 8) and the vaccine allocation strategy based on the number of newly confirmed and suspected cases in each region (Strategy 5) achieved the best epidemic prevention and control effects. The two vaccine allocation strategies that should not be adopted based on these data were the vaccine allocation strategy based on the number of externally imported cases (Strategy 9) and the average allocation strategy (Strategy 12).

Particle swarm optimisation is applicable to many types of problems in a variety of scientific fields, such as obtaining the optimal portfolio of venture capital and predicting the heat transfer coefficient [23,24]. Compared with other mathematical and evolutionary algorithms, this algorithm is computationally more efficient and easier to implement [25]. In our study, the particle swarm algorithm allocated more resources to regions with low prevention and control capabilities; thus, the level of prevention and control capability is the most important factor in determining the allocation of vaccine resources. Interestingly, in regions with a large population and high prevention and control

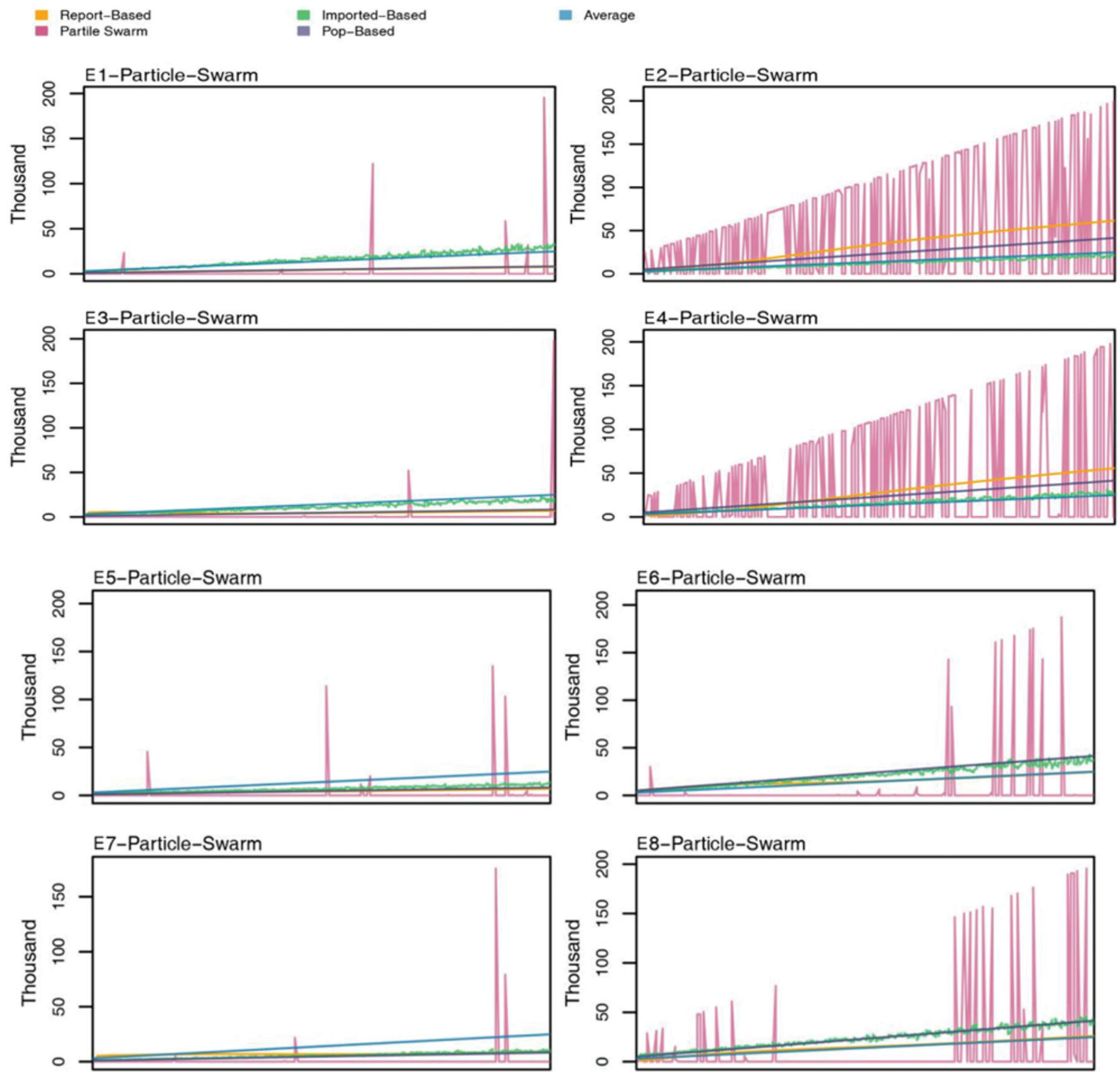

Figure 5. Number of allocations for the vaccine allocation strategy using particle swarm optimisation in the eight-region model.

region capabilities, the particle swarm algorithm initially allocated more resources to the region with fewer initial infection cases. This is consistent with the general conclusion of previous studies that priority should be given to regions where it is possible to prevent more infections [26]. If resources are allocated to regions with a larger number of initial infections at the beginning of the outbreak, the epidemic in regions with a smaller number of initial infections may get out of control more quickly, and more vaccine resources may be required to control it later. Therefore, the limited resources should first be allocated to the regions that are not yet fully erupted and easier to control.

In addition, we found that most vaccine allocation strategies were influenced by historical epidemics or population size and exerted unexpected epidemic prevention and control effects. This conclusion overcomes the traditional shortcomings of establishing a prediction model for research in a single region. On one hand, vaccine allocation strategies based on the cumulative number of confirmed or suspected cases (Strategy 1 and 3) were found to be affected by the bias of historical epidemics. These two strategies prioritise the allocation of vaccine resources to regions with large outbreaks but ignore the possibility that regions with small outbreaks are also regions with low prevention and control capabilities. Consequently, subsequent vaccine resources would not be transferred to regions where the epidemic was developing rapidly, leading to the inefficient allocation of resources. On the other hand, vaccine allocation strategies based on the number of confirmed and suspected cases adjusted for the population of the region (Strategies 4 and 7) were largely found to ignore the fact that low-population regions may also have low prevention and

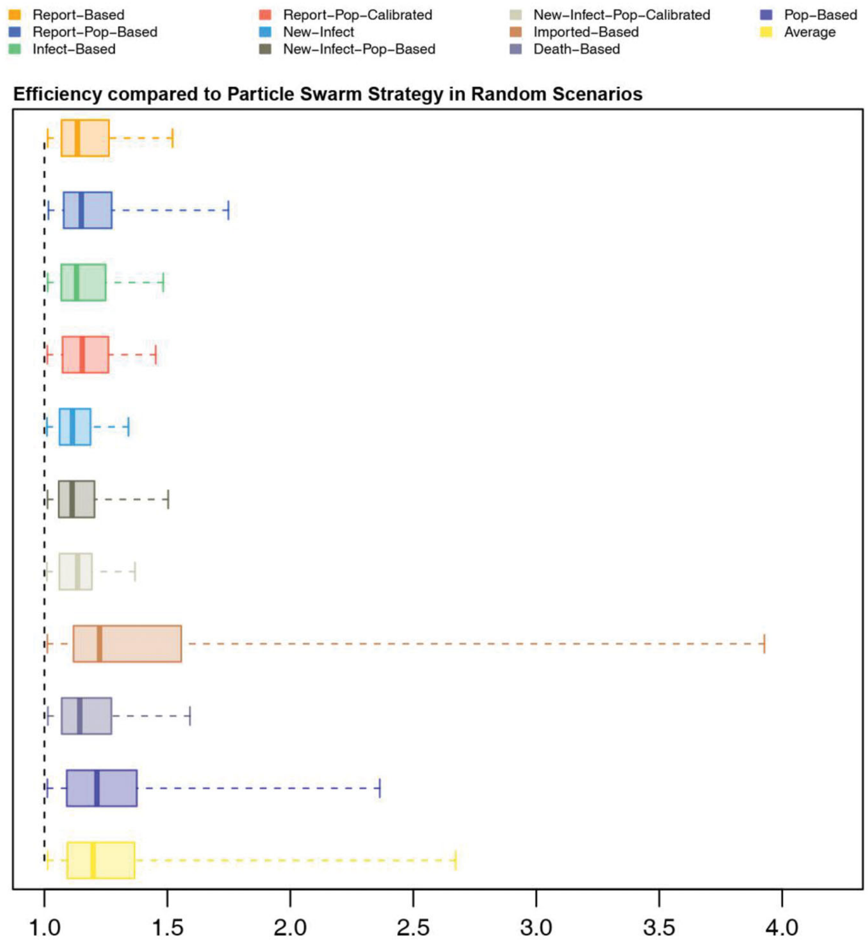

Figure 6. Multiples of the final number of confirmed cases for 11 vaccine allocation strategies in random scenarios relative to the vaccine allocation strategy based on particle swarm optimisation.

control capabilities. Similarly, vaccine allocation strategies based on the proportion of confirmed and suspected cases in the total population (Strategies 2 and 6) gave a higher priority to regions with small populations, which led to the possibility that vaccine resources would be assigned to regions with small populations but high prevention and control capabilities. Compared with the strategies mentioned above, Strategy 5, which uses the number of newly confirmed and suspected cases in each region as the weight of allocation, was the most stable and showed sufficient epidemic prevention and control effects. Because the allocation of vaccine resources according to the growth rate of the epidemic in each region was time-sensitive and flexible, this strategy would not be affected by historical epidemics or demographic factors. Therefore, when dealing with a multi-regional epidemic, Strategy 5 would be a good choice.

Finally, we found that the next four vaccine allocation strategies evaluated (Strategies 9, 10, 11, and 12) provided the lowest levels of protection. First, the vaccine allocation strategy based on the number of externally imported cases (Strategy 9) had the lowest epidemic prevention effect because many imported cases indicates that outside regions are more affected by the epidemic and thus require more vaccine resources. Second, the average allocation strategy (Strategy 12) also performed poorly because it did not consider differences in population size, prevention and control capabilities, or the number of initial infections in different regions. Finally, although the strategy based on the number of deaths (Strategy 10) and the strategy based on the size of the population (Strategy 11) may be fair [27], vaccine deployment based on the standard proportional method is more suitable for situations when vaccines are available long before infections occur in the region [28], which enables static allocation before an outbreak. Therefore, these two strategies were not suitable for the sudden COVID-19 pandemic or the initial deployment of COVID-19 vaccines.

In view of the capabilities of epidemic prevention and control, our study comprehensively and systematically included isolation speed, the degree of social distancing control, and mask-wearing frequency as indicators. Previous studies have shown that the effect of vaccination is limited and the number of infections may increase if non-pharmaceutical interventions are relaxed while adopting vaccination strategies [29]. In addition, the role of masks in controlling the spread of epidemics has been demonstrated by scholars from various disciplines from the perspectives of physical principles, epidemiology, and clinical evidence [30–32]. A cross-sectional study with a sample size of 378,207 found that when mask-wearing is combined with measures such as social distancing, the effect on controlling the epidemic is enhanced [33]. Therefore, combined with the conclusion of this study – namely, that prevention and control capabilities are important factors to consider when developing vaccine allocation strategies – as vaccine promotion increases, maintaining high levels of epidemic prevention and control is a vital prerequisite for ensuring the sustainable development of the economy and society and for preventing further outbreaks of the epidemic.

Our research has certain limitations. Firstly, although our conclusions can be applied to resource allocation in various regions, we did not consider the logistical or ethical issues that may exist following vaccine distribution. Furthermore, the downstream effects of vaccination and non-pharmacological interventions such as social, psychological, and economic costs were not considered and these effects must be considered when performing certain studies on deciding of the appropriate course of action [34]. Secondly, the 12 health-oriented vaccine allocation strategies evaluated in our study do not represent all possible strategies. Future research could focus on a weighted combination of several of these strategies which may yield better results than individual strategies. Thirdly, we did not consider the role of potential seasonal or meteorological factors, such as temperature and humidity, in the spread of the epidemic. However, recent modelling studies have found that humidity is only weakly correlated with an increase in COVID-19 cases, and no effects of latitude or temperature have been found [35]. Fourthly, due to the large time span of the incubation period of the COVID-19, the distribution of the incubation period still needs to be explored in further studies. It is suggested that future studies could set the incubation period to fluctuate with a certain pattern over a larger range to reflect the real-world situation. Fifthly, although this study considered the possibility that a certain proportion of asymptomatic infected individuals who were not isolated or hospitalised had self-healed before the onset of symptoms, the epidemiological pattern and distribution of this group need to be confirmed by further studies. However, we consider that the partially unreported asymptomatic Infections will not inherently change the strategy of vaccine allocation. Lastly, since the probability of retained transmissibility in recovered individuals is still under further study, we did not consider in our model the case of recovered individuals becoming susceptible again or infecting other susceptible individuals, which requires subsequent studies to clarify the relevant parameters to optimise the model. However, this situation will only affect the number of vaccine allocations rather than the allocation strategies because recovered individuals tend to be immune for a period, and we consider the risk that vaccinated susceptible individuals will still become exposed and infected.

5. Conclusion

In conclusion, we constructed a cross-regional SEIR model to compare 12 health-oriented vaccine allocation strategies based on population size, epidemic status, and a particle swarm algorithm. We focussed on regional epidemic prevention and control capabilities, including the degree of social distancing control, the isolation of exposed and infected individuals, and the initial mask-wearing frequency of residents. These factors were the most important basis for the optimal allocation of COVID-19 vaccine resources required to minimise the total number of confirmed cases in all regions. In addition, regional outbreak risk should be considered when making vaccine allocation decisions. Information in this study will provide decision-makers in various countries and regions with tools to determine the optimal resource allocation strategy so that existing resources can be used effectively.

Ethical approval

The authors state that ethical approval is not required for this type of study in the country where the study was conducted.

Author contributions

T.Y. designed the study. Y.L. and W.D. gathered the data and reviewed the statistical analysis applied. W.D. wrote the first draft of the manuscript with contributions from all authors. J.D. was the study guarantor and revised the manuscript text critically.

Disclosure statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be constructed as a potential conflict of interest. The authors have no affiliation with any organisation with a direct or indirect financial interest in the subject matter discussed in the manuscript.

Funding

This study was supported by Beijing Social Science Foundation [grant no. 21JCC123].

Data availability statement

Cause the data supporting the findings of this study is virtual, the authors confirm that the data are available within the article and its supplementary materials.

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