Preplanned Studies

Impact of Regions with COVID-19 Cases on COVID-Zero Regions by Population Mobility — Worldwide, 2021

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Summary

What is already known about this topic?

Reducing population mobility and increasing the vaccination rate for severe acute respiratory syndrome coronavirus 2 can decrease the transmission of coronavirus disease 2019 (COVID-19).

What is added by this report?

In order to reduce the incidence of COVID-19 to the levels of influenza after restoring normal mobility, the efficacy against infection needs to be increased to 40% and the efficacy against symptomatic disease needs to be increased to 90%. The efficacy against infection has a more important impact compared to efficacy against symptomatic disease or death on the transmission of COVID-19 at the population level.

What are the implications for public health practice?

The population should continue maintaining non-pharmaceutical interventions and minimize international movement to prevent transmission of COVID-19. Furthermore, developing new vaccines or promoting booster vaccinations should be considered to increase efficacy.

The development of vaccines has made a great contribution to the fight against coronavirus disease 2019 (COVID-19), but it should be clearly recognized that the elimination of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) requires the combined efforts of humanity. In order to determine how the population mobility among different regions might affect the COVID-19 epidemic, we constructed a transregional mobility dynamics model to assess the relationship between population mobility and the COVID-19 pandemic. Based on a previous study on vaccine efficacy against infection in the United Kingdom (*1*) and a study in Chile on the vaccine protective effects of CoronaVac (*2*), the baseline efficacy, indicated by efficacy against infection (E_{inf}), efficacy against symptomatic disease (E_{sym}), and efficacy against death (E_{dea}) was respectively 30%, 68.3%, and 86%. If the vaccination rate reaches 95%, allowing for transregional movement would result in 234.2 million infections (64.1 million symptomatic cases) and 2.0 million deaths (case fatality rate of 0.85%) within a year in unaffected regions. Increasing E_{inf} and E_{sym} to no less than 40% and 90%, respectively, could reduce the incidence of COVID-19 in COVID-zero regions to influenza-like levels. When the E_{inf} of the vaccine was higher, the E_{sym} could be reduced accordingly. No matter how effective the vaccine was, it could not eliminate COVID-19 in COVID-zero regions, i.e., regions with strong national commitments to suppressing COVID-19 transmission such as China. The human race should continue to develop vaccines and explore new ways to improve vaccine protection against infection in order to eliminate COVID-19 at the global level.

In order to group the transmission risk of COVID-19 in various countries around the world, we used a proportion of existing cases in the overall population of countries to rank and group these countries and regions into three levels, including high-risk regions, medium-risk regions, and low-risk regions. COVID-zero regions were defined as countries or regions committed to reducing the number of domestic cases to zero, such as China. The countries covered by each region were shown in Figure 1A. Considering the disease characteristics of COVID-19, we added categories to include asymptomatic infected cases and divided each category into two according to vaccination status (Figure 1B). The model assumed that the mobility rate between COVID-zero regions and other areas was constant. All parameters used in this model and COVID-19 epidemic data sources were shown in Table 1, and more details of methods were shown in Supplementary Materials, available in http://weekly.chinacdc.cn/.

Based on the study in Chile mentioned above, E_{sym} and E_{dea} of CoronaVac was 68.3% and 86%, respectively (*2*). And the E_{inf} was estimated to 55% by the study produced in the United Kingdom (*1*). Considering the declining immunity in the vaccinated population, E_{inf} was finally estimated to 30%

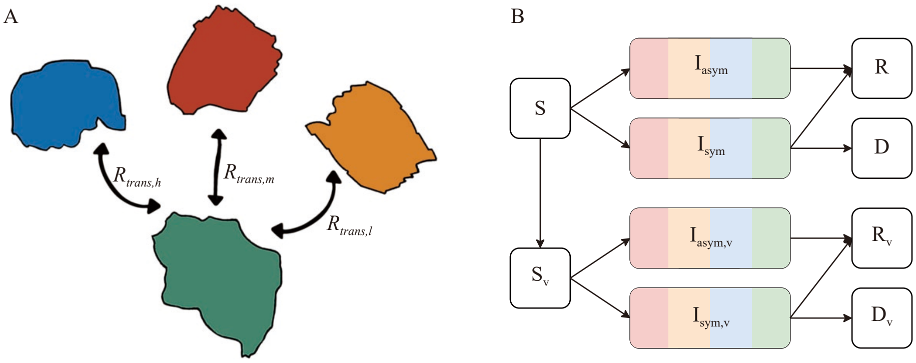

FIGURE 1. Diagrams of the COVID-19 epidemic model. (A) the diagram of transregional mobility of population, (B) epidemic dynamics model compartments.
Note: S, I_{asym}, I_{sym}, R, and D desperately denoted the susceptible, asymptomatic infective, symptomatic infective, removal and dead. And the v subscript indicated COVID-19 vaccination.
Abbreviation: COVID-19=coronavirus disease 2019.

TABLE 1. Estimation of COVID-19 transregional model parameters and data sources.

Label	Value	Reference
R_{trans}	0.0002, 0.0013*	(*3*-*4*)
R_0	2.5	(*5*)
R_{sym}	70%	(*5*)
R_{dea}	2.0%	Calculated †
R_{rem}	1/5.4§	(*6*)
β	0.179	Calculated by R_0
R_{a-s}	75%	(*6*)
E_{inf}	30%	Based on (*1*) ¶
E_{sym}	65.3%	(*2*)
E_{dea}	86%	(*2*)

* 0.0002 was the number of arrivals and departures of January to June 2021 and 0.0013 was from the whole year of 2019. They represented the current population mobility rate and normal mobility rate.
† R_{dea} is the sum of deaths divided by the sum of confirmed cases in all countries.
§ R_{rem} denoted that patients presented to the doctor within 2 days since the onset of symptoms (average 3.4 days) and were no longer transmissible.
¶ More details about the estimation of R_{inf} could be found in Supplementary Materials, available in http://weekly.chinacdc.cn/.

(Supplementary Material, available in http://weekly.chinacdc.cn/). Based on the baseline efficacies of the vaccines, referred to E_{inf}, E_{sym}, and E_{dea} were 30%, 68.3%, and 86%, respectively, the global vaccination rate could reach 95% and then people in other areas could move within COVID-zero regions without non-pharmaceutical interventions (NPIs). Among COVID-zero regions, a total of 234.2 million SARS-CoV-2 infections were projected to occur in one year, of which 170.1 million (72.6%) were asymptomatic cases and 64.1 million (27.4%) are symptomatic cases (Figure 2A), with a total death count of 2.0 million (case fatality rate 0.85%). The highest number of new symptomatic cases per day was estimated 376,600, which would appear on the Day 262 after lifting the restrictions and the highest number of deaths per day was 11,400, which would appear on the Day 266 (Figure 2B) in COVID-zero regions.

On the basis of maintaining the current mobility rate, we explored what kind of combination of vaccine protective efficacy could lift the restrictions. Due to the COVID-19 vaccine having an E_{dea} of 86%, we presented results that assumed E_{dea} to be 90% (Figure 3A). Predictions of other combinations of vaccine protective efficacy could be found in the Supplementary Materials (available in http://weekly.chinacdc.cn/). The results suggested that in order to reduce the annual incidence of COVID-19 to influenza, the vaccine's E_{inf} needed to be increased to more than 40% concurrently with an E_{sym} of at least 60%. If the E_{inf} was increased to 50%, the E_{sym} could decrease to 0%. In addition, when the 3 efficacies reached at least 90%, the annual incidence of COVID-19 was decreased to 0.81/100,000 population.

Finally, we assessed what protective efficacy would be required to restore the population mobility to ensure that the incidence of COVID-19 could be lower than that of influenza. After restoring the population mobility rate of 2019, a higher vaccine protective effect was required. In order to reduce the annual incidence of COVID-19 to that of influenza, the vaccine's E_{inf} and E_{sym} needed to be increased to no less than 40% and 90%, respectively. With a higher E_{inf}, the E_{sym} could be decreased (Figure 3B). When the E_{inf} was increased to 70%, the E_{sym} could be decreased to 0 (Table 2).

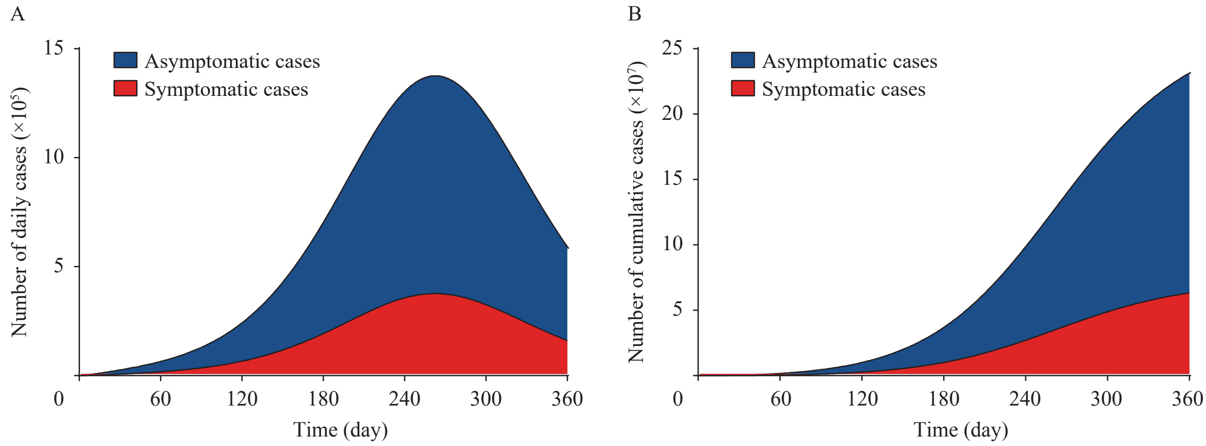

FIGURE 2. Prediction of COVID-19 epidemic after restoring population mobility without NPIs. (A) The number of daily infections, (B) The number of cumulative infections with time..

Note: Blue denoted the asymptomatic cases and red denoted the symptomatic cases. This result was based on the efficacy against infections, symptomatic disease and death was separately 30%, 68.3%, and 86%, and the vaccination rate was 95%.

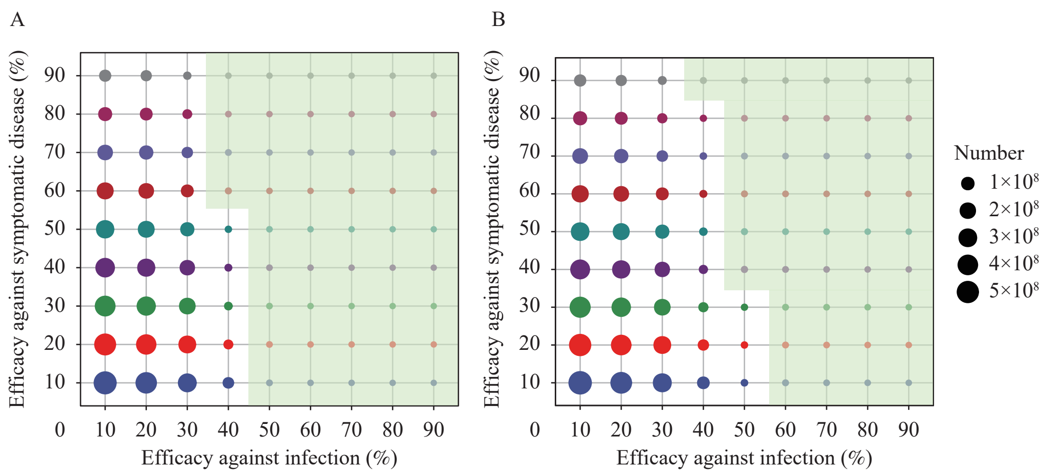

FIGURE 3. The number of COVID-19 cases in response to different vaccine protection at (A) low rate of population mobility, (B) normal rate of population mobility.

Note: The size of the circle denoted the number of COVID-19 cases and the green shadow denoted the annual incidence was lower than influenza with the corresponding efficacy against infection and symptomatic disease and a vaccination rate of 95%, indicated that efficacy against death has a less impact on virus transmission so we only show the prediction of 90% efficacy against death.

TABLE 2. Prediction of COVID-19 epidemic by currently vaccine effectiveness and combinations of threshold efficacies that can reduce the number of infections to influenza.

Vaccination rate (%)	Mobility rate (%)	Vaccine effectiveness			Symptomatic cases	Deaths
		Infection (%)	Symptom (%)	Death (%)*		
95	0.02	30.0	65.3	86.0	64,123,171	2,039,690
95	0.02	40.0	60.0	90.0	1,054,347	28,517
95	0.02	50.0	0.0	90.0	623,887	12,906
95	0.13	40.0	90.0	90.0	706,184	40,565
95	0.13	50.0	40.0	90.0	1,105,650	31,237
95	0.13	60.0	0.0	90.0	627,634	17,808

Abbreviation: COVID-19=coronavirus disease 2019.

* Indicated that efficacy against death has a less impact on virus transmission so we only showed the prediction of 90% efficacy against death.

DISCUSSION

Our model aimed to create a hypothetical scenario in which enough people were vaccinated to assess whether people could move freely and safely without NPIs. There were three main findings of this study. First, based on the assumption of parameters that the E_{inf}, E_{sym}, and E_{dea} were 30%, 65.3%, and 86%, respectively, COVID-19 vaccinations were not enough to provide a sufficient proportion of immunized population to resume normal population mobility without NPIs. Among the three parameters estimating the protective effects of the vaccine, only the E_{inf} was supported by existing evidence. But considering immune escape ability of Delta variant, we thought estimation of 30% was reasonable. It indicated that policymakers should carefully deal with allowing transmission with freedom and all populations should continue to maintain the NPIs in order to avoid a resurgence of COVID-19.

Second, if we assumed that COVID-19 incidence was lower than that of influenza for resuming population mobility, the vaccine E_{inf} should be at least 40%. Simply increasing the E_{sym} and E_{dea} would not do much to control the disease. The E_{inf} had a more important impact on controlling COVID-19 at the population level. Therefore, further research on the efficacy against infection was of vital significance. The results of this study only assumed the minimum value of the protective effects to decrease the incidence of COVID-19 to that of influenza due to the decline in vaccine immunity and the possible emergence of new strains. In any case, resuming international population mobility should be treated with caution to avoid domestic outbreaks.

Finally, we investigated if the vaccine alone could be used to achieve a COVID-zero strategy in COVID-zero regions. Because of population mobility, even if the 3 vaccine efficacies reached 90%, COVID-zero regions would not be able to eliminate COVID-19. This result suggested that as long as there were COVID-19 cases in other countries, vaccinations alone without non-pharmaceutical interventions could not reduce the number of domestic cases to zero. Rationally allotting the COVID-19 vaccines might play a more important role in controlling COVID-19 worldwide.

This study was subject to at least four limitations. First, the vaccine protective efficacy was assumed based on results of the Sinovac vaccine in Chile. However, due to the different types of vaccines used in various countries around the world, this may not accurately reflect results in other regions included in this study. In addition, the estimated mobility rate in this study referred to data of China in 2019 and 2021, and the mobility rate of other countries will differ significantly from that in China. Third, due to China's policy of administering booster vaccinations, the study did not consider the effect of declining immunity on vaccine effectiveness, but this may lead to further issues in predicting disease transmission. Fourth, the emergence of new SARS-CoV-2 strains might significantly increase the risk of disease transmission in a country or region, and the parameters of this model were based on the characteristics of current strains. If new variants of concern emerge, researchers need to re-model the risk of disease transmission after acquiring the information about the characteristics of new strains.

The key to controlling COVID-19 lies in the development and widespread use of vaccines that are more effective at preventing infection. People still need to maintain adequate NPIs to avoid the risk of COVID-19 recurrence.

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SUPPLEMENTARY MATERIALS

Model Assumptions

1. The natural growth and mortality rate of the population were not considered.
2. The mobility probability of people in the same area was consistent.
3. Recovered cases would not be reinfected with coronavirus disease 2019 (COVID-19).
4. The protective efficacy of the vaccine will not diminish during the forecast period.
5. The rates of population mobility between different regions were consistent and stable.
6. The time taken by the movement of people was ignored.

Grouping Results

We collected the COVID-19 epidemic data of 194 countries and regions except China through the COVID-19 global data of Dingxiangyuan Website (*1*) which included confirmed cases, recovered cases, and deaths up to October 10, 2021 and the population data collected by the World Health Organization (WHO) until October 10, 2021. The prevalence rate of COVID-19 ($R_{pre,i}$) in each country or region was calculated by the following methods:

$$R_{pre,i} = \frac{n_{acc,i} - n_{rec,i} - n_{dea,i}}{N_i} \times 100\%$$

$n_{acc,i}$ denoted the cumulative number of infections, $n_{rec,i}$ represented the cumulative number of recovered cases, $n_{dea,i}$ denoted the cumulative number of deaths, and N_i was the population of country (or region) i.

The 194 countries were ranked by quintile into high risk, medium risk, and low risk regions. China has been selected as a representative country for the COVID-zero regions due to its ongoing zero-COVID-19 prevention and control strategy. The grouping result was shown in the Supplementary Table S1.

SUPPLEMENTARY TABLE S1. The detailed grouping results based on the prevalence of COVID-19 within 194 countries or regions.

Low risk region		Medium risk region		High risk region	
Country or region	Prevalence (/100,000)	Country or region	Prevalence (/100,000)	Country or region	Prevalence (/100,000)
Chad	0.14	Dominican Republic	91.30	Iran	495.50
Niger	0.49	Djibouti	92.51	Cuba	521.52
Gambia	0.54	The Republic of Korea	96.26	Oman	583.34
Senegal	1.25	Monaco	96.83	Ukraine	606.80
Burkina Faso	1.62	Philippines	98.45	Turkey	640.37
Bhutan	2.20	Spain	105.77	Lesotho	651.28
Mali	2.76	Panama	108.84	Singapore	661.37
Liberia	2.79	Congo	116.33	Bahamas	663.96
Zambia	3.67	Czechia	124.86	North Macedonia	691.11
Madagascar	4.94	Equatorial Guinea	127.01	Israel	710.03
Nigeria	5.17	Hungary	129.19	Moldova	710.32
Comoros	5.63	Central African Republic	130.64	Guyana	710.94
Mozambique	6.43	Falkland Islands	136.89	Seychelles	718.04
Kenya	7.49	Italy	139.27	Armenia	760.45
Saudi Arabia	7.57	Cape Verde	152.34	Brunei	795.00
Sudan	8.53	Nicaragua	161.58	Anguilla	824.19
South Sudan	9.44	Greenland	172.09	Bulgaria	873.81
Guinea	9.70	Iceland	172.75	Georgia	883.76
Bangladesh	10.16	Montserrat	172.98	Romania	904.68
Paraguay	10.77	Vietnam	175.20	Belize	956.69
Ghana	15.30	Denmark	179.53	Latvia	999.82
New Zealand	17.52	Algeria	182.49	Saint Lucia	1,034.69

TABLE S1. (Continued)

Low risk region		Medium risk region		High risk region	
Country or region	Prevalence (/100,000)	Country or region	Prevalence (/100,000)	Country or region	Prevalence (/100,000)
Mauritania	20.28	Jordan	190.29	Jamaica	1,036.55
Uzbekistan	21.16	San Marino	191.53	Barbados	1,105.54
India	21.55	Canada	196.76	Bosnia and Herzegovina	1,107.93
Malawi	22.89	Ecuador	198.26	Mauritius	1,124.16
Kuwait	23.04	Andorra	199.31	Libya	1,152.96
Sierra Leone	23.08	Bolivia	203.64	Dominica	1,198.76
Yemen	24.84	Brazil	208.87	Isle of Man	1,228.95
Pakistan	26.07	Turks and Caicos Islands	209.21	Estonia	1,307.31
Benin	26.78	Guernsey	210.52	Lithuania	1,398.40
Democratic Republic of Congo	28.12	Iraq	212.04	Antigua and Barbuda	1,471.49
Zimbabwe	28.74	Azerbaijan	216.25	Fiji	1,497.08
Ethiopia	29.41	Gabon	217.73	Palestine	1,526.13
Togo	30.95	Malta	221.21	Montenegro	1,530.60
Japan	31.32	Indonesia	222.68	Grenada	1,748.15
Egypt	34.66	Cayman Islands	223.68	Norway	1,910.30
Angola	35.39	Guatemala	227.54	Costa Rica	1,938.34
Guinea-Bissau	37.75	Sri Lanka	238.31	Finland	2,053.73
Papua New Guinea	41.57	Aruba	243.52	United Kingdom	2,165.33
Tanzania	41.96	Laos	249.69	Saint Kitts and Nevis	2,286.48
Morocco	42.29	Thailand	251.62	Mongolia	2,335.06
Rwanda	42.91	El Salvador	269.31	Honduras	2,509.91
Haiti	44.14	Botswana	281.85	Bermuda	2,580.47
Cote d'Ivoire	48.33	Belarus	292.94	Suriname	2,714.13
Kyrgyzstan	48.53	Mexico	296.26	Greece	2,725.79
Argentina	50.25	Germany	310.60	United States	2,731.09
Cameroon	50.66	Luxembourg	312.52	Slovakia	2,832.00
Cambodia	53.11	Portugal	335.31	New Caledonia	3,168.48
South Africa	56.52	Sao Tome and Principe	365.03	Saint Vincent and the Grenadines	3,411.54
Syria	58.55	Australia	365.17	Eswatini	3,625.69
Uruguay	58.73	Austria	368.74	Kazakhstan	4,475.39
Afghanistan	60.30	Liechtenstein	374.96	Sint Maarten (Dutch part)	5,388.14
Colombia	60.32	Faeroe Islands	378.59	Switzerland	6,005.94
Chile	63.40	Lebanon	391.62	Ireland	7,350.34
Qatar	64.42	Gibraltar	391.80	Curacao	7,475.07
Uganda	65.72	Jersey	395.59	French Polynesia	8,281.83
Namibia	66.04	Maldives	396.27	Cyprus	9,804.61
Somalia	66.05	Malaysia	398.72	France	10,123.30
United Arab Emirates	67.92	Trinidad and Tobago	426.87	Belgium	10,503.50
Bahrain	68.35	Albania	437.07	Sweden	10,983.86
Myanmar	69.79	British Virgin Islands	439.86	Netherlands	11,607.85
Nepal	79.25	Poland	464.92	Slovenia	13,917.69
Venezuela	83.12	Russia	474.02	Serbia	14,227.67
Tunisia	86.69	Croatia	477.59		

Model Formulation

Considering that the effectiveness of COVID-19 vaccination was mainly focused on avoiding infection, avoiding symptomatic disease, and avoiding severe illness and death, this study extended the traditional epidemic model to include asymptomatic infection compartment and five corresponding compartments for vaccination. In addition, in order to assess the impact of population mobility on the spread of COVID-19, we assumed that high, medium, and low-risk regions would have a mobility rate of R_{trans} with COVID-zero regions. To describe this flow, we randomly selected a population of size $R_{trans} \times N_{clean}$ from the total population of the clean region and a population of the same number from other regions separately to exchange. Using this method, we could realize the population mobility with the constant total population of each region.

Given the unknown safety of the vaccine in infants and young children, we assumed that this population would not be vaccinated. According to the population age distribution announced by China in 2020, infants aged 0–4 accounted for about 5% of the total population. Therefore, we assumed that the maximum proportion of vaccination was 95%. This study focused on the epidemic trend of COVID-19 when a fairly high proportion of people have been vaccinated and international mobility resumed normal levels. Therefore, the starting of the prediction was that 95% of people have been vaccinated and no new vaccinations have taken place after all regions were totally opened.

Model Equations

$$\frac{dS_i}{dt} = -\beta \times S_i \times \frac{\left[\left(I_{sym,i} + I_{sym,v,i}\right) + r_{a-s} \times \left(I_{asym,i} + I_{asym,v,i}\right)\right]}{N_i} - Out_{S_i} + In_{S_i}$$

$$\frac{dS_{v,i}}{dt} = -\beta \times (1 - e_{inf}) \times S_{v,i} \times \left[\left(I_{sym,i} + I_{sym,v,i}\right) + r_{a-s} \times \left(I_{asym,i} + I_{asym,v,i}\right)\right]/N_i - Out_{S_{v,i}} + In_{S_{v,i}}$$

$$\frac{dI_{sym,i}}{dt} = r_{sym} \times \beta \times r_{sym} \times S_i \times \left[\left(I_{sym,i} + I_{sym,v,i}\right) + r_{a-s} \times \left(I_{asym,i} + I_{asym,v,i}\right)\right]/N_i - Out_{I_{sym,i}} + In_{I_{sym,i}}$$

$$\frac{dI_{asym,i}}{dt} = (1 - r_{sym}) \times \beta \times r_{sym} \times S_i \times \left[\left(I_{sym,i} + I_{sym,v,i}\right) + r_{a-s} \times \left(I_{asym,i} + I_{asym,v,i}\right)\right]/N_i - Out_{I_{asym,i}} + In_{I_{asym,i}}$$

$$\frac{dI_{sym,v,i}}{dt} = r_{sym} \times \left(1 - e_{sym}\right) \times \beta \times (1 - e_{inf}) \times S_{v,i} \times \left[\left(I_{sym,i} + I_{sym,v,i}\right) + r_{a-s} \times \left(I_{asym,i} + I_{asym,v,i}\right)\right]/N_i - Out_{I_{sym,v,i}} + In_{I_{sym,v,i}}$$

$$\frac{dI_{asym,v,i}}{dt} = \left[1 - r_{sym} \times \left(1 - e_{sym}\right)\right] \times \beta \times (1 - e_{inf}) \times S_{v,i} \times \left[\left(I_{sym,i} + I_{sym,v,i}\right) + r_{a-s} \times \left(I_{asym,i} + I_{asym,v,i}\right)\right]/N_i - Out_{I_{asym,v,i}} + In_{I_{asym,v,i}}$$

$$\frac{dR_i}{dt} = r_{rec} \times \left(I_{sym,i} + I_{asym,i} + I_{sym,v,i} + I_{asym,v,i}\right) - Out_{R_i} + In_{R_i}$$

$$\frac{dD_i}{dt} = r_{dea} \times I_{sym,i} + \left(1 - e_{dea}\right) \times r_{dea} \times I_{sym,v,i}$$

Symbol i included 0, 1, 2, 3 indicating clean, low risk, medium risk, and high-risk regions. We used the symbol j to represent each compartment and the number of population mobility in different regions could be described by following equations.

For the COVID-zero Regions:

$$Out_{j,0} = \sum_{1}^{3} R_{trans} \times N_{j,0}$$

$$In_{j,0} = \sum_{i=1}^{3} \frac{R_{trans} \times N_{j,0} \times N_{j,i}}{N_i}$$

For the high risk, medium risk, and low risk regions (*i*=1, 2, 3)

$$Out_{j,i} = \frac{R_{trans} \times N_{j,0} \times N_{j,i}}{N_i}$$

$$In_{j,0} = R_{trans} \times N_{j,0}$$

Parameter Estimation of E_{inf}

At present, there were no definitive studies on the effectiveness of CoronaVac in preventing infection. After reviewing the literature, we found that in August 2021, Paul Elliott et al. (*2*) analyzed the efficacy against infection of COVID-19 vaccines administered in the UK. The conclusion was that the vaccine was 49% to 62% effective in preventing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in people aged 18 to 64 years old. Taking into account the higher efficacy of the Oxford/AstraZeneca COVID-19 vaccine in its published Phase III clinical data than CoronaVac, and the immune decline in the population after vaccination, we finally made an E_{inf} estimate of 30%.

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