Supplementary Materials

Contents

Estimation of clinical severity

Using Garkse's[1] method, we adjusted the right censoring data by weighting the denominators of the time interval distributions. The numerator was the cumulative number of cases on the cut-off date of the analysis, and the denominator was weighted based on the density distribution of the time interval. This method allowed the exclusion of cases in the early stages of outbreak when the final outcome has not yet been observed. The method of obtaining interval parameters could be found in the published article. IFR, IHR and HFR were estimated stratified by age group, and 95% confidence intervals (CIs) were estimated by binomial distributions.

$$IFR(t_2) = \frac{D(t_2)}{\sum_{t_1=0}^{t_2} F(t_2-t_1)C(t_1)} \quad (1)$$

$$IHR(t_2) = \frac{H(t_2)}{\sum_{t_1=0}^{t_2} F(t_2-t_1)C(t_1)} \quad (2)$$

$$HFR(t_2) = \frac{D(t_2)}{\sum_{t_1=0}^{t_2} F(t_2-t_1)H(t_1)} \quad (3)$$

Where the numerator refers to the cumulative number of cases with predefined endpoints on the cut-off date of the analysis, t_2 (H: hospitalization infection; D: death), and the denominator refers to a weighted sum of daily (t_1) reported total number of infections or hospitalization cases. The weights are based on the density distribution of the time interval from infection to hospitalization, from infection to death, from hospitalization to death (F).

Comparation of difference

We adopted a general approach[2], rather than classical method, to perform statistical test between clinical severity/disease burden by constructing a confidence limit of difference of mean value with the following two equations.

$$\mathrm{L} = \hat{\theta}_1 - \hat{\theta}_2 - \mathrm{Z}_{\alpha/2}\sqrt{\frac{\left(\hat{\theta}_1 - \mathrm{l}_1\right)^2}{\mathrm{Z}_{\alpha/2}{}^2} + \frac{\left(\mathrm{u}_2 - \hat{\theta}_2\right)^2}{\mathrm{Z}_{\frac{\alpha}{2}}{}^2}}$$

$$= \hat{\theta}_1 - \hat{\theta}_2 - \sqrt{\left(\hat{\theta}_1 - \mathrm{l}_1\right)^2 + \left(\mathrm{u}_2 - \hat{\theta}_2\right)^2} \quad (1)$$

and

$$\mathrm{U} = \hat{\theta}_1 - \hat{\theta}_2 + \sqrt{\left(\mathrm{u}_1 - \hat{\theta}_1\right)^2 + \left(\hat{\theta}_2 - \mathrm{l}_2\right)^2} \quad (2)$$

Where $\hat{\theta}_i$ is the point estimate of clinical severity/disease burden, with $\hat{\theta}_1$ and $\hat{\theta}_2$ represent the mean clinical severity/disease burden of the two cities to be compared; $Z_{\alpha/2}$ is the upper $\alpha/2$ quantile of the standard normal distribution; l_1 and u_1 represent the lower and upper limit of the predicted clinical severity/disease burden of Shanghai, while l_2 and u_2 for Hong Kong to be compared. If the constructed limit covers the zero, it indicates no significant difference is tested. If the constructed limit doesn't cover the zero, it indicates there is significant difference between two clinical severity/disease burden indicators.

Sensitivity analysis

During the epidemic in Hong Kong, the methods used for case detection also changed dynamically. In the early stage, RT-PCR test was mainly used, and RAT was added to expand the case screening subsequently. We performed sensitivity analysis based on the overall ascertainment ratio of the test method reported in the study[3], and re-estimated the disease burden and clinical severity.

Random forest (RF) regression model

Random forest regression is an ensemble learning based algorithm that performs regression tasks by building multiple decision trees and integrating their predictions. The RF model averages or weights the predictions of multiple decision trees to get the final regression result. Mean Squared Error (MSE) is commonly used to evaluate performance of regression models, which measures the average squared error between the predicted value and the true value. Increase in MSE (%) of one variable refers to the average amount of increase in the MSE of the model after removing this variable, which can be used to evaluate the importance of explanatory variables to dependent variables, namely the strength of the correlation between explanatory variables and dependent variables. The CART regression tree in the RF is based on the mean of the leaf nodes, so the prediction of the RF is the average of the predicted values of all trees. The formulas are as follows:

$$\mathrm{MSE} = \frac{1}{n}\sum (x_i - y_i)^2$$

$$\underbrace{min}_{A,s}\left[\underbrace{min}_{c_1}\sum_{x_i \in D_1(A,s)}(y_i - c_1)^2 + \underbrace{min}_{c_2}\sum_{x_i \in D_2(A,s)}(y_i - c_2)^2\right]$$

Where c_1 is the sample output mean of D_1 dataset, and c_2 is the sample output mean of D_2 dataset; for the datasets D_1 and D_2 divided into two sides of feature A by the corresponding partition point s, the minimum MSE of two sets and the minimum sum of MSE are obtained.

Extreme Gradient Boosting (XGBoost) model

The method of machine learning XGBoost (eXtreme Gradient Boosting) is also based on residual optimization algorithm. Through the establishment of multiple regression trees, the predicted value of the tree group is as close as possible to the true value and has the maximum generalization ability. SHapley Additive exPlanations (SHAP) is an approach derived from game theory, in which all features are treated as contributors. SHAP values above 0 are regarded as risk effects and below 0 as protective effects. XGBoost model was constructed to calculate the SHAP values of all features in all samples, which reflected the importance of features and the positive or negative contributions. The following function is the main algorithmic principle.

$$Obj(\theta) = L(\theta) + \Omega(\theta) = \sum_i L(\hat{y}_i, y_i) + \sum_k \Omega(f_k), f_k \in F$$

Where L is the training loss function. $L(\hat{y}_i, y_i)$ represents the training loss function for each sample, where $\hat{y}_i$ represents the true value of the i sample and y_i represents the estimated value. Ω is regularization function that evaluates the model complexity, where k is the number of trees, F is the set of all possible regression trees.

Table S1. Case definition, identification and surveillance of Shanghai and Hong Kong, China

Case information	Shanghai	Source	Hong Kong, China	Source
Case definition	Confirmed COVID-19 cases: suspected cases (epidemiological history within 14 days and clinical manifestations such as fever and/or respiratory symptoms) with one of the following etiological or serological evidence: 1) positive nucleic acid test for novel coronavirus; 2) those without vaccination were positive for both IgM and IgG antibodies specific to the novel coronavirus.	The website of the National Health Commission (NHC): Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment (trial ninth edition) http://www.nhc.gov.cn/yzygj/s7653p/202203/a354cb3151b74cfdbac6b2e909f311e6.shtml	Confirmed COVID-19 cases: definition is generally the same as the guidelines used in mainland China.	The website of the Centre for Health Protection of the Department of Health of Hong Kong
	Severe/Critical COVID-19 case: severe cases referred to those patients with at least one of the following conditions: breathing problems, low oxygen saturation, low PaO2/FiO2 (PaO2 denotes partial pressure of oxygen in arterial blood; FiO2 denotes fraction of inspired oxygen), or progressive symptoms combined with pulmonary imaging showing obvious progress of lesions (>50%) within 24-48 hours. Critical cases referred to patients who met any one of the following three criteria: respiratory failure, shock, or organ failure that required intensive care unit admission.	the COVID-19 Prevention and Control Protocol (eighth edition) http://www.nhc.gov.cn/xcs/zhengcwj/202105/6f1e8ec6c4a540d99fafef52fc86d0f8.shtml	Severe/Critical COVID-19 case: definition is generally the same as the guidelines used in mainland China.	
	Hospitalization case: hospitalization cases referred to those mild but worsens; moderate/severe/critical cases; risk factors (age≥60; underlying diseases; immune dysfunction; organ transplantation; obesity; perinatal		Hospitalization case: hospitalization cases referred to those moderate/severe/critical cases; high risk groups (the elderly, aged≤5, pregnant>28weeks, underlying diseases or suppressed immunity).	https://www.ha.org.hk/visitor/ha_visitor_index.asp?Content_ID=264500&Dimension=100

	women; heavy smokers; the unvaccinated).			&Ver=HTML&Lang=CHIGB https://sc.isd.gov.hk/TuniS/www.info.gov.hk/gia/general/202202/15/P2022021500421.htm?fontSize=1
	COVID-19 deaths: deaths caused by pneumonia or respiratory failure due to SARS-CoV-2 are classified as COVID-19 deaths, while deaths caused by other diseases or underlying diseases, such as cardiovascular and cerebrovascular diseases and myocardial infarction, are not classified as COVID-19 deaths.	The website of World Health Organization (WHO): International Guidelines for Certification and Classification (Coding) of COVID-19 as Cause of Death https://www.who.int/publications/m/item/international-guidelines-for-certification-and-classification-(coding)-of-covid-19-as-cause-of-death	COVID-19 deaths: a death in a person with positive SARS-CoV-2 result and died within 28 days of the first positive specimen collection day, which mean that underlying cause of death may have been unrelated to COVID-19.	https://www.coronavirus.gov.hk/pdf/5th_wave_statistics/5th_wave_statistics_20220322.pdf
Case identification	Nucleic acid detection by RT-PCR was the gold standard for the diagnosis of COVID-19 infections. Two kinds of RT-PCR kits were used for large-scale nucleic acid screening (BioGerm, Lot No. 20200304A; Bioperfectus, Lot No. JC10223-1N).	Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment (trial ninth edition) http://www.nhc.gov.cn/yzygj/s7653p/202203/a354cb3151b74cfdbac6b2e909f311e6.shtml	On February 25, 2022, the Hong Kong government announced that a positive result of a rapid antigen test could also be considered the gold standard for confirming COVID-19 cases, as same as the positive result of a nucleic acid test.	Hong Kong Special Administrative Region Government Press Release: Speech at the Briefing on the latest situation of COVID-19 Cases

Case surveillance	1) Multiple rounds of mass nucleic acid screenings and self-performed rapid antigen test (RAT) screenings as a supplement to detect infection cases (any positive results of antigen test need to be confirmed by nucleic acid test). 2) Routine case surveillance included symptom-based surveillance of medical institutions, contact tracing, epidemiological investigations and high-risk group screening	the COVID-19 Prevention and Control Protocol (eighth edition) http://www.nhc.gov.cn/xcs/zhengcwj/202105/6f1e8ec6c4a540d99fafef52fc86d0f8.shtml	1) The nucleic acid test was only performed on key populations, and non-mandatory antigen screening was implemented for all individuals. 2) The case surveillance system sticks to symptom-based surveillance in medical institutions and monitoring of specific occupational groups and high-risk groups, which was unable to achieve timely contact tracing and epidemiological investigation. This means that most of the confirmed cases counted by the case surveillance of Hong Kong were symptomatic patients and the majority of asymptomatic infections were missed.	https://sc.isd.gov.hk/TuniS/www.info.gov.hk/gia/general/202202/26/P2022022600668.htm?fontSize=1
Case data	Daily reported case data from the website of Shanghai Health Commission	https://wsjkw.sh.gov.cn/	Daily reported cases data from the website of the Centre for Health Protection of the Department of Health of Hong Kong.	https://www.coronavirus.gov.hk/pdf/5th_wave_statistics/5th_wave_statistics_20220322.pdf

Table S2. Case data of Shanghai and Hong Kong, China

Case data	Shanghai		Hong Kong, China	
	Definition	**Value**	**Definition**	**Value**
Infection case	NA	-	NA	-
Reported conformed case	Cumulative PCR-confirmed infections, since Feb 26, 2022.	627,115	Cumulative reported cases by PCR/RAT, since Dec 31, 2021.	745,910/445,669 (RT-PCR/RAT)
Reported symptomatic case	Cumulative PCR-confirmed symptomatic infections.	58,137	NA	-
Hospitalization case	NA	-	Current hospitalized cases: • hospitalized critical cases • hospitalized serious cases • hospitalized stable/satisfactory cases Cumulative discharged cases	1420 • 34 • 67 • 1319 48,001
Severe/Critical case	NA	-	NA	-
Reported death case	Cumulative deceased cases.	588	Cumulative deceased cases.	9095
Population size	Resident population at the end of 2021.	24,894,300	Resident population in the middle of 2021	7,394,700

Table S3. Parameters source

Parameters	Classification	Shanghai	Source	Hong Kong, China		Source
Age distribution	deceased cases	daily new deceased cases	The official websites of Shanghai municipal Health Commissions;	Cumulative deceased cases by age group.		The Centre for Health Protection of the Department of Health; and the Hospital Authority of Hong Kong, China
		568 deaths (Before May 15)	Huang et al., 2022[4]			
	confirmed cases	612,597 confirmed cases		Cumulative reported cases by age group.		
	severe/critical patients	1485 severe/critical patients		-		
Vaccination coverage	deceased cases	568 deceased cases		Cumulative deceased cases.		
	severe/critical patients	1485 severe/critical patients		-		
	confirmed cases	612,597 confirmed cases		Cumulative reported cases.		
	resident population	Vaccinated/full vaccinated rate	The official websites of Shanghai municipal Health Commissions	Population with 1^{st}/ 2^{nd}/ 3^{rd}/ 4^{th} vaccine dose		
Sensitivity	RT–PCR/RAT	BioGerm: 0.944; Bioperfectus: 0.949.	Lu et al., 2020[5]	Ascertainment rate by PCR:	by PCR+RAT:	Lau et al., 2022[3]
Interval between	infection and symptom onset	1.91 days (95% CI: 0.25-14.28)	Yu et al., 2022	0-11: 16% (13-21%);	0-11: 33% (26-42%);	
	symptom and hospital admission	0.92 days (95% CI: 0.13-6.61)		12-19: 13% (12-14%);	12-19: 25% (23-28%);	
	hospital admission and death	6.92 days (95% CI: 0.53-29.52)		20-29: 24% (23-26%);	20-29: 43% (40-46%);	
	infection and severe/critical illness	5.7 days (95% CI: 4.1-7.8)		30-39: 27% (25-31%);	30-39: 49% (45-56%);	
				40-49: 26% (25-29%);	40-49: 44% (41-49%);	
				50-59: 29% (27-32%);	50-59: 44% (41-49%);	
				60+: 28% (24-34%);	60+: 41% (35-50%);	
				Overall: 25% (23-27%)	Overall: 41% (38-45%)	

Table S4. Possible risk factors of clinical severity and disease burden between Shanghai and Hong Kong, China.

Risk factors	Variables	Shanghai	Sources	Hong Kong, China	Sources
Medical resource	Doctors per 1000 population	3.752	1)https://wsjkw.sh.gov.cn/tjsj2/20220704/a540b90305ae4c54bf870b3804c6f84c.html 2)https://baijiahao.baidu.com/s?id=1729165454139565402&wfr=spider&for=pc 3)the Xinhua News Agency: https://baijiahao.baidu.com/s?id=1730253936556442424&wfr=spider&for=pc 4)https://www.163.com/dy/article/H62CBQAC05341282.html	2.097	https://www.ha.org.hk/visitor/ha_index.asp?Lang=CHIB5
	Hospital beds per 1000 population	18.78		4.873	
	ICU beds per 100000 population	6.14		7.1	
	Nurses per 1000 population	6.05		8.64	
Testing capacity	PCR test per 1000 population per day	363.6	Press conference on COVID-19 prevention and control: https://baijiahao.baidu.com/s?id=1732223200448122486&wfr=spider&for=pc	80.97	1)http://www.xinhuanet.com/home.htm 2)https://sputniknews.cn/20220217/1039355592.html
	RAT per 1000 population per day	733.0		-	
Vaccination status	≥1 dose vaccination rate	Overall: 95.2%	1)http://wsjkw.sh.gov.cn/xwfb/20220429/56cf0206f02b4690a80f762b40e3d749.html 2)https://www.shanghai.gov.cn/nw4411/20220310/8a9111cefd4e44bc838a9ac48270760b.html?siteId=1	Overall: 84.75%	https://www.coronavirus.gov.hk/chi/5th-wave-statistics.html
	Full vaccination rate	Aged 60+: 62% Overall: 95.1%		Aged 60+: 62.05% Overall: 71.00%	
	Booster vaccination rate	Aged 60+: 38% Overall: 42.74%		Aged 60+: 25.95% Overall: 28.38%	
Demographic characteristic	Age structure	Aged 0-9: 7.13% Aged 10-19: 5.53% Aged 20-29: 14.96% Aged 30-39: 20.25% Aged 40-49: 14.61%	https://tjj.sh.gov.cn/tjnj/20220309/0e01088a76754b448de6d608c42dad0f.html	Aged 0-9: 7.19% Aged 10-19: 7.69% Aged 20-29: 10.89% Aged 30-39: 12.62% Aged 40-49: 16.23%	https://www.censtatd.gov.hk/sc/

		Aged 50-59: 14.15% Aged 60-69: 13.72% Aged 70-79: 6.3% Aged 80+: 3.36%		Aged 50-59: 16.73% Aged 60-69: 15.35% Aged 70-79: 7.88% Aged 80+: 5.43%	
	Population density per km^2	3926		6800	
	Proportion of people at high risk (%)	29.1		27.7	
	Living area (m^2)	35.3		15.8	
Socioeconomic characteristic	Human Development Index (HDI)	0.893	https://tjj.sh.gov.cn/tjnj/20220309/0e01088a76754b448de6d608c42dad0f.html	0.949	1)https://www.censtatd.gov.hk/sc/ 2)https://www.cn-healthcare.com/articlewm/20220910/content-1433181.html
	Life expectancy (years)	84.11		85.35	
	Average years of schooling	12.2		12.5	
	Per capita GDP ($\times 10^4$ dollar)	2.69		4.97	
NPIs*	Stringency Index	81.94	1)https://ourworldindata.org/policy-responses-covid 2)https://www.pudong.gov.cn/026002/20220329/671806.html 3)https://www.shanghai.gov.cn/qjzccs/20220401/b3fd5ac909114b5693a1fb1cc58c8149.html 4)https://www.shanghai.gov.cn/nw12344/20220401/08e4592510cb4b68b50c546184a05cf2.html	75.00	1)https://ourworldindata.org/policy-responses-covid 2)https://www.coronavirus.gov.hk/sim/inbound-travel-faq.html 3)https://sc.isd.gov.hk/TuniS/www.info.gov.hk/gia/general/202202/05/P2022020500185.htm?fontSize=1 4)https://www.info.gov.hk/gia/general/202108/10/P2021081000555.htm
	School/Workplace closures	4		4	
	Cancellation of public events	3		2	
	Stay-at-Home Restrictions	4		3	
	Facial coverings	4		4	
	International and Domestic Travel	2		1	
	Public transport	2		1	
	Testing policy	4		3	
	Contact tracing	2		1	
Underlying disease	Cardiovascular mortality (per 100,000 people)	371.93	https://baijiahao.baidu.com/s?id=1726232988298998682&wfr=spider&for=pc	146.43	1)https://www.ha.org.hk/visitor/ha_index.asp?Lang=CHIB5 2) https://www.censtatd.gov.hk/sc/
	Cancer mortality (per 100,000 people)	270.53		199.98	

* The additional details about NPIs can be found in Table S10.

Table S5. Search strategy and terms

Database	Step	Search strategy
PubMed	#1	Title/Abstract: 2019-nCoV OR “coronavirus disease 2019” OR COVID-19 OR “severe acute respiratory syndrome coronavirus 2” OR SARS-CoV-2
	#2	MeSH Terms: SARS-CoV-2 OR COVID-19
	#3	#1 OR #2
	#4	Title/Abstract: VOC OR “Variant of Concern” OR “Variants of Concern” OR variant* OR mutant* OR mutation* OR “Omicron” OR “B.1.1.529” OR “GR/484A” OR “21K” OR “21L” OR “21M” OR “BA.1” OR “BA.2” OR “BA” OR “BA.2.12.1”
	#5	Title/Abstract: IFR* OR serology confirmed infection fatality risk OR infection fatality risk OR mortality OR fatality OR death OR infection rate
	#6	Language: English
	#7	Nov 1, 2021 to Oct 30, 2023
	#8	#3 AND #4 AND #5 AND #6 AND #7
Web of Science	#1	Title/Abstract: 2019-nCoV OR “coronavirus disease 2019” OR COVID-19 OR “severe acute respiratory syndrome coronavirus 2” OR SARS-CoV-2
	#2	Title/Abstract: VOC OR “Variant of Concern” OR “Variants of Concern” OR variant* OR mutant* OR mutation* OR “Omicron” OR “B.1.1.529” OR “GR/484A” OR “21K” OR “21L” OR “21M” OR “BA.1” OR “BA.2” OR “BA” OR “BA.2.12.1”
	#3	Title/Abstract: IFR* OR serology confirmed infection fatality risk OR infection fatality risk OR mortality OR fatality OR death OR infection rate
	#4	Language: English
	#5	2021/11/01 to 2023/10/30
	#6	#1 AND #2 AND #3 AND #4 AND #5
Embase	#1	Title/Abstract: 2019-nCoV OR “coronavirus disease 2019” OR COVID-19 OR “severe acute respiratory syndrome coronavirus 2” OR SARS-CoV-2
	#2	Title/Abstract: VOC OR “Variant of Concern” OR “Variants of Concern” OR variant* OR mutant* OR mutation* OR “Omicron” OR “B.1.1.529” OR “GR/484A” OR “21K” OR “21 L” OR “21 M” OR “BA.1” OR “BA.2” OR “BA” OR “BA.2.12.1”
	#3	Title/Abstract: IFR* OR serology confirmed infection fatality risk OR infection fatality risk OR mortality OR fatality OR death OR infection rate
	#4	Language: English
	#5	2021/11/01 to 2023/10/30
	#6	#1 AND #2 AND #3 AND #4 AND #5

EuropePMC	#1	Title/Abstract: 2019-nCoV OR “coronavirus disease 2019” OR COVID-19 OR “severe acute respiratory syndrome coronavirus 2” OR SARS-CoV-2
	#2	Title/Abstract: VOC OR “Variant of Concern” OR “Variants of Concern” OR variant* OR mutant* OR mutation* OR “Omicron” OR “B.1.1.529” OR “GR/484A” OR “21K” OR “21 L” OR “21 M” OR “BA.1” OR “BA.2” OR “BA” OR “BA.2.12.1”
	#3	Title/Abstract: IFR* OR serology confirmed infection fatality risk OR infection fatality risk OR mortality OR fatality OR death OR infection rate
	#4	Language: English
	#5	2021/11/01 to 2023/10/30
	#6	#1 AND #2 AND #3 AND #4 AND #5

Table S6. Summary of studies reporting infection, mortality or infection fatality ratio (IFR) of COVID-19 caused by Omicron

Authors (year)	Location	Time	Variant	Methods	Case definition	Data sources/Case identification	Study participants	Results
Madhi et al., Viruses (2023)[6]	Gauteng, South Africa	Oct 2021-Mar 2022	Omicron BA.1	Cross-sectional population-based serosurvey	The serology testing for anti-nucleocapsid (anti-N) and anti-spike (anti-S) IgG was carried out on dried blood spot samples obtained from the participants	Data sources included daily recorded COVID-19 cases, hospitalizations and deaths to 17 November 2022 from the National Institute for Communicable Diseases (NICD) in South Africa, as well as excess deaths (all excess deaths were assumed to be COVID-19 deaths) until 12 November 2022 from the South African Medical Research Council	3345 households, including 1052 (31.4%) enrolled in the previous survey. Dried blood spots were obtained from 7510 individuals, including 2420 (32.2%) with paired samples	**Infection fatality risk (IFR)** Overall: 0.02% **Cumulative recorded death rate per 100,000 population** 11.6
Mseka et al., EClinicalMedicine (2023)[7]	Malawi	Apr 2021-Apr 2022	Omicron	The study used a stratified multistage probability sample design, a random systematic sample of households was selected from each PSU within each health zone to the extent feasible.	SARS-CoV-2 Receptor Binding Domain protein immunoglobulin were measured qualitatively in sera using the WANTAI SARS-CoV-2 total antibody commercial ELISA kit. As a confirmatory assay, a multiplexed MSD immunoassay was used to measure anti-SARS-CoV-2 IgG antibodies against Spike, Nucleocapsid and Receptor Binding Domain.	Data regarding daily cases, hospitalizations, and deaths were sourced from the Public Health Institute of Malawi (PHIM). In brief, the routine national COVID-19 reporting system works as follows: data from multiple sources at district level covering a 24-h period (6am–6am) are sent to national level through the national Public Health Emergency Operations Centre (PHEOC).	4639 participants from 1415 households, with 4619 samples from the participants analyzed.	**Infection fatality risk (IFR)** Overall: 1.15% (95% CI, 1.00–1.34)

Erikstrup et al., The Lancet Regional Health – Europe (2022)[8]	Denmark	Jan 2022-Apr 2022	Omicron	The study collected blood samples from blood donors from each of the five administrative regions in Denmark and tested for anti-N IgG antibodies	Anti-N IgG measurements for blood donors who donated blood in the study period	(1) SARS-CoV-2 RT-PCR test results measured in oropharyngeal swaps from residents in Denmark based on the Danish Microbiological Database;12 (2) information on underlying diseases based on diagnosis codes from the Danish National Patient Registry;13 (3) information on vital status and region of residence from the Danish Civil Registration System; (4) registrations of death from the Danish Register of Causes of Death; and (5) COVID-19 vaccination data from the Danish Vaccination Register. Population counts from the first quarter of 2022 were obtained from Statistics Denmark	A total of 43 088 donations from 35 309 Danish blood donors aged 17−72 years were screened. In November 2021, 1.2% (103/8701) of donors had detectable anti-N IgG antibodies.	**Infection fatality risk (IFR)** 30-Day mortality (per 100,000) Overall: 6.2 (5.1-7.5) 17-35 years: 1.6 (0.9−3.1) 36-50 years: 4.1 (2.6−6.6) 51-60 years: 7.6 (5.2−11.3) 61-72 years: 15.1 (11.5−19.9) 60-Day mortality (per 100,000) Overall: 10.2 (8.8−11.9) 17-35 years: 2.6 (1.6−4.3) 36-50 years: 5.8 (3.9−8.7) 51-60 years: 14.6 (11.0−19.4) 61-72 years: 24.6 (19.8−30.5)
Eales et al., PLOS Biology (2023)[9]	England	Sep 2021-Mar 2022	Omicron	The Real-time Assessment of Community Transmission-1 (REACT-1) study estimated swab positivity for (SARS-CoV-2) infection in England approximately monthly from May 2020 to March 2022.	-	The study analyzed the changing relationship between prevalence of swab positivity and the IFR and IHR over this period in England, using publicly available data for the daily number of deaths and hospitalizations, REACT-1 swab positivity data	-	**Infection fatality risk (IFR)** Overall: 0.069% (0.066%, 0.072%)
Rahman et al., Health Sci. (2023)[10]	Bangladesh	Dec 2021-Oct 2022	Omicron	-	-	The clade and Pango lineages were assigned by using Nextclade v2.8.1. SARS-CoV-2 infections and fatality data were collected from the Institute of Epidemiology Disease Control and Research (IEDCR), Bangladesh.	-	**Infection fatality risk (IFR)** Overall: 0.313%

Zhang et al., Scientific Reports (2023)[11]	Osaka, Japan	Dec 2021-Jan 2022	Omicron	The present study aimed to estimate the infection fatality risk (IFR) and ascertainment bias of SARS-CoV-2 for six epidemic waves in Japan from February 2020 to January 2022. Smoothing spline function was employed to reconstruct the age-specific cumulative incidence of infection	-	The study used two types of datasets: (i) surveillance-based datasets containing the cumulative numbers of confirmed cases and deaths in each epidemic wave and (ii) sero-epidemiological datasets conducted in a serial cross-sectional manner.	-	**Infection fatality risk (IFR)** Overall: 124/42367 (0.29%) 20-39 years: 0% (0%, 0%) 40-59 years: 0.02% (0.01%, 0.04%) 60+ years: 1.26% (0.90%, 2.54%)
Chen et al., BMC Infectious Diseases (2023)[12]	Six countries: India, Indonesia, Nepal, Malaysia, Bangladesh and Myanmar.	Jan 2022-Oct 2022	Omicron	The study proposed a Susceptible-Vaccinated-Exposed-Infectious-Hospitalized-Death-Recovered model with a time-varying transmission rate $\beta(t)$ to ft the multiple waves of the COVID-19 pandemic and to estimate the IFR and $R_0(t)$ in the aforementioned six countries.	-	-	-	**Infection fatality risk (IFR)** India: 0.03 % Indonesia: 0.049% Malaysia: 0.14% Nepal: 0.035% Bangladesh: 0.014 % Myanmar: 0.025%
Colman et al., Journal of Theoretical Biology (2023)[13]	England, UK	Jan 2022-Mar 2022	Omicron	By calibrating the model against surveillance data, the study estimated the case ascertainment rate, defined as the proportion of infections that were reported through diagnostic testing; the incidence, defined as the number of newly infected individuals	The study considered tests that are negative for the S target gene and positive for the two other targets, known as S-gene target failure (SGTF), to be a proxy for the Alpha and Omicron BA.1 variant.	They are primarily concerned with daily Pillar 1 and 2 case data (UK coronavirus dashboard, 2022a), hereafter referred to as diagnostic test cases, which represent tests done in health care settings and the community, respectively	-	**Infection fatality risk (IFR)** 25-34 years: 0.009% 35-49 years: 0.02% 50-69 years: 0.19% 70+ years: 2.2%

				each day; and the IFR				
Sigal et al., Nature Reviews (2022)[14]	USA	Dec 2021-Mar 2022	Omicron	-	-	The study used data from the Delta and Omicron infection waves in the USA available from the Centers for Disease Control and Prevention	-	**Infection fatality risk (IFR)** 0.15%
Marziano et al. Influenza Other Respi Viruses (2023)[15]	Italy	Dec 2021-Feb 2022	Omicron BA.1	The study developed an age-structured stochastic model, based on a susceptible-infectious-removed-susceptible (SIRS) scheme to simulate SARS-CoV-2 transmission and vaccination.	-	All the numerators refer to numbers reported to the Italian Integrated Surveillance System.	-	**Infection fatality risk (IFR)** 0.05% (95%CI: 0.04–0.08)

Table S7. Data sources from Our World in Data

Type	Variable	Description	Time Span	Link	Data published by
Test	New tests per thousand (7day smoothed)	The series is smoothed by averaging daily figures over a rolling 7-day window. Not all countries report testing data on a daily basis. To generate this series, we assume that testing changed equally on a daily basis over any periods in which no data was reported. This produces a complete series of daily figures, which is then averaged over a rolling 7-day window. Tests may refer to the number of tests performed or the number of people tested – depending on which is reported by the particular country.	Jan 8, 2020-Jun 23, 2022	https://ourworldindata.org/coronavirus-testing#testing-for-covid-19-background-the-our-world-in-data-covid-19-testing-dataset	For source details see ourworldindata.org/coronavirus-testing#source-information-country-by-country
Vaccine	Total boosters per hundred	-	Dec 2, 2020-Apr 13, 2023	https://github.com/owid/covid-19-data/tree/master/public/data/vaccinations/locations.csv	-
	People fully vaccinated per hundred				
	People vaccinated per hundred				
NPIs	Containment index	OxCGRT measures the variation in governments' responses using its COVID-19 Government Response Stringency Index. This composite measure is a simple additive score of nine indicators measured on an ordinal scale, rescaled to vary from 0 to 100. Please note that this measure is for comparative purposes only, and should not be interpreted as a rating of the appropriateness or effectiveness of a country's response.	Jan 1, 2020-Dec 31, 2022	https://www.bsg.ox.ac.uk/research/research-projects/oxford-covid-19-government-response-tracker	Thomas Hale, Noam Angrist, Rafael Goldszmidt, Beatriz Kira, Anna Petherick, Toby Phillips, Samuel Webster, Emily Cameron-Blake, Laura Hallas, Saptarshi Majumdar, and Helen Tatlow. (2021). "A global panel database of pandemic policies (Oxford
	School closures	0 - No measures			

		1 - recommend closing 2 - Require closing 3 - Require closing all levels No data - blank			COVID-19 Government Response Tracker).” Nature Human Behavior. https://doi.org/10.1038/s41562-021-01079-8
	Workplace closures	0 - No measures 1 - recommend closing (or work from home) 2 - require closing (or work from home) for some sectors or categories of workers 3 - require closing (or work from home) all but essential workplaces (e.g. grocery stores, doctors) No data - blank			
	Cancel public events	0 - No measures 1 - Recommend cancelling 2 - Require cancelling No data - blank			
	Restriction gatherings	0 - No restrictions 1 - Restrictions on very large gatherings (the limit is above 1,000 people) 2 - Restrictions on gatherings between 100-1,000 people 3 - Restrictions on gatherings between 10-100 people 4 - Restrictions on gatherings of less than 10 people No data - blank			
	Close public transport	0 - No measures 1 - Recommend closing (or significantly reduce volume/route/means of transport available) 2 - Require closing (or prohibit most citizens from using it)			

	Public information campaigns	0 -No COVID-19 public information campaign 1 - public officials urging caution about COVID-19 2 - coordinated public information campaign (e.g. across traditional and social media) No data - blank			
	Stay home requirements	0 - No measures 1 - recommend not leaving house 2 - require not leaving house with exceptions for daily exercise, grocery shopping, and 'essential' trips 3 - Require not leaving house with minimal exceptions (e.g. allowed to leave only once every few days, or only one person can leave at a time, etc.) No data - blank			
	Restrictions internal movements	0 - No measures 1 - Recommend movement restriction 2 - Restrict movement			
	International travel controls	0 - No measures 1 - Screening 2 - Quarantine arrivals from high-risk regions 3 - Ban on high-risk regions 4 - Total border closure No data - blank			
	Contract tracing	0 - No contact tracing 1 - Limited contact tracing - not done for all cases 2 - Comprehensive contact tracing - done for all cases			

		No data			
	Facial coverings	0 - No policy 1 - Recommended 2 - Required in some specified shared/public spaces outside the home with other people present, or some situations when social distancing not possible 3 - Required in all shared/public spaces outside the home with other people present or all situations when social distancing not possible 4 - Required outside the home at all times, regardless of location or presence of other people			
	Testing policy	0 - No testing policy 1 - Only those who both (a) have symptoms AND (b) meet specific criteria (e.g., key workers, admitted to hospital, came into contact with a known case, returned from overseas) 2 - testing of anyone showing COVID-19 symptoms 3 - open public testing (e.g., "drive through" testing available to asymptomatic people) No data			
	Close public transport	-			
Economics	Income support	These metric captures if the government is covering the salaries or providing direct cash payments, universal basic income, or similar, of people who lose their jobs or cannot	Jan 1, 2020-Dec 31, 2022	https://www.bsg.ox.ac.uk/research/research-projects/oxford-covid-19-government-response-tracker	

		work. (Includes payments to firms if explicitly linked to payroll/ salaries). 0 - no income support 1 - government is replacing less than 50% of lost salary (or if a flat sum, it is less than 50% median salary) 2 - government is replacing 50% or more of lost salary			
	GDP per capita, PPP (constant 2017 international $)	GDP per capita based on purchasing power parity (PPP). PPP GDP is gross domestic product converted to international dollars using purchasing power parity rates. An international dollar has the same purchasing power over GDP as the U.S. dollar has in the United States.		https://datacatalog.worldbank.org/search/dataset/0037712/World-Development-Indicators	World Development Indicators - World Bank (2022.05.26)
	Domestic private health expenditure per capita, PPP (current international $)	Current private expenditures on health per capita expressed in international dollars at purchasing power parity.	2000-2019	https://datacatalog.worldbank.org/search/dataset/0037712/World-Development-Indicators	World Development Indicators - World Bank (2022.05.26)
Case	Daily new estimated infections of covid-19 (ICL, mean)	Values are for the mean estimate.	Aug 6, 2020-Dec 25, 2022	https://github.com/mrc-ide/global-lmic-reports/tree/master/data	MRC Centre for Global Infectious Disease Analysis, Imperial College London
	Daily new estimated infections of covid-19 (IHME, mean)	Values are for the mean estimate.	Feb 4, 2020-Dec 12, 2022	http://www.healthdata.org/covid/data-downloads	Institute for Health Metrics and Evaluation
	Daily new estimated infections of covid-19 (LSHTM, median)	Values are for the mean estimate.	Jan 9, 2020-Aug 11, 2020	https://cmmid.github.io/topics/covid19/global_cfr_estimates.html	The Centre for Mathematical Modelling of Infectious Diseases, London School of Hygiene & Tropical Medicine
	Daily new estimated infections of covid-19 (YYG, mean)	Values are for the mean estimate.	Dec 26, 2019-Oct 4, 2020	https://github.com/youyanggu/covid19_projections/tree/master/projections	Youyang Gu

	Daily new confirmed cases of covid-19	-	Jan 3, 2020-Apr 12, 2023	https://covid19.who.int/data	WHO COVID-19 Dashboard. Geneva: World Health Organization, 2020.
	Daily new confirmed deaths due to covid-19	-	Jan 3, 2020-Apr 12, 2023	https://covid19.who.int/data	WHO COVID-19 Dashboard. Geneva: World Health Organization, 2020.
Medical sources	Physicians (per 1,000 people)	Physicians include generalist and specialist medical practitioners.	1960-2019	https://datacatalog.worldbank.org/search/dataset/0037712/World-Development-Indicators	World Development Indicators - World Bank (2022.05.26)
	Public health expenditure pc GDP	-	1880-2021	https://nextjournal.com/fiona-spooner/government-health-expenditure	Our World in Data
	Critical care beds (per 100,000)	-	2011-2018	https://docs.google.com/spreadsheets/d/1nSDwFWmnqvcP5Ut_epcntxjZrR8PcnU6enupT8G5d0s/edit	OECD; Eurostat; World Bank; National Government Records and other sources
	Hospital beds (per 1,000 people)	Hospital beds include inpatient beds available in public, private, general, and specialized hospitals and rehabilitation centers. In most cases beds for both acute and chronic care are included.	1960-2019	https://datacatalog.worldbank.org/search/dataset/0037712/World-Development-Indicators	World Development Indicators - World Bank (2022.05.26)
Underlying disease	Cardiovascular diseases death rate (per 1,000 people)	Annual number of deaths from cardiovascular disease per 100,000 people. Cardiovascular disease (CVD) is a general term that describes a disease of the heart or blood vessels. It can impact the supply of blood to the heart muscle, the brain, or other parts of the body. Cardiovascular diseases are the leading cause of death globally.	1990 – 2019	http://ghdx.healthdata.org/gbd-results-tool	Institute for Health Metrics and Evaluation, Global Burden of Disease (2019)

Table S8. Definitions of indicators of clinical severity and disease burden

Indicators	Definitions
Infection rate	The number of new COVID-19 infections in the total population during a certain period of time.
Hospitalization rate	The number of hospitalized COVID-19 patients in the total population during a certain period of time.
Mortality rate	The number of deaths of COVID-19 in the total population during a certain period of time.
IHR (infection-hospitalization ratio)	The ratio between the number of hospitalized COVID-19 patients and the total number of COVID-19 infections.
IFR (infection-fatality ratio)	The ratio between the number of deaths of COVID-19 and the total number of COVID-19 infections.
HFR (hospitalization-fatality ratio)	The ratio between the number of deaths of COVID-19 and the total number of hospitalized COVID-19 patients.

Table S9. Comparison of the differences in disease burden and clinical severity of COVID-19 caused by Omicron BA.2 variant between Shanghai and Hong Kong, China.

The constructed limit [*L-U*] doesn't cover the zero, indicating there is significant difference between two clinical severity/disease burden indicators.

Age Group	Infection rate per 100 persons			Mortality rate per 100,000 persons			Adjusted infection-fatality risk (IFR) (%)		
	Hong Kong, China	Shanghai	[*L-U*]	Hong Kong, China	Shanghai	[*L-U*]	Hong Kong, China	Shanghai	[*L-U*]
3-17	45.87 (45.76-45.98)	1.67 (1.66-1.69)	[44.09-44.3]	1.19 (0.45-1.93)	0 (0-0)	[0.45-1.93]	0.003 (0.001-0.004)	0 (0-0)	[0.001-0.004]
18-39	42.12 (42.05-42.19)	2.2 (2.19-2.21)	[39.85-39.99]	2.02 (1.4-2.65)	0.02 (0-0.04)	[1.38-2.63]	0.005 (0.003-0.006)	0.001 (0.001-0.001)	[0.002-0.005]
40-59	40.35 (40.29-40.41)	3.43 (3.42-3.44)	[36.85-36.98]	12.97 (11.51-14.43)	0.32 (0.19-0.45)	[11.19-14.11]	0.032 (0.029-0.036)	0.009 (0.008-0.01)	[0.019-0.027]
60-79	43.58 (43.51-43.66)	3.65 (3.63-3.67)	[39.86-40.01]	132.78 (127.32-138.23)	4.6 (3.87-5.32)	[122.68-133.68]	0.305 (0.292-0.317)	0.126 (0.111-0.134)	[0.164-0.198]
80+	44.37 (44.22-44.53)	2.88 (2.84-2.92)	[41.34-41.65]	1622.8 (1583.56-1662.05)	57.17 (51.63-62.71)	[1526-1605.26]	3.657 (3.57-3.745)	1.989 (1.755-2.106)	[1.522-1.918]
All	42.45 (42.41-42.48)	2.74 (2.73-2.74)	[39.67-39.75]	124.90 (122.33-127.46)	2.42 (2.23-2.62)	[119.9-125.05]	0.294 (0.288-0.300)	0.089 (0.078-0.094)	[0.198-0.218]

Table S10. Comparison of Shanghai and Hong Kong's major NPIs during the Omicron BA.2 variant epidemic period.

NPIs	Shanghai	Sources	Hong Kong, China	Sources
School closures	1) Closure of all kindergartens, nurseries, primary, secondary, vocational, and training schools (2022/03/12) 2) University closure (2022/03/15).	https://mp.weixin.qq.com/s/_yiS-7IhSbp6J9vmQQBYDQ	1) Closure of all kindergartens, nurseries, primary, secondary, vocational, and training schools (2022/02/15). 2) Universities switched to online classes (2022/02/07).	http://sz.bendibao.com/news/2022215/882694.htm https://learning.sohu.com/a/523607761_340756
Workplace closures	All enterprises and factories suspended production (2022/3/28).	https://baijiahao.baidu.com/s?id=1728594624146968541&wfr=spider&for=pc	After 6 PM, dine-in services at restaurants are prohibited, and the closure of bars, beauty salons, gyms, malls, theme parks, and similar venues was enforced (2022/01/07).	https://baijiahao.baidu.com/s?id=1721105341283567001&wfr=spider&for=pc
Cancellation of public events	Limiting gatherings: Suspension of gathering activities, such as large-scale exhibitions, cultural performances and others (2022/03/15).	https://baijiahao.baidu.com/s?id=1727354297326963152&wfr=spider&for=pc	Hospitals suspend visits, maintain the 4-person gathering limit, and mask mandate, while the government cancels large events and non-essential gatherings.	https://baijiahao.baidu.com/s?id=1721105341283567001&wfr=spider&for=pc
Stay-at-Home Restrictions	Community confinement: Implement "2+12" control measures for the residential community where the close contacts lived or worked. "2" refers to the confinement for 2 days and two nucleic acid tests which have a 24-hour interval at least, and the next stage "12" refers that the community is strictly managed.	https://sghexport.shobserver.com/html/baijiahao/2022/03/14/683716.html https://new.qq.com/omn/20211203/20211203A05BRO00.html	Suspected cases, as directed in writing, should avoid testing centers and stay at home while awaiting results to minimize transmission risk.	https://sc.isd.gov.hk/TuniS/www.info.gov.hk/gia/general/202202/05/P2022020500185.htm?fontSize=1
Facial coverings	Universal facemask policies: A graphic version of Guidelines for Wearing Masks in Public Science was released by the National Health Commission of China	https://mp.weixin.qq.com/s/iUPvUHV9GSTEkHMI_xFZiQ	Universal facemask policies: The Prevention and Control of Disease (Wearing of Masks) Regulation	https://www.info.gov.hk/gia/general/202108/10/P2021081000555.htm
International Travel	Fuse measures for international scheduled passenger flights	http://www.caac.gov.cn/XXGK/XXGK/TZTG/202104/t20210429_207386.html	Ban on flights and entry from Australia, Canada, France, India, Pakistan, the Philippines, the UK, and the US to Hong Kong (2022/01/08).	https://baijiahao.baidu.com/s?id=1721105341283567001&wfr=spider&for=pc

	Airport diversion of inbound flights: The entry point was transferred from Shanghai Pudong Airport to other airports at 12 cities (2022/03/21).	http://news.carnoc.com/list/580/580595.html	Mandatory 14-day quarantine required for all, irrespective of nationality or travel documents.	https://www.info.gov.hk/gia/general/202108/10/P2021081000555.htm
	Quarantine for inbound travelers at designated facilities: 14 days of centralized isolation in designated hotels.	http://sh.bendibao.com/news/20211212/246484.shtm		
	Home-quarantine: After 14 days of centralized isolation, those who have a fixed place of residence in Shanghai and meet the conditions for home health monitoring will undergo 7-day home health monitoring.	http://sh.bendibao.com/news/20211212/246484.shtm		
Domestic Travel	Travel restrictions for at-risk groups: Three-color dynamic management of health code: green code, yellow code and red code. The travel and access to public places will be limited for people with yellow code and red code.	http://sh.bendibao.com/news/2020221/217272.shtm	Local and international cruises temporarily suspended (2022/01/07).	https://baijiahao.baidu.com/s?id=1721105341283567001&wfr=spider&for=pc
	All persons coming from or passing through high-risk or medium-risk areas in China should receive centralized quarantine (from high-risk areas) or strict community health monitoring (from medium-risk areas), combining with nucleic acid tests.	https://www.shanghai.gov.cn/sjzccs/20211029/d380895773214 68d86b5f0048f419c1f.html		
Public transport	Public transportation closures of long-distance bus: The Shanghai Bus Terminals suspend operations (2022/3/14).	https://mp.weixin.qq.com/s/dku0LLKZUf1hidcQcjCEZQ	Partial bus route suspensions.	https://www.sohu.com/a/533602199_121119292
Testing policy	Occupation-based screening: Increased frequency of health monitoring and nucleic acid screening will be tailored for the front-line staff at ports, medical staff in fever clinics and other high-risk positions	http://shanghai.xinmin.cn/xmsq/2021/08/20/32012714.html	Mandatory nucleic acid testing: 1) Mandatory triple testing: Enforced for clinical suspicion of COVID-19. The initial test must be completed within the first three days following the announcement of	https://sc.isd.gov.hk/TuniS/www.info.gov.hk/gia/general/202202/05/P2022020500185.htm?fontSize=1

	Multiple PCR-based screenings of high-risk groups: 1) 2 nucleic acid screenings within 48 hours, with the adoption of lockdown (2022/3/16-17) 2) 1 nucleic acid screening within 48 hours, with the adoption of lockdown (2022/03/23-24) 3) 1 nucleic acid screening within 48 hours, with the adoption of lockdown (2022/03/26-27) 4) 1 nucleic acid screening in residential communities with positive infections recorded from April 1 to 5, mainly using mixed sampling (2022/04/06-07). 5) 1 nucleic acid test per day (2022/04/18-21)	https://mp.weixin.qq.com/s/ZJSpoQYjGupSBOsWtSr_vA https://mp.weixin.qq.com/s/VU5d7WNiv7HF6DASXCaYNQ https://mp.weixin.qq.com/s/_OKOPwbPfOw1Zi48FOvF4w https://mp.weixin.qq.com/s/QXtV0k0vDYZQkPJ0W2XDDA https://mp.weixin.qq.com/s/vU7zkW0SeoqizeU50JLg3g https://mp.weixin.qq.com/s/K-4LVOff1yW9ExUyrwBzlw	mandatory testing. Subsequent tests are required between the 4th and 6th days and the 7th and 9th days, respectively, from the initiation of compulsory testing (2022/02/05-18). 2) Mandatory testing for those living or working with relevant cases on specified dates by the Department with self-monitoring for 21 days 3) Mandatory testing (within two days of being notified) for anyone residing with a quarantined person in the 14 days before or on the quarantine start date (report results to the government within three days via phone, fax, or email)	
	Multiple PCR-based screenings of general population: 1) 1 nucleic acid screening within 48 hours (2022/03/18-20) 2) 2 nucleic acid screenings were separately done on March 28 and 30 (2022/03/28-30) 3) 1 nucleic acid screening (2022/04/01) 4) 1 nucleic acid screening (2022/04/04) 5) 1 nucleic acid screening (2022/04/10) 6) 1 nucleic acid screening (2022/04/26) 7) At least 1 nucleic acid screening for the entire Shanghai (2022/05/01-07)	https://mp.weixin.qq.com/s/r6OBkpYSHRezqzHXXVclkw https://mp.weixin.qq.com/s/JHHfabFmTO1GQ7hxd5QdYQ https://mp.weixin.qq.com/s/jHQoG8YOmCGs6sMxJam_fQ https://mp.weixin.qq.com/s/HWcx2Hv6ONo3tJlduFMYrw https://mp.weixin.qq.com/s/1_3NkXSIKTAUEJBGwIyQkQ https://mp.weixin.qq.com/s/AIlpPep2E1HEC2SEIIT9MA https://mp.weixin.qq.com/s/HxQr4RSZIjbwrvoteDM6Vg		

	Antigen-based screening of general population: 1) 1 antigen screening in non-high-risk areas (2022/03/26-27) 2) 1 antigen screening (2022/04/03) 3) 1 antigen screening (2022/04/09)	https://mp.weixin.qq.com/s/_OKOPwbPfOw1Zi48FOvF4w https://mp.weixin.qq.com/s/HWcx2Hv6ONo3tJlduFMYrw https://mp.weixin.qq.com/s/L36p7Jrf4HNfARkNzEx-qg	Mandatory antigen testing: Daily rapid antigen testing for all Hong Kong citizens, with positive results to be reported within 24 hours (2022/04/08-10). Voluntary antigen testing: Distributing voluntary virus rapid test kits to residents and staff in response to sewage samples testing positive.	https://www.kankanews.com/detail/kKyJr8eJEye https://sc.isd.gov.hk/TuniS/www.info.gov.hk/gia/general/202202/04/P2022020400623.htm
	-	-	Sewage virus testing: The Environmental Protection Department and Drainage Services Department, with HKU collaboration, intensify COVID-19 testing in sewage samples across districts.	https://sc.isd.gov.hk/TuniS/www.info.gov.hk/gia/general/202202/05/P2022020500609.htm
Symptom-based surveillance	Symptom surveillance at fever clinics: Routine monitoring and screening at fever patients	http://shanghai.xinmin.cn/xmsq/2021/08/20/32012714.html	Symptom-based surveillance in medical institutions and monitoring of specific occupational groups and high-risk groups.	https://sc.isd.gov.hk/TuniS/www.info.gov.hk/gia/general/202202/26/P2022022600668.htm?fontSize=1
Contact tracing	1) Tracing, quarantine and testing of close contacts: 14 days of centralized isolation plus 7 days of home-quarantine, coupled with regular nucleic acid testing. 2) Tracing, quarantine and testing of contacts of contacts: 14 days of centralized isolation, coupled with regular nucleic acid testing	https://mp.weixin.qq.com/s/p1a4A1BrI1q6bZb-IRoxXw https://baijiahao.baidu.com/s?id=1709212142402363456&wfr=spider&for=pc	The government actively tracked individuals who had visited specific locations and might have been infected, enforced compliance with testing notices, and considered non-compliance a criminal offense, imposing a fixed penalty.	https://sc.isd.gov.hk/TuniS/www.info.gov.hk/gia/general/202202/05/P2022020500185.htm?fontSize=1
Case isolation	Isolation of cases in designated facilities: Several hospitals are set as designated hospitals for medical treatment	https://mp.weixin.qq.com/s/XZLTWktIMLABGZ-9Eum1Qw	Asymptomatic/mild cases mostly self-isolated at home, while moderate/severe/critical cases and high-risk groups were admitted to hospitals for treatment.	https://sc.isd.gov.hk/TuniS/www.info.gov.hk/gia/general/202202/15/P2022021500421.htm?fontSize=1
	Makeshift isolation hospitals were gradually opened (2022/03/23).	https://mp.weixin.qq.com/s/eCQPcwUC9iMirNWmKGGkLw	Collaborated with the mainland to establish a temporary isolation hospital	https://baijiahao.baidu.com/s?id=1725209913834130236&wfr=spider&for=pc

Grid management of high-risk /non-high-risk areas	Implemented lockdown for key-areas when launched nucleic acid screening (2022/03/16)	https://mp.weixin.qq.com/s/ZJSpoQYjGupSBOsWtSr_vA	-	-
Lockdown	1) Lockdown of eastern Shanghai (2022/03/28) 2) Lockdown of western Shanghai (2022/04/01)	https://mp.weixin.qq.com/s/Ufza89hhBGZsiGPTHoC5aQ	-	-

Figure S1. Disease burden of COVID-19 caused by Omicron BA.2 variant in Hong Kong, China
The number represents the median estimates, and the error bar represents the 95% confidence interval.

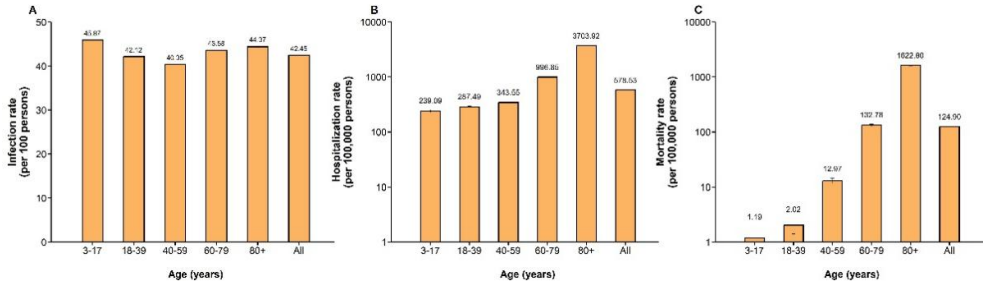


Figure S2. Clinical severity of COVID-19 caused by Omicron BA.2 variant in Hong Kong, China
The number represents the median estimates, and the error bar represents the 95% confidence interval.

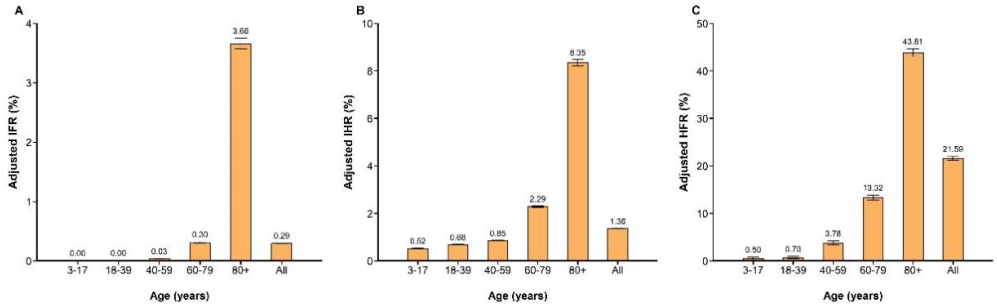


Figure S3. Sensitivity analysis of disease burden and clinical severity by adjusting ascertainment rate
The number represents the median estimates, and the error bar represents the 95% confidence interval. The sensitivity analysis was based on the range of the overall ascertainment ratio of COVID-19 infections. (A-C) The adjustment of ascertainment rates to the upper limit of the confidence interval. (D-E) The adjustment of ascertainment rates to the lower limit of the confidence interval.

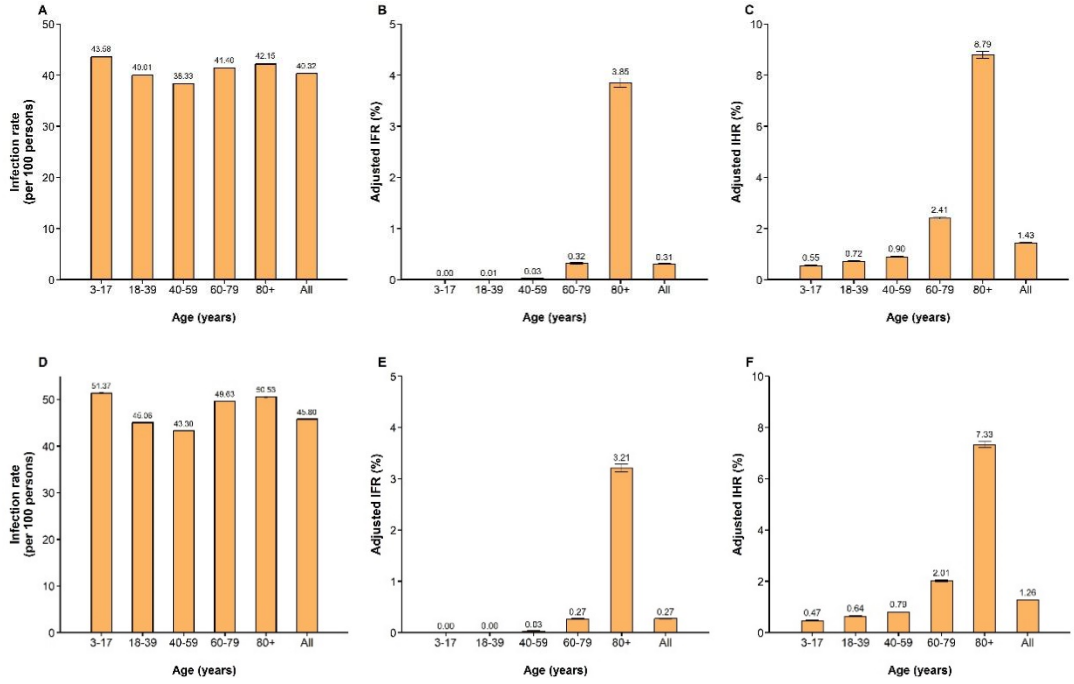


Figure S4. Correlation coefficient of explanatory variables

The correlation coefficient between pairwise predictors was calculated. Correlation heat maps are sorted according to the results of hierarchical clustering. The number represents the value and direction of the correlation coefficient of the two variables in the corresponding row and column, visualized in the form of a circle.

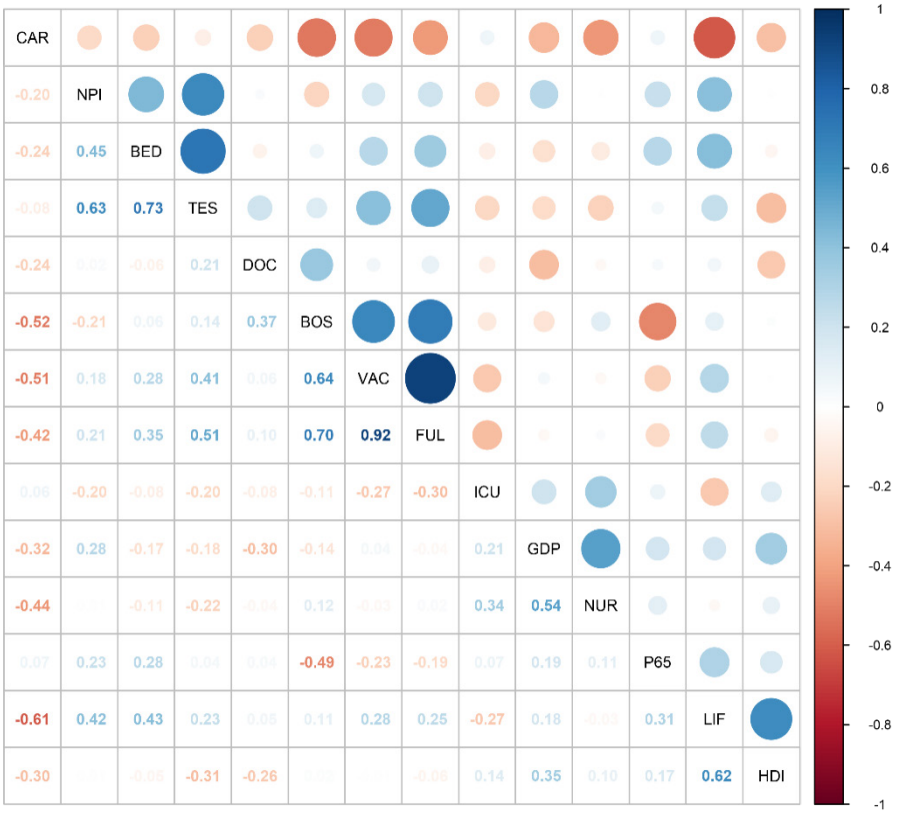


Figure S5. The SHAP values of variable importance by XGBoost model
In the SHAP summary plot, each row represents a feature and the horizontal coordinate is the SHAP value. The bar chart on the left shows the importance ranking of the variables based on the total average SHAP value, while the beeswarm chart on the right shows the SHAP value for each feature of each sample, with a dot representing a sample and color representing the feature value (yellow for high value, purple for low value).

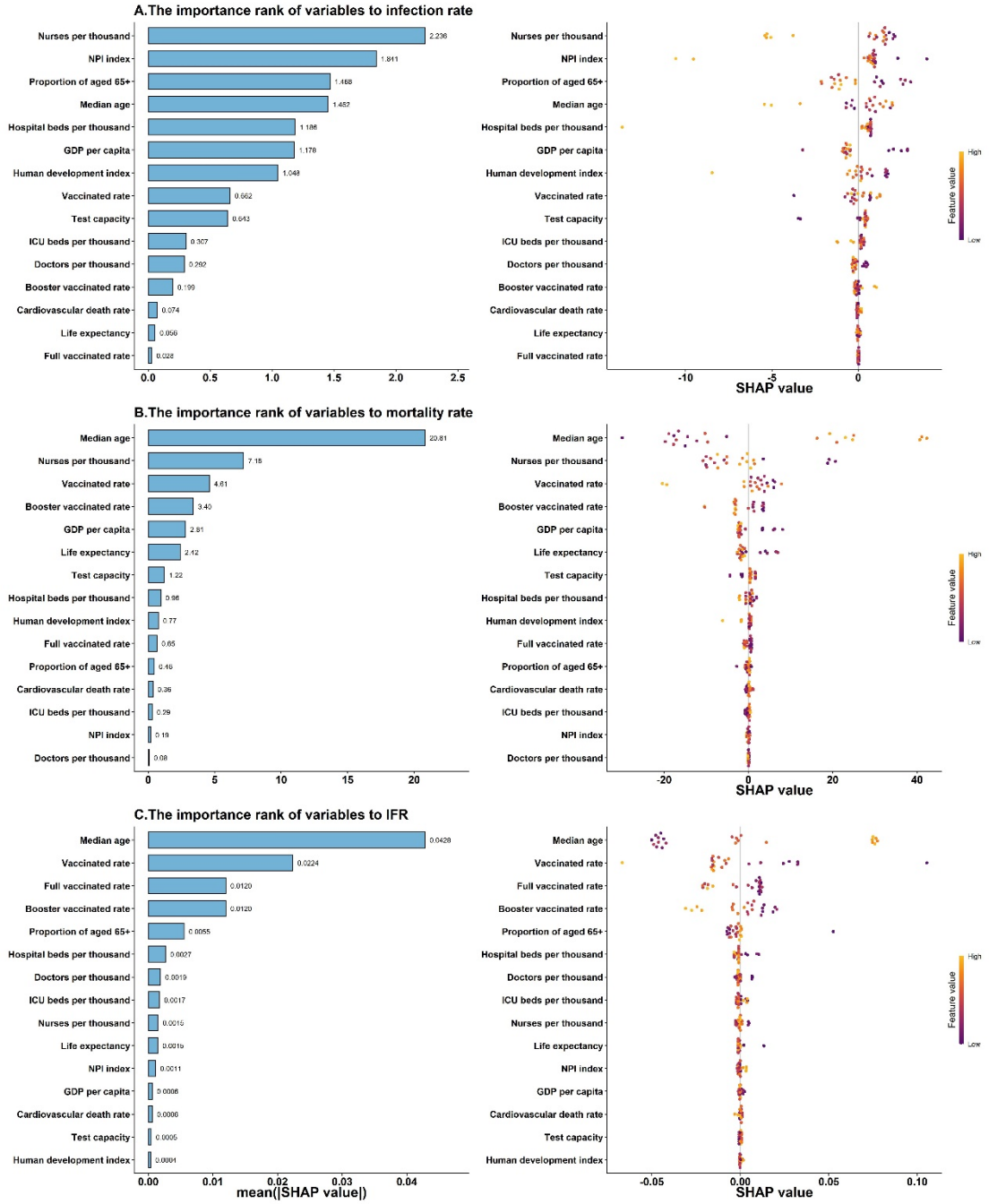
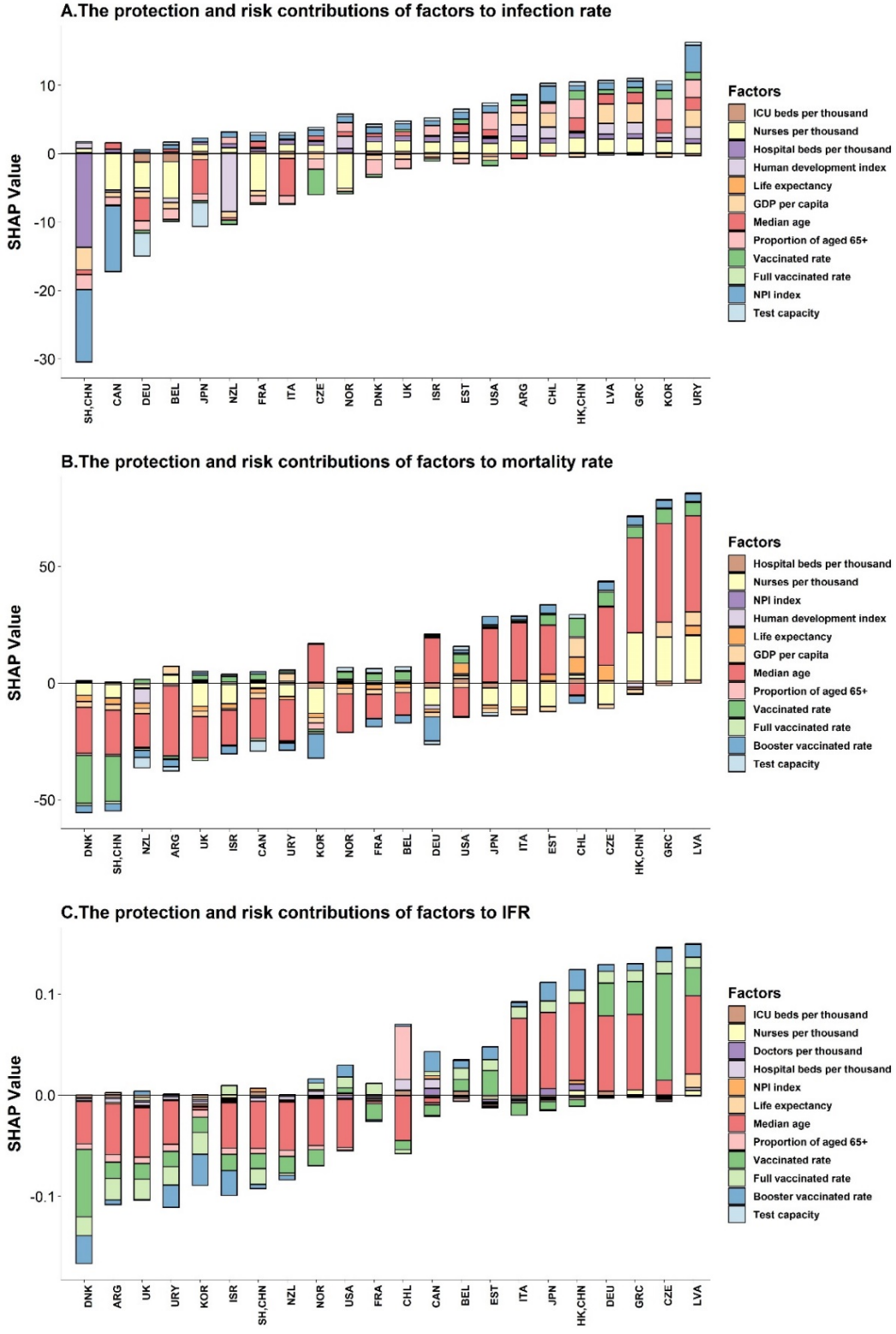


Figure S6. The protection and risk contributions of factors to the clinical severity and disease burden by XGBoost model

In the bar chart, countries/cities are roughly ranked according to disease burden or clinical severity, with the value increasing from left to right. The SHAP values reflected the importance of each factor for each country/city. The SHAP values above 0 are considered risk contributions, and those below 0 as protective contributions to clinical severity and disease burden.



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