CHINA CDC WEEKLY

CCDCweekly

中 国 疾 病 预 防 控 制 中 心 周 报

CHINA DAILY

Because of the large population, unbalanced regional development, and insufficient total medical resources, China will face the risk of serious runs of medical and health resources if the "lying flat" strategy is adopted.

China CDC Weekly

COVID-19 ISSUE (26)

CHINESE CENTER FOR DISEASE CONTROL AND PREVENTION

Preplanned Studies

Preliminary Study of the Protectiveness of Vaccination Against the COVID-19 in the Outbreak of VOC Omicron BA.2 — Jilin City, Jilin Province, China, March 3–April 12, 2022

Xuebin Fan[1,&]; Shan Lu[2,&]; Lu Bai[1]; Haican Liu[2]; Junshao Fu[1]; Xiaoxun Jin[1]; Yulong He[3]; Jinxing Lu[2]; Xiaoping Dong[4,5,6,7,#]

Summary

What is already known about this topic?

An outbreak of coronavirus disease 2019 (COVID-19) of Omicron BA.2 emerged in Jilin City since March 3, 2022, which involved in 27,036 cases by April 12. The vaccination program with inactivated COVID-19 vaccines has been implemented since the beginning of 2021.

What is added by this report?

The incidences of moderate, severe, and critical cases in the whole population of the group of 0+1 dose were 1.82-, 9.49-, and 3.85-fold higher than those in the group of 2 doses, and 5.03-, 44.47-, and ∞-fold higher than those received 3 doses vaccination. For the population ≥60 years, the incidences of moderate, severe, and critical cases in the group of 0+1 dose were 29.92, 9.62, and 4.27 per 100,000, showing 4.13-, 43.72-, and 4.85-fold higher than 2 doses, as well as 13.28-, 22.37-, and ∞-fold higher than 3 doses.

What are the implications for public health practice?

The incidences of each type of COVID-19 in the population who were fully vaccinated or booster vaccinated in Jilin City were significantly lower than those who were unvaccinated and/or partially vaccinated. Booster vaccination with homologous inactivated vaccines induces stronger protectiveness for COVID-19 caused by variant of concern (VOC) Omicron.

An outbreak of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron BA.2 strain occurred in Jilin City, Jilin Province, China. By April 12, a total of 27,036 cases had been diagnosed by the reverse transcription-polymerase chain reaction (RT-PCR) as SARS-CoV-2 and reported via the internet-based national direct reporting system for infectious disease. The clinical severity of those cases was typed according to the Diagnosis and Treatment Protocol for COVID-19 Patient (9th edition) issued by the National Health Commission (NHC) (1). Among them, 13,164 cases were asymptomatic, 13,629 were mild, 196 were moderate, 32 were severe, and 13 were critical. A total of 241 cases were diagnosed as COVID-19, accounting for 0.89% of all COVID-19 cases. There were 2 fatal SARS-CoV-2 positive cases reported who died from other diseases. The SARS-CoV-2 Omicron BA.2 strain shows a great impact on transmission and immunity globally. Numerous studies have revealed that the vaccine effectiveness on COVID-19 transmission of Omicron strains is markedly reduced, regardless of the types of vaccines (2–5). In this report, the vaccine protectiveness on COVID-19 induced pneumonia and more severe clinical types of 241 cases in Jilin City were preliminarily analyzed.

Jilin City is the 2nd largest city in Jilin Province with a registered population of 3,623,713. Among them, 25.6% (915,090) were 60 years and/or older. The COVID-19 vaccination program has been implemented in Jilin City since the beginning of 2021. All people were vaccinated with domestic inactivated vaccines. By March 3, the coverages of COVID-19 full (2 doses) and booster (3 doses) vaccination in the general population were 81.1% (2,937,342) and 32.1% (1,163,069), while those in the population ≥60 years were 79.5% (727,950) and 29.8% (272,943), respectively. In addition, there were 68,347 people who received 1 dose vaccine but had not finished the full vaccination by March 3.

The general population, the population ≥60 years, and <60 years in Jilin City was divided into 3 groups, unvaccinated plus received 1 dose (0+1 dose), full vaccination (2 doses), and booster vaccination (3 doses). More COVID-19 cases distributed in the group of 0+1 dose (n=121) than that of 2 doses (n=90) and 3 doses (n=30). Among them, 2 moderate cases and 1 severe case received only 1 dose of the vaccine. The distribution of the clinical severity in the different

groups of ages and vaccinations was summarized in Table 1. In general population, higher ratios of severe (21.5%) and critical (7.4%) cases were in the group of 0+1 dose, whilst lower ratios were in the groups of 2 doses (5.6% of severe and 4.4% of critical) and 3 doses (3.3% of severe and 0% of critical). Among those 241 cases, 127 cases were at ages of ≥60 years and 117 were <60 years. Markedly more numbers and higher ratios of critical cases were in the group of ≥60 years. Only 1 case <60 years displayed a critical phenotype and did not receive vaccination. There were no critical cases in the group of <60 years who received 2 doses of vaccination, and no severe or critical cases who received 3 doses.

The incidences (1/100,000) of COVID-19 in different vaccination groups were further calculated. For the general population in Jilin City, the incidences of moderate, severe, and critical cases in the group of 0+1 dose were 12.53, 4.08, and 1.31 per 100,000, respectively, which were 1.82-, 9.49-, and 3.85-fold higher than those in the group of 2 doses, and 5.03- and 44.47-fold higher than the moderate and severe cases that received 3 doses of vaccination (Figure 1A). For the population ≥60 years, the incidences of moderate, severe, and critical cases in the group of 0+1 dose were 29.92, 9.62, and 4.27 per 100,000, respectively, which were remarkably higher than that of the general population. The incidences of moderate, severe, and critical cases in the group of 0+1 dose were 4.13-, 43.72-, and 4.85-fold higher than those in the group of 2 doses, 13.28- and 22.37-fold higher than moderate and severe ones in the group of 3 doses, respectively (Figure 1B). Contrarily, the incidence of COVID-19 in the population <60 years of 0+1 dose group was lower, showing 9.82-, 1.60, and 0.20 per 100,000 in moderate, severe, and critical phenotypes, respectively. There were no critical cases in the group of 2 doses and no severe and critical cases in that of 3 doses. The incidences of moderate and severe disease of 0+1 group were 3.70- and 4.85-fold higher than that of patients receiving 2 doses, while the incidence of moderate cases was 3.81-fold higher than that receiving 3 doses (Figure 1C). The incidence of each type of

COVID-19 in the population who were fully vaccinated or booster vaccinated in Jilin City is significantly lower than those who were unvaccinated and/or partially vaccinated. Booster vaccination induces stronger protectiveness for COVID-19 both in the population ≥60 years and <60 years.

DISCUSSION

As a variant of concern (VOC), SARS-CoV-2 Omicron BA.2 strain attracted great attention worldwide since it emerged in South Africa at the end of 2021, due to numerous amino acid substitutions in the region of the viral spite protein (6–7). Great impact on immunity, particularly on vaccine effectiveness in disease transmission, has been already addressed, regardless of the types of available COVID-19 vaccines (8–11). In line with another study (8), the preliminary data in the Omicron BA.2 strain-associated outbreak in Jilin City here have again verified the protectiveness of vaccination with inactivated vaccine against COVID-19, especially the severe and critical phenotypes. Such protectiveness is notable in the population ≥60 years.

Booster vaccination of COVID-19 vaccine has been implemented since the emergence of VOC Delta in the middle of 2021 and remarkably accelerated since the emergence of VOC Omicron globally. Heterologous vaccination of different types of vaccine has shown the advantage in the titers of serum neutralizing antibody and in the vaccine effectiveness against disease transmission and symptomatic disease in the real world. However, homologous vaccination has also revealed reliable vaccine effectiveness against COVID-19 (5,12–13). Similar to many areas in China, the inactivated vaccines manufactured by domestic pharmaceutical companies, mainly Sinovac and Sinopharm COVID-19 vaccine (Vero cell) inactivated, were predominantly used in Jilin City. It needs to be emphasized that all booster vaccinations in Jilin City were homologous vaccination with inactivated vaccine. The data in this report reveals the special significance in China and other countries with predominant usage of inactivated vaccine, that booster vaccination with

TABLE 1. The distribution of clinical severity phenotypes in different vaccination groups.

Age (years)	0+1 dose			2 doses			3 doses			Total (n)
	Moderate	Severe	Critical	Moderate	Severe	Critical	Moderate	Severe	Critical	
≥60	56 (68.3%)	18 (22.0%)	8 (9.8%)	33 (86.8%)	1 (2.6%)	4 (10.5%)	6 (85.7%)	1 (14.3%)	0 (0%)	127
<60	30 (76.9%)	8 (20.5%)	1 (2.6%)	48 (92.3%)	4 (7.6%)	0 (0%)	23 (100%)	0 (0%)	0 (0%)	114
Total	86 (71.7%)	26 (21.5%)	9 (7.4%)	81 (90.0%)	5 (5.6%)	4 (4.4%)	29 (96.7%)	1 (3.3%)	0 (0%)	241

A

B

C
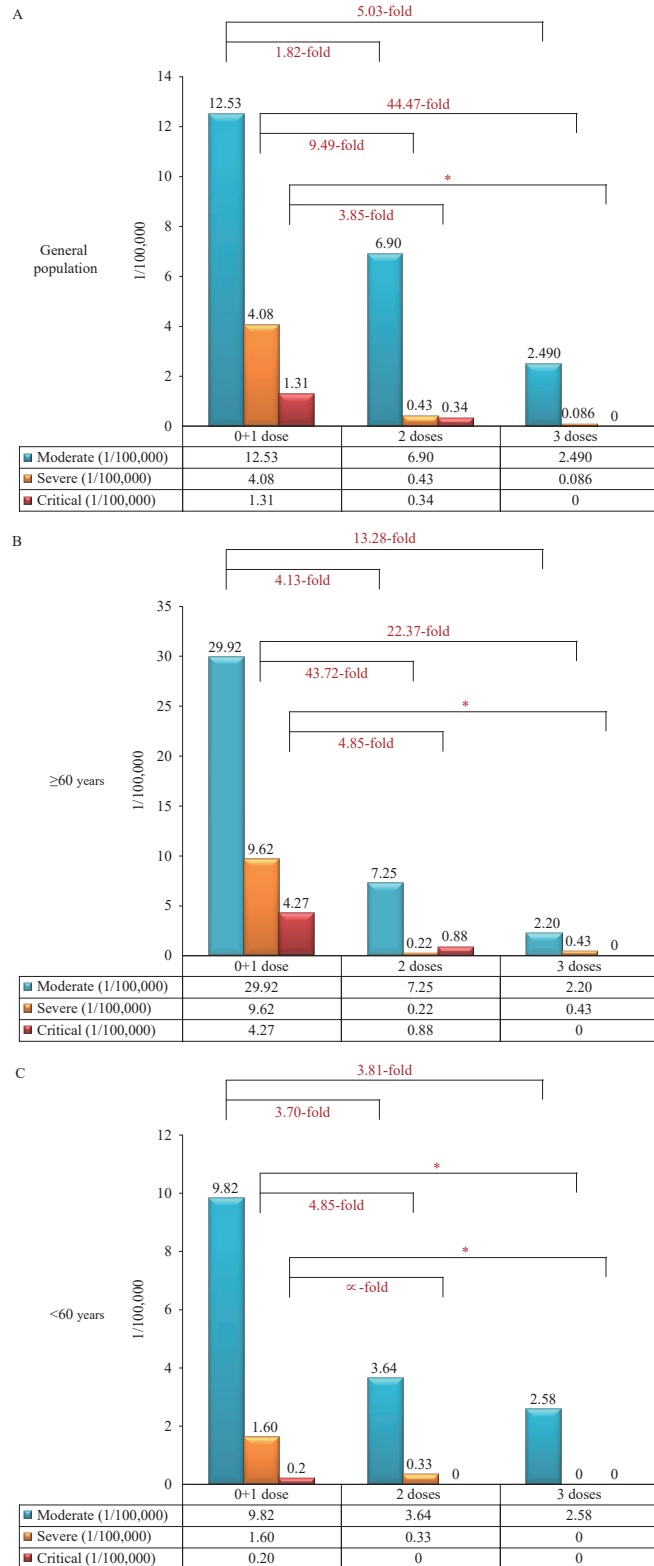
FIGURE 1. The incidences of COVID-19 in the groups of unvaccinated and partially vaccinated (0+1 dose), fully vaccinated (2 doses), and booster vaccinated (3 doses). (A) In the whole population; (B) the population ≥60 years; (C) the population <60 years.
Note: the X-fold changes in the incidence between groups are indicated.
Abbreviation: COVID-19=coronavirus disease 2019.
* Uncalculatable as there are no cases in the group to be compared.

homologous inactivated vaccine can produce reliable protectiveness to COVID-19 caused by VOC Omicron.

Although the exact effectiveness of inactivated COVID-19 vaccines against transmission, asymptomatic, and mild COVID-19 of VOC Omicron BA.2 in Jilin City is still unexplored, preliminary protective data to COVID-19 here is strong enough to indicate the public significance of the strategy of full and booster vaccination, particularly for the elderly population who has markedly higher risk of having critical and fatal outcomes. Variation of SARS-CoV-2 seems to be inevitable and the impact of newly emerged variants on transmission, immunity, and severity is also unpredictable. Booster vaccination, either homologous or heterologous, probably repeatedly, may be one of the limited specific interventions for relief of the impact of COVID-19 in the future.

This study was subject to some limitations. The preliminary real-world analysis here was a straightforward comparison of incidences of the 3 outcomes of COVID-19 during the outbreak in Jilin City from March 3 to April 12 by vaccination status. The analyses did not control for potential confounding variables, such as the presence of comorbidities and the time since vaccination, although the stratification by age group did provide some ability to control for subject age. Moreover, different antiviral medications, e.g., anti-serum from convalescent patients, antiviral monoclonal antibody, and the antiviral Paxlovid, were applied in clinical settings, which might affect the final outcomes. Further collection and analysis of the relevant data potentially affecting the vaccine effectiveness of those patients are deserved.

Corresponding author: Xiaoping Dong, dongxp238@sina.com.

¹ Jilin Municipal Center for Disease Control and Prevention, Jilin City, Jilin Province, China; ² State Key Laboratory for Infectious Disease Prevention and Control, National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China; ³ Tongliao Municipal Center for Disease Control and Prevention, Tongliao City, Inner Mongolia Autonomous Region, China; ⁴ State Key Laboratory for Infectious Disease Prevention and Control, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases (Zhejiang University), National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China; ⁵ Center for Biosafety Mega-Science, Chinese Academy of Sciences, Wuhan City, Hubei Province, China; ⁶ China Academy of Chinese Medical Sciences, Beijing, China; ⁷ Shanghai Institute of Infectious Disease and Biosafety, Shanghai, China.
& Joint first authors.

REFERENCES

1. National Health Commission of the People's Repbulic of China. The diagnosis and treatment protocol for COVID-19 patient (the 9th Edition, in Chinese). 2022. http://www.nhc.gov.cn/yzygj/s7653p/202203/b74ade1ba4494583805a3d2e40093d88/files/ef09aa4070244620b010951b088b8a27.pdf. (In Chinese). [2022-4-17].

2. Altarawneh HN, Chemaitelly H, Hasan MR, Ayoub HH, Qassim S, AlMukdad S, et al. Protection against the omicron variant from previous SARS-CoV-2 infection. N Engl J Med 2022;386(13):1288 – 90. http://dx.doi.org/10.1056/NEJMc2200133.

3. Suryawanshi RK, Chen IP, Ma TC, Syed AM, Brazer N, Saldhi P, et al. Limited cross-variant immunity after infection with the SARS-CoV-2 omicron variant without vaccination. medRxiv 2022. http://dx.doi.org/10.1101/2022.01.13.22269243.

4. Smith DJ, Hakim AJ, Leung GM, Xu WB, Schluter WW, Novak RT, et al. COVID-19 mortality and vaccine coverage - Hong Kong special administrative region, China, January 6, 2022-March 21, 2022. MMWR Morb Mortal Wkly Rep 2022;71(15):545 – 8. http://dx.doi.org/10.15585/mmwr.mm7115e1.

5. Magen O, Waxman JG, Makov-Assif M, Vered R, Dicker D, Hernán MA, et al. Fourth dose of BNT162b2 mRNA COVID-19 vaccine in a nationwide setting. N Engl J Med 2022. http://dx.doi.org/10.1056/NEJMoa2201688.

6. European Centre for Disease Prevention and Control. SARS-CoV-2 variants of concern as of 7 April 2022. https://www.ecdc.europa.eu/en/COVID-19/variants-concern. [2022-4-17].

7. Kawaoka Y, Uraki R, Kiso M, Iida S, Imai M, Takashita E, et al. Characterization and antiviral susceptibility of SARS-CoV-2 Omicron/BA.2. Res Sq 2022. http://dx.doi.org/10.21203/rs.3.rs-1375091/v1.

8. Plumb ID, Feldstein LR, Barkley E, Posner AB, Bregman HS, Hagen MB, et al. Effectiveness of COVID-19 mRNA vaccination in preventing COVID-19-associated hospitalization among adults with previous SARS-CoV-2 Infection - United States, June 2021-February 2022. MMWR Morb Mortal Wkly Rep 2022;71(15):549 – 55. http://dx.doi.org/10.15585/mmwr.mm7115e2.

9. Temsah MH, Aljamaan F, Alenezi S, Alhasan K, Alrabiaah A, Assiri R, et al. SARS-CoV-2 omicron variant: exploring healthcare workers' awareness and perception of vaccine effectiveness: a national survey during the first week of WHO variant alert. Front Public Health 2022;10:878159. http://dx.doi.org/10.3389/fpubh.2022.878159.

10. Lusvarghi S, Pollett SD, Neerukonda SN, Wang W, Wang R, Vassell R, et al. SARS-CoV-2 BA variant is neutralized by vaccine booster-elicited serum, but evades most convalescent serum and therapeutic antibodies.. 1 Sci Transl Med 2022eabn8543. http://dx.doi.org/10.1126/scitranslmed.abn8543.

11. Rajpal VR, Sharma S, Kumar A, Chand S, Joshi L, Chandra A, et al. 'Is Omicron mild'? Testing this narrative with the mutational landscape of its three lineages and response to existing vaccines and therapeutic antibodies. J Med Virol 2022. http://dx.doi.org/10.1002/jmv.27749.

12. Natarajan K, Prasad N, Dascomb K, Irving SA, Yang DH, Gaglani M, et al. Effectiveness of homologous and heterologous COVID-19 booster doses following 1 Ad.26.COV2.S (Janssen [Johnson & Johnson]) vaccine dose against COVID-19-associated emergency department and urgent care encounters and hospitalizations among adults - VISION network, 10 States, December 2021-March 2022. MMWR Morb Mortal Wkly Rep 2022;71(13):495-502. http://dx.doi.org/10.15585/mmwr.mm7113e2.

13. Glatman-Freedman A, Bromberg M, Hershkovitz Y, Sefty H, Kaufman Z, Dichtiar R, et al. Effectiveness of BNT162b2 vaccine booster against SARS-CoV-2 infection and breakthrough complications, israel. Emerg Infect Dis 2022;28(5):948 – 56. http://dx.doi.org/10.3201/eid2805.220141.

SARS-CoV-2 Omicron Variant is Expected to Retain Most of the Spike Protein Specific Dominant T-Cell Epitopes Presented by COVID-19 Vaccines — Worldwide, 2021

Jiajing Jiang[1]; Yingying Du[1,#]; Tao Peng[2,#]

Summary

What is already known about this topic?

The newly emerged variant of Omicron, which carries many of the mutations found in other variants of concern (VOCs), as well as a great number of new mutations that may enhance its immune escape, has spread rapidly around the world. This has raised public concern about the effectiveness of the current coronavirus disease 2019 (COVID-19) vaccine.

What is added by this report?

In this study, different bioinformatic softwares were applied to predict the dominant Omicron spike (S) protein cytotoxic T lymphocyte (CTL) and T helper (Th) epitopes in representative world population and Chinese population. Compared to the original severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) S protein, limited mutations were identified within the dominant CTL and Th epitopes in Omicron variant.

What are the implications for public health practice?

The results of this study suggested that the current COVID-19 vaccine-induced T-cell immunity may still provide significant protection against Omicron variant infection in fully vaccinated individuals.

The World Health Organization (WHO) categorized the new B.1.1.529 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant (Omicron) as a variant of concern (VOC) on November 26, 2021. Since then, this newly emerged variant has placed the world on high alert. Compared to other VOCs, Omicron has an unusual constellation of mutations. It contains over 50 mutations in various locations of its genome. In the spike protein gene, Omicron has over 30 mutations, doubling the number associated with the Delta variant. In the receptor binding domain (RBD) alone, Omicron has over 10 mutations while Delta only has 2. Many of these mutations have been shown to enhance the interaction between the viral spike and the cellular receptor angiotensin-converting enzyme 2 (ACE2). Based on this observation, it is predicted that the Omicron variant could be highly contagious.

In general, a vaccine provides two arms of immune protection. On one hand, the vaccine results in the production of neutralizing antibodies (NAbs) by B cells. These NAbs bind to the spike protein of the virus and inhibit its ability to infect the host cells. For previously immunized people, the memory humoral immune response is the first line of defense against Omicron infection. Unfortunately, Omicron variant carries many mutations on the spike protein that neutralizing antibodies recognize, reducing vaccinated individuals' immunity to this variant. The human body's second line of defense is heavily reliant on the human leukocyte antigen (HLA)-restricted T-cell response mechanism, in which viral epitopes are presented by dendritic cells to CD8+ T lymphocytes through interactions with HLA class I alleles and CD4+ T lymphocytes through HLA class II alleles. Viral epitope presentation by HLA class I leads to clonal expansion of HLA-restricted CD8+ cytotoxic T lymphocytes (CTLs), which are primed to perform antiviral defense during acute infection. Subsequently, reinfection of the virus is controlled by memory CTLs. The recognition of viral epitope-HLA class II complexes by CD4+ T cell enhances cell-mediated immune response by inducing cytokines and facilitates antibody production by activating B cells. The urgent question right now is how many of the memory CTLs and T helper (Th) epitopes remain in the heavily mutated Omicron variant.

T-cell epitopes were predicted in this paper using IEDB recommended 2020.09 and SYFPEITHI for major histocompatibility complex Class I (MHC Class I), and IEDB recommended 2.22 and Propred for MHC Class II, before real-world data were available to answer this question.

Wuhan-Hu-1 (NCBI Reference Sequence: YP_009724390.1) was obtained from the GenBank database of the National Center for Biotechnology Information (https://www.ncbi.nlm.nih.gov/). EPI ISL:EPI_ISL_6640916 sequence (Omicron) was obtained from the GISAID database (https://www.gisaid.org/).

IEDB recommended 2020.09 (NetMHCpan 4.1EL) (http://tools.immuneepitope.org/mhci/, National Institute of Allergy and Infectious Diseases, USA) and SYFPEITHI (http://www.syfpeithi.de/, BMI Biomedical Informatics, Heidelberg, Germany) were used to predict HLA-A*02:01, HLA-A*11:01 restricted epitopes. NetMHCpan4.1 based on artificial neural network (ANN) applied binding affinity (BA) and mass spectrometry (MS) eluted ligands (EL) data as a model to analyze the affinity between target peptides and their ligands (MHC). This algorithm not only integrates affinity data and mass spectrometry eluted ligand data, but also covers information in the process of antigen processing and presentation (1–2). The smaller the value, the higher the prediction score of the corresponding random natural peptide. SYFPEITHI is based on the motif matrix algorithm (3), according to the natural ligands, T-cell epitopes, or the frequency of amino acids in the binding peptides to predict the target peptides. The anchors and their auxiliary anchors that appear frequently get higher scores in the prediction results. The higher the score, the greater the possibility that the peptide will become an antigenic peptide.

IEDB recommended 2.22 (http://tools.immuneepitope.org/mhcii/, National Institute of Allergy and Infectious Diseases, USA) and Propred (http://www.imtech.res.in/raghava/propred/, Department of Computational Biology, Indraprastha Institute of Information Technology, New Delhi, India) were used to predict HLA-DRB1*01:01 and HLA-DRB1*15:01 restricted epitopes. IEDB recommended 2.22 apply Consensus combined with Combinatorial library (4), SMM-align (5), NN-align (6) to analyze the target peptides and combine their predicted values to obtain more accurate results. Propred based on an algorithm called quantitative affinity matrix (QAM) predicted the score of the sequence by comparing the degree of match between the target sequence and the binding pocket of HLA (7).

In this study, we analyzed 4 representative HLA alleles (including HLA-A*02:01, HLA-A*11:01, HLA-DRB1*01:01, and HLA-DRB*15:01) restricted peptides among which HLA-A*02:01 and HLA-

DRB1*01:01 represented the dominant HLA alleles in the world population, HLA-A*11:01 and HLA-DRB*15:01 represent the dominant HLA alleles in the Chinese population (8–9). Various bio-information software was used to predict the HLA restricted CTL or Th epitopes, and the top ten dominant epitopes were finally screened. The comparison between Wuhan-Hu-1 and Omicron was performed.

There were 17 dominant HLA-A*02:01 restricted CTL epitopes (ranking in the top 10) derived from spike (S) protein of Wuhan-Hu-1, among which 2 epitopes mutated in Omicron variant (Table 1). These mutations in Omicron variant exhibited minor decline in epitope rank and may slightly impair corresponding CTL response in viral clearance. However, 15 dominant HLA-DRB1*01:01 restricted Th epitopes in S protein of Wuhan-Hu-1 (ranking in the top ten) remain consistent in Omicron (Table 1). These results indicate that dominant protective CTL and Th epitopes derived from original Wuhan-Hu-1 strain or vaccines constructed based on Wuhan-Hu-1 still provided good T cell protection for convalescents or vaccinated individuals, although limited mutations were found within dominant CTL epitopes in a large proportion of the world's population.

There were 12 dominant HLA-A*11:01-restricted CTL epitopes (ranking in the top 10) in the S protein of Wuhan-Hu-1, of which 3 epitopes mutated in Omicron variant (Table 2). Similarly, three of the top-ten dominant HLA-DRB1*15:01 restricted Th epitopes of Wuhan-Hu-1 strain S protein mutated in Omicron variant (Table 2). The mutations in the CTL epitopes may lead to a decrease in CTL against Omicron variant, while the mutated Th epitopes, may alter its capacity to promote T cell mediated immune response via cytokines and antibody generation via B cell activation, thus may have some impact on protective effect of vaccine against Omicron variant.

DISCUSSION

Since the WHO designated Omicron as a VOC, Omicron has caused concern for the world for its significant transmissibility and infectivity. Previously, Delta variant, also classified as VOC, had been spreading rapidly worldwide and causing serious outbreaks due to its high transmissibility, short incubation period, and high viral load (10). Reduced levels of neutralizing antibody in serum against the Delta variant in vaccinated people and patients who recovered from coronavirus disease 2019 (COVID-19)

TABLE 1. Comparison of HLA-A*02:01-restricted CTL epitopes and HLA-DRB1*01:01-restricted Th epitopes in Wuhan-Hu-1 S protein and Omicron S protein.

HLA-A*02:01 CTL epitopes derived from S Protein	Epitope rank in Wuhan-Hu-1[†]	Epitope mutation exist in Omicron	HLA-DRB1*01:01 Th Epitopes derived from S protein	Epitope rank in Wuhan-Hu-1[§]	Epitope mutation exist in Omicron
YLQPRTFLL	1	No	MFVFLVLLPLVSSQC	1	No
VLNDILSRL	1	L981F	FVFLVLLPLVSSQCV	1	No
TLDSKTQSL	2	No	VVLSFELLHAPATVC	2	No
KIADYNYKL	2	K417N	VLSFELLHAPATVCG	2	No
RLDKVEAEV	3	No	LSFELLHAPATVCGP	2	No
ALNTLVKQL	3	No	VVVLSFELLHAPATV	3	No
FIAGLIAIV	3	No	SFELLHAPATVCGPK	3	No
RLQSLQTYV	4	No	RVVVLSFELLHAPAT	4	No
NLNESLIDL	4	No	VFLVLLPLVSSQCVN	5	No
LLFNKVTLA	5	No	FELLHAPATVCGPKK	6	No
SIIAYTMSL	5	No	FLVLLPLVSSQCVNL	7	No
RLNEVAKNL	6	No	ITRFQTLLALHRSYL	8	No
VVFLHVTYV	7	No	TRFQTLLALHRSYLT	8	No
HLMSFPQSA	8	No	GWTFGAGAALQIPFA	9	No
GLTVLPPLL	8	No	SGWTFGAGAALQIPF	10	No
VLYENQKLI	9	No			
YQDVNCTEV	10	No			

Abbreviations: S=spike; HLA=human leukocyte antigen; CTL=cytotoxic T lymphocytes; Th=T helper.
[†] This rank is derived from the combined ranking of IEDB recommended 2020.09 and SYFPEITHI.
[§] This rank is derived from the combined ranking of IEDB recommended 2.22 and Propred.

TABLE 2. Comparison of HLA-A*11:01-restricted CTL epitopes and HLA-DRB1*15:01-restricted Th epitopes in Wuhan-Hu-1 S protein and Omicron S protein.

HLA-A*11:01 CTL epitopes derived from S protein	Epitope rank in Wuhan-Hu-1[†]	Epitope mutation exist in Omicron	HLA-DRB1*15:01 Th Epitopes derived from S protein	Epitope rank in Wuhan-Hu-1[§]	Epitope mutation exist in Omicron
SVLNDILSR	1	L981F	PTESIVRFPNITNLC	1	No
GVYFASTEK	2	T95I	CSNLLLQYGSFCTQL	2	No
ASANLAATK	2	No	QPTESIVRFPNITNL	2	No
VTYVPAQEK	3	No	TESIVRFPNITNLCP	2	No
SSTASALGK	4	No	SNLLLQYGSFCTQLN	3	N764K
TLKSFTVEK	5	No	ECSNLLLQYGSFCTQ	4	No
GTHWFVTQR	6	No	ESIVRFPNITNLCPF	4	No
NSASFSTFK	7	S371L/S373P/S375F	NLLLQYGSFCTQLNR	5	N764K
GVLTESNKK	8	No	TECSNLLLQYGSFCT	6	No
GVYYHKNNK	8	No	LLLQYGSFCTQLNRA	7	N764K
QIYKTPPIK	9	No	LTDEMIAQYTSALLA	8	No
EILPVSMTK	10	No	DEMIAQYTSALLAGT	9	No
			TDEMIAQYTSALLAG	10	No

Abbreviations: S=spike; HLA=human leukocyte antigen; CTL=cytotoxic T-lymphocytes; Th=T helper.
[†] This rank is derived from the combined ranking of IEDB recommended 2020.09 and SYFPEITHI.
[§] This rank is derived from the combined ranking of IEDB recommended 2.22 and Propred.

have also been reported to contribute to severe outbreaks.

Vaccines are the safest option to achieve herd protection during the SARS-CoV-2 pandemic. Overall, 43% of the global population has been fully vaccinated with COVID-19 vaccine so far. Although some populations had changes in the dominant T-cell epitopes due to Omicron mutation, based on the results from this analysis, more than 70% of the dominant epitopes were still retained. This result predicted that vaccine-induced T-cell immunity may still provide good protection when fully vaccinated individuals are exposed to the Omicron variant.

Some of the mutations in Omicron S protein that cause the changes of the dominant epitopes also exist in other VOCs (for example, T95I of Delta variant and K417N of Beta variant). Reduced recognition capacity of memory T cell to viral epitope-MHC complex due to the mutations may contribute to the immune escape of these variants. Thus, for the next generation of COVID-19 vaccine, the selection of cross-variant conserved T-cell epitopes should be included in the antigen design.

Despite the advancements in bioinformatics software for epitope prediction in recent years, predictions can still be inaccurate. We chose to target HLA-A*11:01/HLA-DRB*15:01 and HLA-A*02:01/HLA-DRB1*01:01 in this study, therefore the prediction results can only be instructive for these populations. The results of this study indicated that as the SARS-CoV-2 virus mutate, variation among T cell epitopes is limited in much of the world's population (representative alleles: HLA-A*02:01 and HLA-DRB1*01:01). Since the mutation rate is up to 23%–25%, mutations in T cell epitopes in the Chinese population (representative alleles: HLA-A*11:01 and HLA-DRB*15:01) should be noticed.

Corresponding authors: Yingying Du, yingyingdu@gzhmu.edu.cn; Tao Peng, pengtao@gibh.ac.cn.

¹ State Key Laboratory of Respiratory Disease, Sino-French Hoffmann Institute, College of Basic Medical Science, Guangzhou Medical University, Guangzhou, Guangdong, China; ² Guangdong South China Vaccine, Guangzhou, Guangdong, China.

REFERENCES

1. Reynisson B, Alvarez B, Paul S, Peters B, Nielsen M. NetMHCpan-4.1 and NetMHCIIpan-4.0: improved predictions of MHC antigen presentation by concurrent motif deconvolution and integration of MS MHC eluted ligand data. Nucleic Acids Res 2020;48(W1):W449 – 54. http://dx.doi.org/10.1093/nar/gkaa379.

2. Hoof I, Peters B, Sidney J, Pedersen LE, Sette A, Lund O, et al. NetMHCpan, a method for MHC class I binding prediction beyond humans. Immunogenetics 2009;61(1):1 – 13. http://dx.doi.org/10.1007/s00251-008-0341-z.

3. Rammensee HG, Bachmann J, Emmerich NPN, Bachor OA, Stevanović S. SYFPEITHI: database for MHC ligands and peptide motifs. Immunogenetics 1999;50(3 – 4):213 – 9. http://dx.doi.org/10.1007/s002510050595.

4. Sidney J, Assarsson E, Moore C, Ngo S, Pinilla C, Sette A, et al. Quantitative peptide binding motifs for 19 human and mouse MHC class I molecules derived using positional scanning combinatorial peptide libraries. Immunome Res 2008;4:2. http://dx.doi.org/10.1186/1745-7580-4-2.

5. Nielsen M, Lundegaard C, Lund O. Prediction of MHC class II binding affinity using SMM-align, a novel stabilization matrix alignment method. BMC Bioinformatics 2007;8:238. http://dx.doi.org/10.1186/1471-2105-8-238.

6. Nielsen M, Lund O. *NN-align*. An artificial neural network-based alignment algorithm for MHC class II peptide binding prediction. BMC Bioinformatics 2009;10:296. http://dx.doi.org/10.1186/1471-2105-10-296.

7. Singh H, Raghava GPS. ProPred: prediction of HLA-DR binding sites. Bioinformatics 2001;17(12):1236 – 7. http://dx.doi.org/10.1093/bioinformatics/17.12.1236.

8. Pajot A, Michel ML, Fazilleau N, Pancré V, Auriault C, Ojcius DM, et al. A mouse model of human adaptive immune functions: *HLA-A2.1-/HLA-DR1*-transgenic *H-2 class I-/class II*-knockout mice. Eur J Immunol 2004;34(11):3060 – 9. http://dx.doi.org/10.1002/eji.200425463.

9. He Y, Li J, Mao W, Zhang D, Liu M, Shan X, et al. HLA common and well-documented alleles in China. HLA 2018;92(4):199 – 205. http://dx.doi.org/10.1111/tan.13358.

10. Allen H, Vusirikala A, Flannagan J, Twohig KA, Zaidi A, Chudasama D, et al. Household transmission of COVID-19 cases associated with SARS-CoV-2 Delta variant (B.1.617.2): national case-control study. Lancet Reg Health Eur 2022;12:100252. http://dx.doi.org/10.1016/j.lanepe.2021.100252.

Preplanned Studies

Comparison of Omicron and Delta Variant Infection COVID-19 Cases — Guangdong Province, China, 2022

Ting Hu[1]; Meng Zhang[1]; Aiping Deng[1]; Yingtao Zhang[1]; Bosheng Li[1]; Yan Li[1]; Min Kang[1,2,#]

Summary

What is already known about this topic?

The Omicron variant has been listed as a variant of concern, but the characteristics still remain unclear.

What is added by this report?

The vaccinated proportion of 65 imported coronavirus disease 2019 cases that were infected with Omicron variant in this study was 89.23%, which was higher than Delta cases. Most imported cases infected with Omicron were tested positive using polymerase chain reaction after entering Guangdong within 3 days, a shorter period than Delta.

What are the implications for public health practice?

Under this observation, the international travelers infected with Omicron variant were detected positive earlier after entry than those infected with Delta variant. Breakthrough infections occurred in most Omicron cases in this study, but vaccination was still effective to reduce the incidence of severe illness. Omicron surveillance should be strengthened.

The Omicron variant was first identified in South Africa on November 9, 2021, and the World Health Organization (WHO) designated it as a variant of concern (VOC) on November 26, 2021, only 17 days passed (1). Due to the Omicron variant, the number of coronavirus disease 2019 (COVID-19) cases worldwide is growing rapidly. On December 13, 2021, Guangzhou City confirmed a Canada imported COVID-19 case, which was sequenced as Omicron (B.1.1.529) variant. Guangdong had reported a total of 65 imported COVID-19 cases infected with the Omicron variant (Omicron cases in brief) by second-generation sequencing as date of December 31, 2021. We selected 78 imported cases infected with the Delta variant (Delta cases in brief) reported in Guangdong from May to June, 2021, the first 2 months when Delta variant was discovered in Guangdong. These 78 Delta cases were compared with 65 Omicron cases. The results showed that 89.23% of Omicron cases

completed whole course of vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), higher than that of Delta cases. Overall, 92.19% imported Omicron cases tested SARS-CoV-2 nucleic acid positive after entering Guangdong within 3 days, which was earlier than Delta cases.

Information about these COVID-19 cases was collected by disease report cards and epidemiological investigation report in the China Information System for Disease Control and Prevention. Categorical variables were compared by chi-square test, continuous variables were compared by nonparametric test of Mann-Whitney U test. Data analysis was conducted by software IBM SPSS Statistics (version 25.0, IBM Corp, Chicago, USA). All statistical tests were 2-sided with α value at 0.05.

Among the 65 Omicron cases, 41 cases (63.08%) were male, 36.92% were female; 35.38% of Omicron cases were 21–30 years old, 21.54% were 31–40 years old, the mean age of Omicron cases was 34.2 years old, younger than Delta cases that had a mean age of 40.2 years old. Out of 65 Omicron cases, 56 cases were normal passengers, and 9 cases were flight crew members, of whom 8 were from Ethiopian Airlines and 1 was from Israel Airlines. However, no flight crew members were reported in the 78 Delta cases, as Table 1 shows. Also, 65 Omicron cases came from 16 countries, of which 29 cases (44.62%) came from America, followed by Ethiopia, Canada, and Democratic Republic of the Congo. Overall, 78 Delta cases came from 20 countries, of which 27 cases (34.62%) came from South Africa, followed by Saudi Arabia, India, and the United Arab Emirates (not listed in table).

As more people were vaccinated against SARS-CoV-2, the proportion of Omicron cases that were vaccinated was significantly higher than the Delta cases. Except 7 cases without history of vaccination against SARS-CoV-2, the other 58 cases (89.23%) all completed the whole course of vaccination, including 2 cases receiving 1 dose of Johnson & Johnson vaccine.

TABLE 1. Comparison between 65 imported cases infected with Omicron variant and 78 imported cases infected with Delta variant.

Variable	Cases infected with Omicron variant (%) (n=65)	Cases infected with Delta variant (%) (n=78)	Chi-square test	P value
Gender				
Male	41 (63.08)	62 (79.49)	4.74	0.029*
Female	24 (36.92)	16 (20.51)		
Age (years)				
1–10	4 (6.15)	2 (2.56)		
11–20	2 (3.08)	0 (0.00)		
21–30	23 (35.38)	12 (15.38)		
31–40	14 (21.54)	26 (33.33)	14.28	0.027*
41–50	13 (20.00)	26 (33.33)		
51–60	7 (10.77)	7 (8.97)		
61–70	2 (3.08)	5 (6.41)		
Type of traveler				
Passenger	56 (86.15)	71 (91.03)		
Flight crew	9 (13.85)	0 (0.00)	16.73	0.000*
Seaman	0 (0.00)	7 (8.97)		
Doses of coronavirus vaccine				
None	7 (10.77)	55 (70.51)		
1	2 (3.08)	0 (0.00)		
2	42 (64.62)	22 (28.21)	56.03	0.000*
3	11 (16.92)	1 (1.28)		
4	3 (4.62)	0 (0.00)		
Days from entry to SARS-CoV-2 nucleic acid positive[†]				
0–3	59 (92.19)	41 (52.56)		
4–7	5 (7.81)	32 (41.03)	26.82	0.000*
8–10	0 (0.00)	4 (5.13)		
11–14	0 (0.00)	1 (1.28)		
Ct values of SARS-CoV-2 nucleic acid[§]				
ORF1ab gene				
Median (Range)	25.0 (15.0–39.0)	27.0 (14.0–37.0)	−0.948	0.343
N gene				
Median (Range)	24.0 (14.0–38.0)	25.0 (12.0–35.0)	−0.851	0.395

Abbreviations: SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; Ct values=cycle threshold value; ORF1ab gene=open reading frame 1ab gene; N gene=nucleocapsid protein gene.
* $P<0.05$, the difference is statistically significant.
[†] An imported COVID-19 infected Omicron variant was considered infection during centralized quarantine in other province, so days from entry to test SARS-CoV-2 nucleic acid positive were not calculated.
[§] Using nonparametric test of Mann-Whitney U test, the statistic for P value was Z.

Further, 3 cases were vaccinated with 4 doses, and 11 cases were vaccinated with 3 doses. Among Delta cases, only 29.49% completed the whole course of vaccination, and 70.51% were never vaccinated. It seemed that breakthrough infection was more common in Omicron cases than Delta cases in this study.

Among 65 Omicron cases, 59 cases all tested positive for SARS-CoV-2 nucleic acid after entering Guangdong within 3 days, 5 cases within 4–7 days, except for 1 special case who was quarantined in another province for 14 days and tested positive for nucleic acid after returning to Guangdong where we considered he was likely infected during transition to centralized quarantine. As for Delta cases, 52.56%

were tested positive using polymerase chain reaction (PCR) after entering Guangdong within 3 days, 41.03% in 4–7 days, 5.13% in 8–10 days, and 1.28% in 14 days. The period from entry into Guangdong to testing positive among Omicron cases was much shorter than Delta cases. Therefore, we speculated that the incubation period of Omicron variant was shorter than the Delta variant.

We still compared the cycle threshold value (Ct value) of open reading frame 1ab (ORF1ab) gene and nucleocapsid protein (N) gene when cases were confirmed positive using PCR for the first time between two groups. For Omicron cases, the median Ct value of ORF1ab and N gene was 25.0 (with range of 15.0 to 39.0) and 24.0 (with a range of 14.0 to 38.0), respectively. For Delta cases, the median Ct value of ORF1ab and N gene was 27.0 (with a range of 14.0 to 37.0) and 25.0 (with a range of 12.0 to 35.0), respectively. The difference in Ct values between two groups was of no statistical significance. The results revealed the viral load of Omicron cases was not significantly higher than Delta cases.

We collected the most severe clinical states of 65 Omicron cases by following up to January 16, 2022. Among them, 11 cases were diagnosed as asymptomatic, 54 cases were diagnosed as patients where 25 were classified as ordinary cases, 29 were classified as mild cases, and no cases were deemed critical or severe. We also analyzed the symptoms among 65 cases (Figure 1). The most common symptom was coughing which occurred in 21 cases (32.31%), followed by pharyngoxerosis (29.23%), fever (26.15%), and throat pain (12.31%). Other

symptoms such as diarrhea, headaches, and stuffy or runny noses also occurred in some cases. The proportion with symptoms was lower than that of the local epidemic by SARS-CoV-2 Delta in Guangzhou, where 75% of cases had a fever and 74% of cases coughed (2).

According to the results, we should be on alert of local outbreaks caused by the Omicron variant. Guangdong had a local outbreak with 16 Omicron cases between January 13 and January 16, 2022, involving Zhuhai, Zhongshan, and Meizhou City. We roughly calculated the incubation period (time from exposure to date of illness onset or notification) among the 14 cases, except 2 cases who did not have clear dates of onset. The mean incubation period was 3.2 days, which was shorter than the 4.4 days of Delta variant in the former study (3).

DISCUSSION

Guangdong first found COVID-19 cases infected with Omicron variant on December 13, 2021, then the number of imported Omicron cases exceeded Delta cases in the same period. The in-process vaccination of the population may provide limited protection against infection due to the Omicron variant, but it was effective to reduce the incidence of severe illness.

According to the available evidence, the mean incubation period of Omicron variant was shorter than that of the Delta variant among both imported cases and local cases. The WHO also reported that the Omicron variant has a growth advantage with a
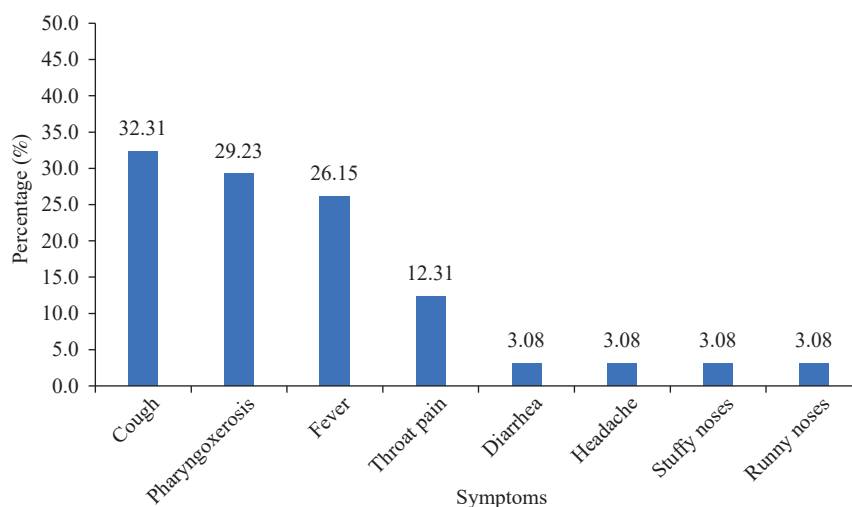

FIGURE 1. Symptoms among 65 COVID-19 cases infected with Omicron variant.
Abbreviation: COVID-19=coronavirus disease 2019.

doubling time of 2–3 days compared with the Delta variant (*4*), which may provide evidence that transmission capacity of the Omicron variant was stronger than Delta. On the other hand, breakthrough infection occurred in most Omicron cases in this study, this may be caused by high vaccination coverage in the whole population during Omicron epidemic. However, former study provided evidence that the Omicron mutations favored the escape of current vaccines than Delta (*5*). The result showed that personal protective measures, including wearing masks and maintaining social distance, should be taken even with complete vaccination against SARS-CoV-2. We also observed the symptoms caused by Omicron variant seemed to be relatively mild, the proportion of severe and critical cases was relatively low due to the contribution of vaccination (*6*). The viral load of hosts infected with Omicron variant was not statistically higher than that of Delta.

This study had two limitations. First, as of December 31, 2021, only 65 imported Omicron cases were reported in Guangdong Province, China. The limited cases may not show us a whole view of this novel variant. Second, this research was based on the field work of emergency responding, the designation and quality control were relatively limited. Further research is needed to obtain more evidence on characteristics of Omicron variant in future, including immune escape, transmission dynamics such as incubation period, the generation time, the serial interval, et al.

Our research reminds us that we need to beware of the rebound of local outbreak by Omicron variant. Travelers entering China should be in closed loop management. Considering most imported Omicron cases were found within 7 days after entry, we suggest shortening the quarantine period from 14 days to 7 days. We also should avoid transmission risk during centralized or home quarantine, especially aerosol transmission (*7–8*), which is relatively difficult to prevent. We should insist on nonpharmaceutical interventions, and Omicron surveillance should be strengthened to ensure early confirmation and treatment.

＃ Corresponding author: Min Kang, kangmin@yeah.net.

1 Guangdong Provincial Center for Disease Control and Prevention, Guangzhou City, Guangdong Province, China; 2 School of Public Health, Southern Medical University, Guangzhou City, Guangdong Province, China.

REFERENCES

1. World Health Organization. Weekly epidemiological update on COVID-19 - 30 November 2021. 2021. https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---30-november-2021. [2022-1-17].
2. Wang YP, Chen RC, Hu FY, Lan Y, Yang ZW, Zhan C, et al. Transmission, viral kinetics and clinical characteristics of the emergent SARS-CoV-2 Delta VOC in Guangzhou, China. EClinicalMedicine 2021;40:101129. http://dx.doi.org/10.1016/j.eclinm.2021.101129.
3. Zhang M, Xiao JP, Deng AP, Zhang YT, Zhuang YL, Hu T, et al. Transmission dynamics of an outbreak of the COVID-19 Delta variant B.1.617.2 - Guangdong province, China, May–June 2021. China CDC Wkly 2021;3(27):584 – 6. http://dx.doi.org/10.46234/ccdcw2021.148.
4. World Health Organization. Weekly epidemiological update on COVID-19 - 28 December 2021. 2021. https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---28-december-2021. [2022-1-17].
5. Chen JH, Wang R, Gilby NB, Wei GW. Omicron variant (B1.1.529): infectivity, vaccine breakthrough, and antibody resistance. J Chem Inf Model 2022;62(2):412 – 22. http://dx.doi.org/10.1021/acs.jcim.1c01451.
6. Abdullah F, Myers J, Basu D, Tintinger G, Ueckermann V, Mathebula M, et al. Decreased severity of disease during the first global Omicron variant COVID-19 outbreak in a large hospital in Tshwane, South Africa. Int J Infect Dis 2022;116:38 – 42. http://dx.doi.org/10.1016/j.ijid.2021.12.357.
7. Kang M, Wei JJ, Yuan J, Guo JX, Zhang YT, Hang J, et al. Probable evidence of fecal aerosol transmission of SARS-CoV-2 in a high-rise building. Ann Intern Med 2020;173(12):974 – 80. http://dx.doi.org/10.7326/M20-0928.
8. Wong SC, Au AKW, Chen H, Yuen LLH, Li X, Lung DC, et al. Transmission of Omicron (B1.1.529) - SARS-CoV-2 variant of concern in a designated quarantine hotel for travelers: a challenge of elimination strategy of COVID-19. Lancet Reg Health West Pac 2022;18:100360. http://dx.doi.org/10.1016/j.lanwpc.2021.100360.

Preplanned Studies

Change of Disease Spectrum Characteristics of Psychiatric Inpatients Before and After Lockdown Lifted During the COVID-19 Pandemic — Wuhan City, Hubei Province, China, 2021

Jingfang Liu[1]; Xuan Gong[1]; Xiaofen Li[1]; Zhiying Wan[1,#]; Hongqiang Sun[2,#]; Lijun Kang[1]; Zhongchun Liu[1]

Summary

What is already known about this topic?

The coronavirus disease 2019 (COVID-19) pandemic poses a significant threat to mental health globally and may change the proportion of hospitalized patients.

What is added by this report?

This report analyzed and compared the disease characteristics of psychiatric inpatients one year before and after Wuhan lifted lockdown during COVID-19. About 50% of the inpatients were diagnosed with bipolar disorder; females and adolescents had a higher prevalence of mental disorders.

What are the implications for public health practice?

More attention should be paid to the mental health of children, adolescents, and females.

In recent decades, the prevalence of mental disorders has increased in China and worldwide. The coronavirus disease 2019 (COVID-19) spread worldwide in less than 2 months from late December 2019. Numerous studies have shown that COVID-19 poses a significant threat to physical and mental health among the general population (1). Factors such as chronic stress and social isolation may increase the risk of emotional deterioration for some people (2), which may increase psychosis risk and proportion of inpatients. We conducted a retrospective cohort study of analyzing and comparing the disease characteristics of psychiatric inpatients 1 year before and after Wuhan lifted lockdown during COVID-19. The data were extracted from the information management system of the mental health center of the third-level hospital in Wuhan City, Hubei Province, China, from April 8, 2019 to April 9, 2021, which included gender, age, Wuhan residential registration (*hukou*), and disease diagnosis. Taking the date of lifting lockdown in Wuhan (April 8, 2020) as the cut-off point, the disease

characteristics of psychiatric inpatients before and after one year were compared. Results showed that nearly half of inpatients were diagnosed with bipolar disorder, and most tended to be younger and female. This study suggests that more attention should be paid to the mental health of females and adolescents, and it is necessary to conduct studies that are multicenter and have more extended observation periods.

On January 23, 2020, Wuhan was under lockdown to control the pandemic, significantly reducing access to services. Renmin Hospital of Wuhan University was appointed as a designated hospital for ordinary and severe COVID-19 patients. No new inpatients were admitted to other departments except emergency and fever clinics. With the effort of the whole society, Wuhan was lifted from lockdown on April 8, 2020 into the period of normalized epidemic prevention and control. All departments only began to receive new inpatients after strict disinfection. Therefore, in this study, April 8, 2020 was taken as the time node to compare the disease spectrum characteristics of psychiatric inpatients before and after one year and provide references for mental health assessment and prevention over the coming years.

This retrospective cohort analysis was conducted on patients with mental disorders hospitalized between April 8, 2019 and April 9, 2021 in the mental health center of the third-level hospital in Wuhan, Hubei, China. This period was divided into two phases. "Phase 1" (i.e., from April 8, 2019 to April 8, 2020) represents the period before Wuhan lifted the lockdown. "Phase 2" (i.e., from April 9, 2020 to April 9, 2021) was Wuhan's normalized epidemic prevention and control stage. Data from the electronic medical record in the information management system were used, which contained information on demographic characteristics (gender, age, Wuhan *hukou*) and disease diagnosis (somatoform disorders, bipolar disorder, sleep disorders, depressive disorder,

stress-related disorder, emotional and behavioral disorders in children and adolescents, anxiety disorder, schizophrenia spectrum disorder, psychoactive substances-induced mental disorders, organic mental disorder, obsessive-compulsive disorder, and other mental disorders). Qualified psychiatrists were responsible for defining and classifying the diagnosis according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) (3).

Continuous data were expressed as mean and standard deviation, categorical data regarding the number of patients (percentage). Continuous data were analyzed using the two-sample t-test. Differences between categorical data were evaluated using the Fisher's Exact test or the Pearson chi-squared test. Statistical analysis was performed using IBM SPSS Statistics for Windows (version 21.0, IBM Corp., Armonk, NY, USA). And $P<0.05$ was considered statistically significant.

Between April 8, 2019 and April 9, 2021, 10,863 inpatients were treated in the Department of Psychiatry at Renmin Hospital of Wuhan University. The total number of inpatients in Phase 1 and Phase 2 was 6,664 (61.3%), 4,199 (38.7%), respectively, with a 36.98% reduction in Phase 2 compared to Phase 1. Comparison of demographic characteristics between both phases: the prevalence of female inpatients in Phase 2 was higher than that in Phase 1 (61.1% *vs.* 55.9%; *P*<0.01); the average age in Phase 2 was younger than that in Phase 1 (33.52±16.52 *vs.* 34.55±16.10; *P*<0.01); the prevalence of inpatients with non-Wuhan *hukou* in Phase 2 was higher than that in Phase 1 (61.5% *vs.* 59.0%; *P*<0.05) (Supplementary Table S1, available in http://weekly. chinacdc.cn/).

The top 3 disease diagnoses in both phases were bipolar disorder (44.6% *vs.* 46.7%), schizophrenia spectrum disorder (19.7% *vs.* 16.9%), and depressive disorder (17.9% *vs.* 16.6%). The distribution of disease diagnosis among inpatients in the Phase 2 was compared with the Phase 1: the proportion of inpatients with bipolar disorder increased (46.7% *vs.* 44.6%, *P*<0.05); emotional and behavioral disorders in children and adolescents increased (3.4% *vs.* 1.6%; *P*<0.01); schizophrenia spectrum disorder decreased (16.9% *vs.* 19.7%; *P*<0.01) (Table 1). The disease

TABLE 1. Inpatients' disease diagnosis distribution in Phase 1 and Phase 2.

| Variety of disease	Phase 1 (n=6,664)	Phase 2 (n=4,199)	χ^2	*P*-value
Somatoform disorders				
Yes	84 (1.3%)	53 (1.3%)	0.00	0.994
No	6,580 (98.7%)	4,146 (98.7%)		
Bipolar disorder				
Yes	2,975 (44.6%)	1,959 (46.7%)	4.20	0.040
No	3,689 (55.4%)	2,240 (53.3%)		
Sleep Disorders				
Yes	59 (0.9%)	29 (0.7%)	1.22	0.270
No	6,605 (99.1%)	4,170 (99.3%)		
Depressive disorders				
Yes	1,196 (17.9%)	696 (16.6%)	3.37	0.066
No	5,468 (82.1%)	3,503 (83.4%)		
Stress-related disorder				
Yes	36 (0.5%)	15 (0.4%)	1.85	0.174
No	6,628 (99.5%)	4,184 (99.6%)		
Emotional and behavioral disorders in children and adolescents				
Yes	107 (1.6%)	144 (3.4%)	37.96	<0.001
No	6,557 (98.4%)	4,055 (96.6%)		
Anxiety disorders				
Yes	417 (6.3%)	298 (7.1%)	2.95	0.086
No	6,247 (93.7%)	3,901 (92.9%)		
Schizophrenia spectrum disorder				
Yes	1,315 (19.7%)	711 (16.9%)	13.31	<0.001
No	5,349 (80.3%)	3,488 (83.1%)		
Psychoactive substances-induced mental disorders				
Yes	46 (0.7%)	23 (0.5%)	0.83	0.363
No	6,618 (99.3%)	4,176 (99.5%)		
Organic mental disorder				
Yes	232 (3.5%)	169 (4.0%)	2.14	0.144
No	6,432 (96.5%)	4,030 (96.0%)		
Obsessive-compulsive disorder				
Yes	65 (1.0%)	37 (0.9%)	0.25	0.620
No	6,599 (99%)	4,162 (99.1%)		
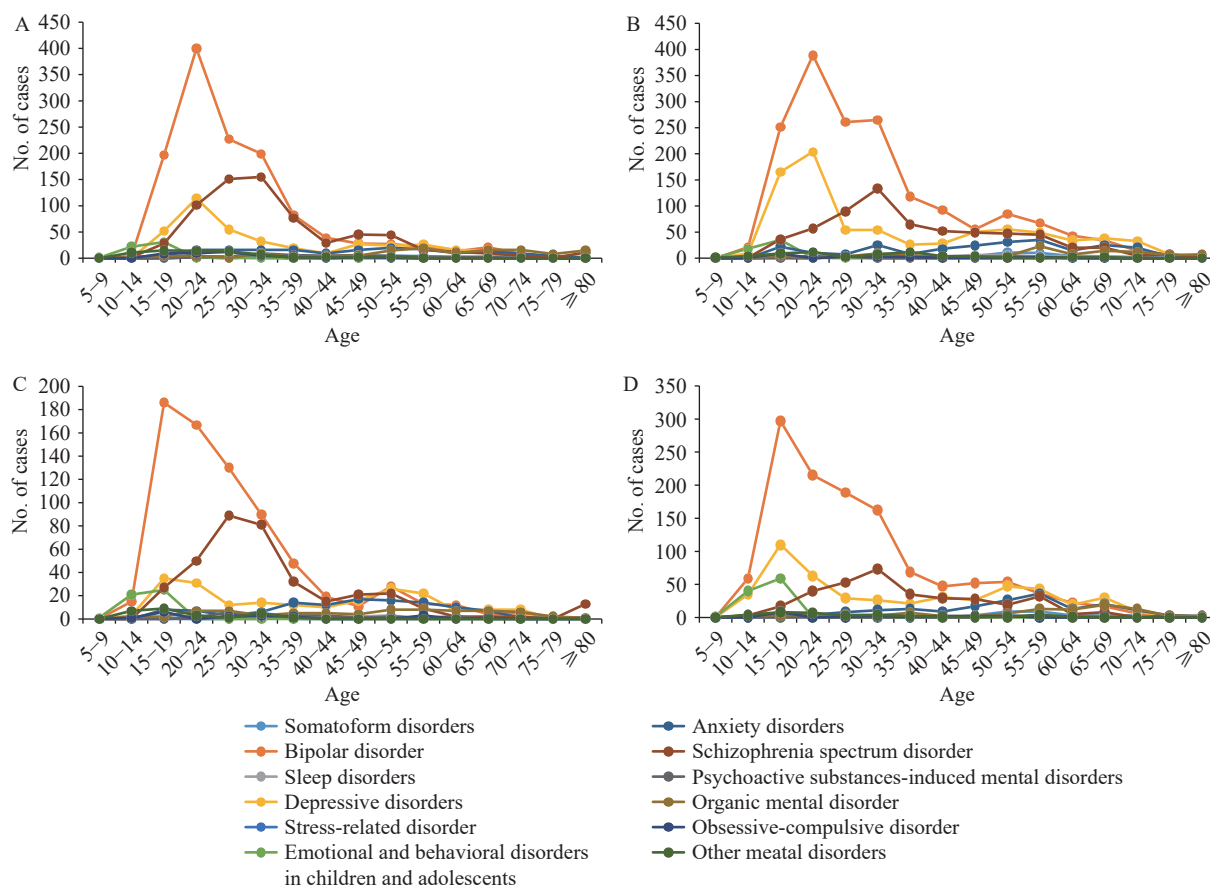
FIGURE 1. Disease distribution of inpatients by gender and age in Phase 1 and Phase 2. (A) Male in Phase 1; (B) Female in Phase 1; (C) Male in Phase 2; (D) Female in Phase 2.

diagnoses distribution by gender at different age groups in Phases 1 and 2 is shown in Figure 1. The disease distribution proportions of inpatients by gender in Phase 1 and Phase 2 are separately shown in Supplementary Figures S1–S2 (available in http://weekly.chinacdc.cn/). A detailed comparison of the two stages of disease diagnosis distribution among demographic characteristics is presented in Supplementary Table S2 (available in http://weekly.chinacdc.cn/).

DISCUSSION

The disease characteristics of psychiatric inpatients were changed after Wuhan lifted lockdown during the COVID-19 pandemic. This study showed that nearly half of the inpatients were diagnosed with bipolar disorder, and the overall average age tended to be younger.

Inpatients with mental disorders have significantly decreased since epidemic prevention and control were implemented. COVID-19 poses a tremendous challenge to healthcare systems around the world. When sporadic cases of the virus occurred in local areas, most medical procedures and related tests were highly restricted or more complex than before to reduce the risk of spreading the virus. Some patients with mental disorders in stable condition who preferred regular outpatient review or online consultation were not hospitalized for treatment until out of control (4). On the other hand, with the support of the state and government in recent decades, many local mental health institutions have been rapidly established to undertake the treatment and management of some patients with psychiatric disorders.

This study showed that the top three mental disorders were bipolar disorder, schizophrenia spectrum disorder, and depressive disorder. However, the prevalence of bipolar disorder has increased significantly, and females had a higher prevalence than males. The pathogenesis of bipolar disorder has been unknown and may be related to genetic, lifestyle, and environmental exposures (e.g., poor diet, physical

inactivity, and childhood trauma) (*5*). Most individuals with bipolar disorders are easily misdiagnosed or not accurately diagnosed until years later (*6*). Females had higher psychiatric disorders than the general population, which may be related to endocrine factors, such as polycystic ovary syndrome (*7*). More than 70% of individuals with bipolar disorders have been onset before 25-year-old (*8*). It is emphasized that early detection, timely diagnosis and treatment, and family and social support are the need for illness outcomes.

The prevalence of emotional and behavioral disorders in children and adolescents has increased significantly after the outbreak. Many schools and educational institutions changed teaching methods since the COVID-19 pandemic, and students began to study by home-based learning or online training. Peer activities and communication were hindered, and the unexpected situation changed their typical growth, learning, playing, and interacting. It impeded the growth and development of young human minds, especially the brain development of the youngest ones (*9*). Secondary school students faced more academic pressure from the entrance examination. Meanwhile, their parents also faced many challenges such as their work, family income, and children's education, increasing the risk of their stress. Parental stress was associated with children's emotional and behavioral problems (*10*). Therefore, the uncertainty of their future academics, individual relationships, inactivity, and parent-child relationship posed some severe threats to their mental health. More attention should be paid to the mental health of children and adolescents by the collaboration of parents, teachers, psychologists, and psychiatrists.

This study was subject to several limitations. First, data for this study were only obtained from one hospital, so the small sample size limited the representativeness. Second, the lack of information about patients may have influenced the analysis. Third, a relatively short period, just one year, was observed in this study. Future studies, especially multicenter and more extended observation period studies, are needed.

Conflicts of interest: No conflicts of interest.

Corresponding authors: Zhiying Wan, 1032242656@qq.com; Hongqiang Sun, Sunhq@bjmu.edu.cn.

---

1 Department of Psychiatry, Renmin Hospital of Wuhan University, Wuhan City, Hubei Province, China; 2 Peking University Sixth Hospital, Peking University Institute of Mental Health, NHC Key Laboratory of Mental Health (Peking University), National Clinical Research Center for Mental Disorders (Peking University Sixth Hospital), National Center for Mental Health, Chinese Center for Disease Control and Prevention, Beijing, China.

REFERENCES

1. Wang CY, Pan RY, Wan XY, Tan YL, Xu LK, McIntyre RS, et al. A longitudinal study on the mental health of general population during the COVID-19 epidemic in China. Brain Behav Immun 2020;87:40 – 8. http://dx.doi.org/10.1016/j.bbi.2020.04.028.

2. Shi L, Lu ZA, Que JY, Huang XL, Liu L, Ran MS, et al. Prevalence of and risk factors associated with mental health symptoms among the general population in china during the coronavirus disease 2019 pandemic. JAMA Netw Open 2020;3(7):e2014053. http://dx.doi.org/10.1001/jamanetworkopen.2020.14053.

3. Blashfield RK, Keeley JW, Flanagan EH, Miles SR. The cycle of classification: DSM-I through DSM-5. Annu Rev Clin Psychol 2014;10:25 – 51. http://dx.doi.org/10.1146/annurev-clinpsy-032813-153639.

4. Yang D, Yang XL, Liu K, Dong ZY. Admission management of patients with severe mental illness during COVID-19. J Int Psychiatry 2020;47(4):650 – 52,665. http://dx.doi.org/10.13479/j.cnki.jip.2020.04.004. (In Chinese).

5. Rowland T, Perry BI, Upthegrove R, Barnes N, Chatterjee J, Gallacher D, et al. Neurotrophins, cytokines, oxidative stress mediators and mood state in bipolar disorder: systematic review and meta-analyses. Br J Psychiatry 2018;213(3):514 – 25. http://dx.doi.org/10.1192/bjp.2018.144.

6. Dagani J, Signorini G, Nielssen O, Bani M, Pastore A, de Girolamo G, et al. Meta-analysis of the interval between the onset and management of bipolar disorder. Can J Psychiatry 2017;62(4):247 – 58. http://dx.doi.org/10.1177/0706743716656607.

7. Rodriguez-Paris D, Remlinger-Molenda A, Kurzawa R, Głowińska A, Spaczyński R, Rybakowski F, et al. Psychiatric disorders in women with polycystic ovary syndrome. Psychiatr Pol 2019;53(4):955 – 66. http://dx.doi.org/10.12740/PP/OnlineFirst/93105.

8. Nowrouzi B, McIntyre RS, MacQueen G, Kennedy SH, Kennedy JL, Ravindran A, et al. Admixture analysis of age at onset in first episode bipolar disorder. J Affect Disord 2016;201:88 – 94. http://dx.doi.org/10.1016/j.jad.2016.04.006.

9. Shah K, Mann S, Singh R, Bangar R, Kulkarni R. Impact of COVID-19 on the mental health of children and adolescents. Cureus 2020;12(8):e10051. http://dx.doi.org/10.7759/cureus.10051.

10. Brown SM, Doom JR, Lechuga-Peña S, Watamura SE, Koppels T. Stress and parenting during the global COVID-19 pandemic. Child Abuse Negl 2020;110(Pt 2):104699. http://dx.doi.org/10.1016/j.chiabu.2020.104699.

SUPPLEMENTARY TABLE S1. Inpatients' characteristics of Phase 1 and Phase 2.

Category	Phase 1 (n=6,664)	Phase 2 (n=4,199)	χ^2/t	*P*-value
Gender				
Male	2,938 (44.1%)	1,634 (38.9%)	28.29	<0.001
Female	3,726 (55.9%)	2,565 (61.1%)		
Age	34.55±16.10	33.52±16.52	3.21	0.001
Wuhan *hukou*				
Yes	2,734 (41.0%)	1,618 (38.5%)	6.67	0.010
No	3,930 (59.0%)	2,581 (61.5%)		
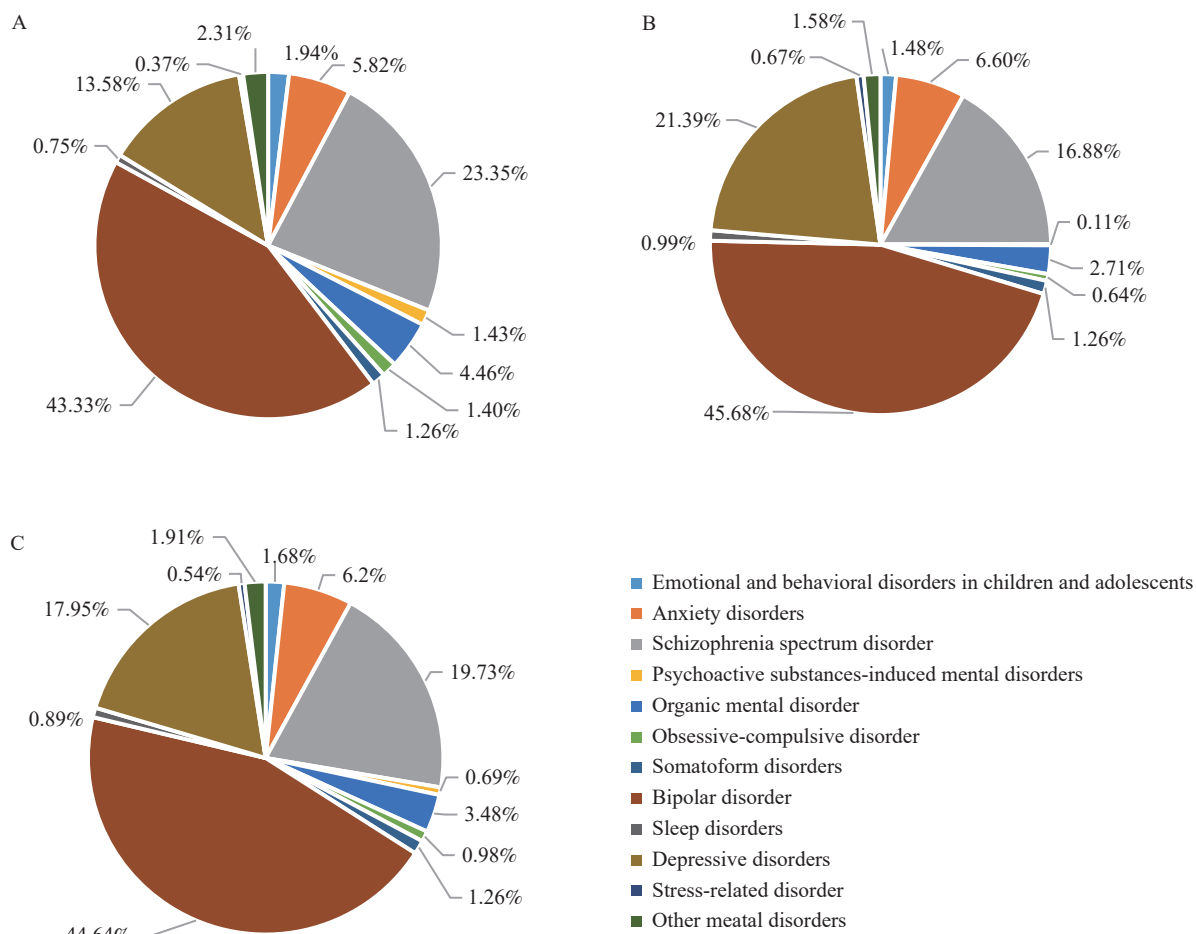
SUPPLEMENTARY FIGURE S1. Disease distribution proportion of inpatients in Phase 1 by gender, (A) male; (B) female; and (C) both.
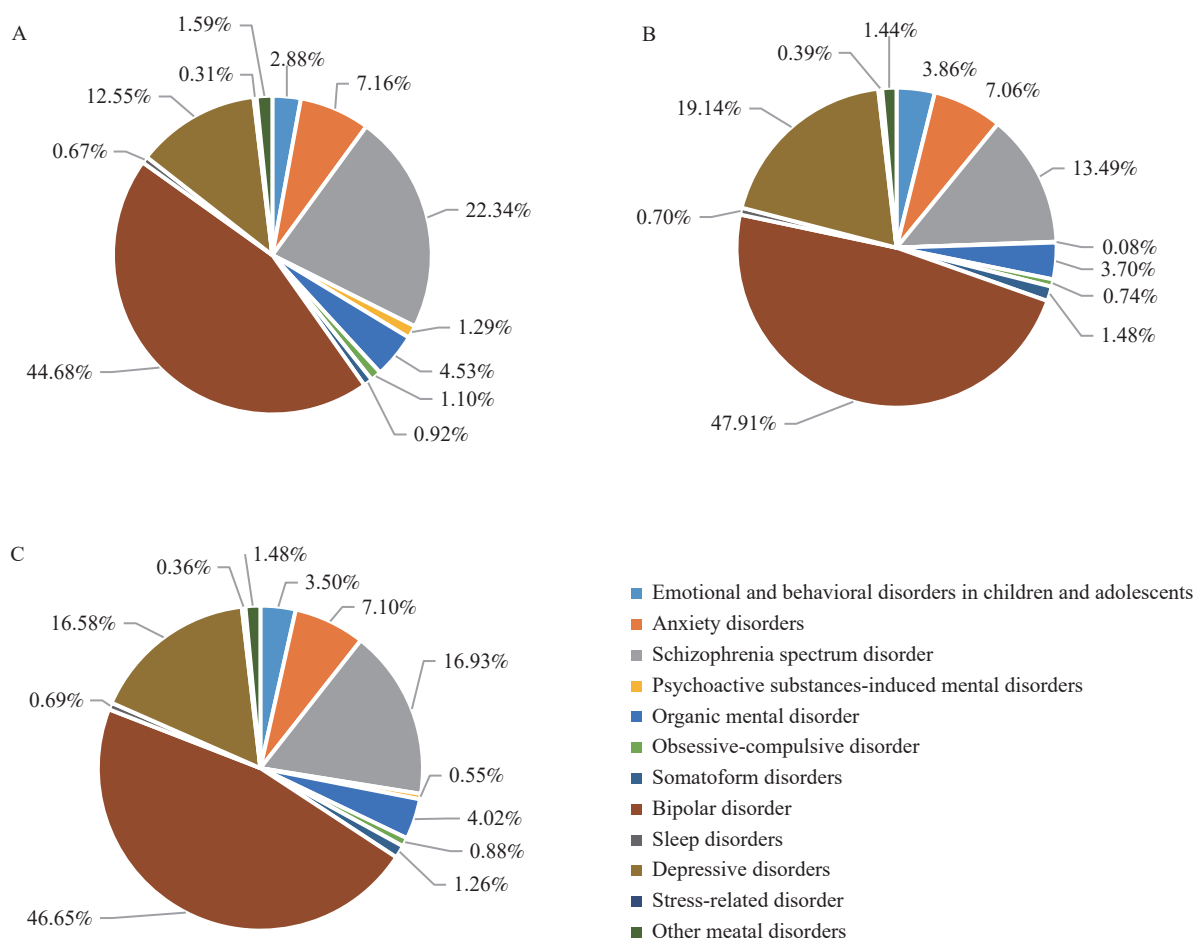
SUPPLEMENTARY FIGURE S2. Disease distribution proportion of inpatients in Phase 2 by gender, (A) male; (B) female; and (C) both.

SUPPLEMENTARY TABLE S2. Inpatients' disease diagnosis distribution among demographic characteristics in Phase 1 and Phase 2.

Variety of disease		Gender		Age	Wuhan *hukou*	
		Male	Female		Yes	No
Somatoform disorders	Phase 1	37 (44.0%)	47 (56.0%)	47.81±15.08	30 (35.7%)	54 (64.3%)
	Phase 2	15 (28.3%)	38 (71.7%)	50.66±16.34	19 (35.8%)	34 (64.2%)
	χ^2/t		3.42	−1.04		0.00
	P-value		0.064	0.299		0.987
Bipolar disorder	Phase 1	1,273 (42.8%)	1,702 (57.2%)	30.50±13.14	1,156 (38.9%)	1,819 (61.1%)
	Phase 2	730 (37.3%)	1,229 (62.7%)	28.70±13.09	707 (36.1%)	1,252 (63.9%)
	χ^2/t		14.96	4.73		3.85
	P-value		<0.001	<0.001		0.050
Sleep disorders	Phase 1	22 (37.3%)	37 (62.7%)	48.88±16.15	26 (44.1%)	33 (55.9%)
	Phase 2	11 (37.9%)	18 (62.1%)	47.07±15.69	9 (31%)	20 (69%)
	χ^2/t		0.003	0.50		1.38
	P-value		0.953	0.619		0.240
Depressive disorders	Phase 1	399 (33.4%)	797 (66.6%)	34.68±17.49	503 (42.1%)	693 (57.9%)
	Phase 2	205 (29.5%)	491 (70.5%)	36.64±18.30	261 (37.5%)	435 (62.5%)
	χ^2/t		3.09	−2.28		3.79
	P-value		0.079	0.023		0.051
Stress-related disorder	Phase 1	11 (30.6%)	25 (69.4%)	40.72±15.99	17 (47.2%)	19 (52.8%)
	Phase 2	5 (33.3%)	10 (66.7%)	35.93±20.16	7 (46.7%)	8 (53.3%)
	χ^2/t		0.04	0.90		0.001
	P-value		0.846	0.372		0.971
Emotional and behavioral disorders in children and adolescents	Phase 1	53 (49.5%)	54 (50.5%)	14.71±2.30	34 (31.8%)	73 (68.2%)
	Phase 2	45 (31.3%)	99 (68.8%)	14.70±1.99	41 (28.5%)	103 (71.5%)
	χ^2/t		8.62	0.04		0.32
	P-value		0.003	0.969		0.572
Anxiety disorders	Phase 1	171 (41%)	246 (59%)	46.94±17.21	19 (46.8%)	222 (48.7%)
	Phase 2	11 (39.3%)	18 (60.7%)	48.77±15.34	14 (48.7%)	153 (51.3%)
	χ^2/t		0.22	−1.46		0.25
	P-value		0.639	0.144		0.617
Schizophrenia spectrum disorder	Phase 1	686 (52.2%)	629 (47.8%)	36.42±13.76	551 (41.9%)	764 (58.1%)
	Phase 2	365 (51.3%)	34 (48.7%)	35.61±14.04	301 (42.3%)	410 (57.7%)
	χ^2/t		0.130.721	1.25		0.04
	P-value			0.211		0.850
Psychoactive substances-induced mental disorders	Phase 1	42(91.3%)	4(8.7%)	41.54±11.93	32 (69.6%)	14 (30.4%)
	Phase 2	21(91.3%)	2(8.7%)	40.13±12.52	13 (56.5%)	10 (43.5%)
	χ^2/t			0.46		1.15
	P-value		1.000*	0.650		0.284
Organic mental disorder	Phase 1	13 (56.5%)	10 (43.5%)	57.23±18.44	11 (51.3%)	11 (48.7%)
	Phase 2	74 (43.8%)	95 (56.2%)	51.59±18.69	80 (47.3%)	89 (52.7%)
	χ^2/t		6.29	3.01		0.61
	P−value		0.012	0.003		0.434
Obsessive-compulsive disorder	Phase 1	41 (63.1%)	24 (36.9%)	27.83±11.78	26 (40%)	39 (60%)
	Phase 2	18 (48.6%)	19 (51.4%)	32.41±16.14	14 (37.8%)	23 (62.2%)
	χ^2/t		2.01	−1.64		0.05
	P-value		0.156	0.103		0.830

* Using the Fisher's Exact test.

Persevere in the Dynamic COVID-Zero Strategy in China to Gain a Precious Time Window for the Future

Jue Liu[1]; Min Liu[1,#]; Wannian Liang[2,3,#]

According to the report of the World Health Organization (WHO), as of April 20, 2022, the cumulative number of confirmed cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the world had exceeded 500 million, with 6.20 million deaths and over 580,000 new confirmed cases on that day (*1*). As many countries have announced to relax quarantine policies, China is facing increasing pressure from overseas imports. All 31 provincial-level administrative divisions (PLADs) of China have reported a total of 191,112 local confirmed cases, with 2,761 new confirmed cases, 17,166 new asymptomatic infections, and 7 new deaths (all in Shanghai Municipality) on April 19 (*2*). Recently, several local outbreaks in clusters have appeared in China, presenting a grim and complex situation with multiple spots, wide coverage, and frequent occurrence (*3*).

Omicron Spreads Quickly and Is Harmful to Those at Risk

The current epidemic was mainly caused by Omicron variant BA.2, which has a short incubation period, strong transmissibility, short serial interval, and a large ability of immune escape (*4–5*). It was found that the basic regeneration number (R_0) of Omicron variant was about 9.5, and its maximum incubation period was about 9 days (*4–5*). The median incubation period was about 3 days, which was significantly shorter than that of the Delta variant (4.3 days) and other variants (5.0 days) (*4–5*). Its median serial interval was about 2.8 days (*4–5*).

It is reported that the proportion of asymptomatic infections of Omicron variant was relatively high (*4*). There are some reasons for this phenomenon. First, the characteristics of Omicron variant caused a higher proportion of asymptomatic infections than that of other variants. Second, some people did not develop symptoms even after being infected because of the coronavirus disease 2019 (COVID-19) vaccination. Third, early detection can find infections at early stages when symptoms have not yet appeared. In addition, the training of medical staff to improve their ability to

correctly conduct diagnosis and treatment, scientifically and reasonably determinate the asymptomatic and confirmed cases, also needed to be strengthened. According to the Statistics on the 5th Wave of COVID-19 in Hong Kong, the population-wide mortality rate caused by Omicron variant was 799 per million and for people over 80 years old was 10,408 per million ((*6–7*). According to the real-world data in Hong Kong, the fatality rate of the Omicron variant (0.76%) was significantly higher than that of influenza (0.1%), and it reached 10.4% among people over 80 years old (*6–7*). The elderly, people with underlying diseases, and those who had not been vaccinated were at high risk of severe illness and death. Of the 8,973 patients who died (0–112 years old) in Hong Kong, 96% were the elderly, and 88% were not fully vaccinated. Fortunately, a large real-world study in Hong Kong showed that three doses of either vaccination against COVID-19 offered very high levels of protection against severe illness and death caused by the Omicron variant (vaccine effectiveness 98.1%, 95% confidence interval: 97.1%, 98.8%) (*8*). Although the total vaccine coverage in the mainland of China is high, compared with adults, the two-dose or booster vaccination rate of the elderly and children was relatively low. In Shanghai, for example, the two-dose vaccination rate for people over 80 years old is only about 15% (*9*). There are still a large proportion of susceptible people.

The Dynamic COVID-Zero Strategy Is Still Required

China should still persevere in the Dynamic COVID-Zero Strategy. Putting people's lives and health first is the fundamental starting point and goal of all prevention and control measures in China. Because of the large population, unbalanced regional development, and insufficient total medical resources, China will face the risk of serious runs of medical and health resources if the "lying flat" strategy is adopted (*10*). The health of many patients with underlying diseases, the elderly, children, and pregnant women

will be seriously threatened, and the steady economic and social development will be seriously affected (*10*).

Dynamic COVID-Zero Strategy is the general guideline for China's fight against COVID-19, which is also a summary of previous experiences in fighting against dozens of domestic clusters of outbreaks since 2020. The multiple rounds of COVID-19 have proved that the Dynamic COVID-Zero Strategy is in line with China's national conditions and is the best option for China to fight the epidemic, which is based on the concept of "people first, life first." China has the capability, the foundation, the conditions, and the toolkits to implement this strategy. Also, China has strong institutional advantages, professional teams, and the support of the public, which will form the greatest protection for life.

The core of the dynamic zero strategy lies in early detection, rapid containment, and cutting off transmission to prevent continuous spread and large-scale rebound of the epidemic (*11*). This is not about "zero infection" or "zero tolerance" of COVID-19, but about science and precision. The premise of precision is to be effective. In the face of the virus, we need to stay ahead. Zero community transmission refers to newly discovered infected persons being comprehensively found in quarantine and controlled populations without the possibility of spreading to the rest of society. The temporary inconveniences in some areas are for longer-term normal life and socioeconomic development of the population more broadly. We need to take a systematic approach and a long-term view to do the best to strike a better balance between epidemic prevention and control with socioeconomic development.

Seize the Opportunities to Gain Precious Time Window for the Future

At present, China has entered the fourth stage of comprehensive epidemic prevention and control, namely, "scientific, accurate, and dynamic COVID-zero" (*10*). Facing the rapidly spreading Omicron, in order to stop the spread of the epidemic in the community as soon as possible, we are supposed to make coordinated efforts to control the outbreak at early stages, including control of at-risk populations, detection, epidemiological investigation, transport, isolation, treatment, and other aspects (*10*). The Dynamic COVID-Zero Strategies adopted by China have won a precious time window for the future. China should seize this opportunity to speed up research and development of specific drugs and vaccines, accelerate the two or three-dose vaccination of the population, especially for the elderly and children, and strengthen the preparedness of resources for the future to finally defeat the virus at a minimal cost.

Corresponding authors: Min Liu, liumin@bjmu.edu.cn; Wannian Liang, liangwn@tsinghua.edu.cn.

1 School of Public Health, Peking University, Beijing, China; 2 Vanke School of Public Health, Tsinghua University, Beijing, China; 3 Institute for Healthy China, Tsinghua University, Beijing, China.

REFERENCES

1. World Health Organization. WHO Coronavirus (COVID-19) Dashboard. World Health Organization; 2022. https://covid19.who.int/. [2022-4-20].
2. National Health Commission. Up to April 19th, the latest situation of COVID-19: National Health Commission; 2022. http://www.nhc.gov.cn/xcs/yqfkdt/202204/378f7fc3484e4b41bb845a0854552a6c.shtml. [2022-4-20]. (In Chinese).
3. National Health Commission. Transcript of the press conference of the joint prevention and control mechanism of the State Council on April 19, 2022. National Health Commission; 2022. http://www.nhc.gov.cn/xcs/fkdt/202204/71904942749945c9a460aed122484c3d.shtml. [2022-4-20]. (In Chinese).
4. Wu Y, Liu J, Liu M, Liang WN. Epidemiological characteristics of SARS-CoV-2 Omicron Variant and the scientific control suggestions. http://dx.doi.org/10.16462/j.cnki.zhjbkz.2022.05.001.
5. Wu Y, Liu J, Liu M, Liang WN. Epidemiologic features and containment of SARS-CoV-2 omicron variant. Chin General Pract 2022;25(1):14 – 9. http://dx.doi.org/10.12114/j.issn.1007-9572.2021.00.348.
6. Smith DJ, Hakim AJ, Leung GM, Xu WB, Schluter WW, Novak RT, et al. COVID-19 mortality and vaccine coverage — Hong Kong special administrative region, China, January 6, 2022–March 21, 2022. China CDC Wkly 2022;71(15):545 – 8. http://dx.doi.org/10.15585/mmwr.mm7115e1.
7. Centre for Health Protection of the Department of Health and the Hospital Authority. The Statistics on 5th Wave of COVID-19 in Hong Kong. Centre for Health Protection of the Department of Health and the Hospital Authority; 2022. https://www.covidvaccine.gov.hk/pdf/5th_wave_statistics.pdf. [2022-4-20]. (In Chinese).
8. McMenamin ME, Nealon J, Lin Y, Wong JY, Cheung JK, Lau EHY, et al. Vaccine effectiveness of two and three doses of BNT162b2 and CoronaVac against COVID-19 in Hong Kong. medRxiv 2022. http://dx.doi.org/10.1101/2022.03.22.22272769.
9. Shen ST. Improve the prevention and control measures and strengthen the treatment force. The People's Daily. 2022 Apr 14. https://wap.peopleapp.com/article/6628510/6504148?share_token=c108dba5-8bdb-45ca-9153-006916645c70. (In Chinese).
10. Ma XW. Curb the spread of the epidemic as soon as possible and resolutely consolidate the hard won achievements in prevention and control. Study Times 2022;1774:1-4. http://paper.cntheory.com/html/2022-04/18/nw.D110000xxsb_20220418_1-A1.htm.(In Chinese).
11. Liu J, Liu M, Liang WN. The dynamic COVID-Zero strategy in China. China CDC Wkly 2022;4(4):74 – 5. http://dx.doi.org/10.46234/ccdcw2022.015.

Indexed by PubMed Central (PMC), Emerging Sources Citation Index (ESCI), Scopus, Chinese Scientific and Technical Papers and Citations, and Chinese Science Citation Database (CSCD)

CCDCweekly

Vol. 4 No. 18 May 6, 2022