Letter to the Editor

Early epidemic control reduced burden of Omicron BA.5 infection in partially vaccinated community

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Submitted Dec 19, 2022. Accepted for publication Oct 20, 2023. Published online Nov 02, 2023.
doi: 10.21037/jtd-22-1824
View this article at: https://dx.doi.org/10.21037/jtd-22-1824

On the mid of June 2022, a new wave of coronavirus disease 2019 (COVID-19) epidemic outbreak in Macao, China. With a top world-ranking population density of 2.18 million/km^2, Macao owns a variety of entertainment venues and cross-border populations. The spread of infection in the community is occurring more rapidly for the current outbreak than in previous waves with an estimated basic reproduction number (R0) was 7.8. There were multiple outbreaks (25 groups) in the community, reaching a single-day peak at 146. As of July 23, a total of 1,810 cases have been confirmed, of which 699 were symptomatic, 1,111 were asymptomatic, and 6 died (1). The phylogenetic analysis showed that reported cases were clustered into severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) BA.5 sub-lineage.

Compared with Omicron BA.2 sub-lineage that previously invaded Hong Kong and Shanghai, China, BA.5 sub-lineage has stronger infectivity and immune evasion ability and is more lung-tropic. Firstly, BA.5 spread faster than BA.2 with estimated growth advantages of 0.10 [95% confidence interval (CI): 0.09–0.11] per day over BA.2 in South Africa (2). Secondly, Tuekprakhon *et al.* found that BA.4/BA.5 display increased evasion of neutralizing antibodies compared with BA.2 against plasma from triple-vaccinated individuals or from individuals who developed a BA.1 infection after vaccination (3). A study in *Nature* pointed out that F486V, R493Q, and L452R became the key to the enhanced immune evasion and cell invasion ability of BA.4/5 (4). Besides, compared with BA.2, BA.5 was more likely to spread in the lungs and the periphery of the lungs of infected hamsters *in vivo* experiments (5). At the same time, the BA.5 mutant strain was also more likely to cause bronchitis, alveolar damage, and lung congestion/bleeding in infected hamsters (5). As of the report in late August in America, the BA.5 strain has accounted for 99.8% of the newly detected strains of Omicron BA.5, and the number of COVID-19 hospitalizations and intensive care unit (ICU) stays continues to increase (6).

Both SARS-CoV-2 inactivated vaccines and messenger RNA (mRNA) vaccines are accessible in Macao, with 587,521 people (about 86.93%) vaccinated with the second dose or above. Similarly, Peru, Chile, Argentina, and Singapore all have relatively high vaccination rates (7) (*Table 1*). However, the lasting time and health burden of the epidemic on society varies widely after experiencing BA.4/5 epidemic. This epidemic ended after 39 days in

Table 1 Epidemic status and vaccination rate in Singapore, Chile, Peru, Argentina, and Macao

Country/region	Started date of BA.4/5 epidemic	The proportion of people aged over 60 years (%)	People fully vaccinated (%)	Booster doses (per 100)	The duration of BA.4/5 epidemic[†] (days)	Deaths in the current outbreak
Singapore	2022.06.12	22.58	91.74	78.57	81+	196
Chile	2022.05.09	19.01	90.60	137.47	115+	2,822
Peru	2022.06.06	13.67	83.33	74.20	87+	2,503
Argentina	2022.05.16	17.46	83.37	66.86	75+	935
Macao	2022.06.18	19.72	86.93	44.58	39	5

[†], the duration of the BA.4/5 epidemic was measured as the August 18, 2022. "+" means the epidemic is still ongoing.

Macao, while other countries were still suffering from the epidemic with 16 times or more deaths than Macao.

Such a large gap in health burden may be attributed to the Macao government's persisting dynamic zero-COVID policy and implemented more active intervention measures in the early stage (Table S1). In the early days of the outbreak, the policy required a 24-hour nucleic acid-negative certificate to leave avoided the risk of infection in mainland China. In addition, three rounds of city-wide nucleic acid testing and timely epidemiological investigations have been carried out to find out the potential transmission risk. In the next few days, the Macao Special Administrative Region (SAR) Government further implemented precise and differentiated strategies in each region to combat the epidemic. When cases were increasingly confirmed in the community, "relatively static" policies were quickly implemented to block the virus transmission in the community. All non-essential industrial and commercial activities that hardly impact people's livelihoods were suspended. With the population flow has been drastically reduced, the newly infected people have been cleared from the social aspect, and time-varying reproductive number (Rt) fell below 1 on July 22, 2022 (Figure S1).

Macao's rapid response against BA.5 is essential to prevent cases from importing into mainland China and to ensure people's health and life normality. In the Greater Bay Area, hundreds of thousands of people travel between Zhuhai and Macao for daily cross-border living or shopping, business, and other activities. If the epidemic cannot be controlled quickly and effectively, large numbers of cases might outbreak in communities and spill over into mainland China. According to the Chinese National Health Commission, about 31 million people older than 60 years have not yet been vaccinated (8), and uncontrolled outbreaks could lead to large numbers of infections and deaths among the elderly. Besides, Macao will not be able to smoothly pass through customs with mainland China for a long time, which will lead to a series of linkages such as a sharp drop in inbound tourists, a "zero" income from the tourism and gaming industry, the closure of a large number of businesses, a surge in unemployed people, and a sharp drop in economic indicators. The lock-in reaction will bring a devastating blow to social livelihood and economic development.

Fortunately, the dynamic zero-COVID policy from the mainland has offered a reference to Macao. Learned from this experience, early non-drug interventions are effective in reducing the health and life burden of the COVID-19 epidemic to people without fully-vaccination. However, prevention and control are both indispensables. When social immunity is not strong, it is particularly important to implement intervention measures as soon as possible in the early stage of the epidemic. But once it subsides, the focus of future work should be to fully understand people's hesitation in vaccination and make targeted solutions to increase the vaccination rate as soon as possible. Nowadays, the Macao Special Administrative Region (SAR) Government has arranged house-to-house visits by community workers to encourage the elderly to get vaccinated. We believe we could combat the COVID-19 pandemic under the concerted efforts of all human beings.

Acknowledgments

We thank Lixi Liang (National Center for Respiratory Medicine, State Key Laboratory of Respiratory Disease & National Clinical Research Center for Respiratory Disease, Guangzhou Institute of Respiratory Health, The First Affiliated Hospital of Guangzhou Medical University,

Guangzhou, China) and Health Bureau, Macao, China for collecting data.
Funding: This work was supported by the Self-Supporting Program of Guangzhou Laboratory (No. SRPG22-007), the Science and Technology Development Fund of Macao SAR (No. 005/2022/ALC), the Science and Technology Program of Guangzhou (No. 2022B01W0003), the Science and Technology Program of Guangzhou (No. 202102100003), the Science and Technology Development Fund of Macao SAR (No. 0045/2021/A), and the Macao University of Science and Technology (No. FRG-20-021-MISE).

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Journal of Thoracic Disease* for the series "Current Status of Diagnosis and Forecast of COVID-19". The article has undergone external peer review.

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-1824/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-1824/coif). The series "Current Status of Diagnosis and Forecast of COVID-19" was commissioned by the editorial office without any funding or sponsorship. Z.Y. served as the unpaid Guest Editor of the series. N.Z. serves as Editor-in-Chief of *Journal of Thoracic Disease*. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Cite this article as: Liang J, Liu Z, Liu R, Li Q, Hon C, Zhong N, Yang Z. Early epidemic control reduced burden of Omicron BA.5 infection in partially vaccinated community. J Thorac Dis 2023;15(12):7162-7164. doi: 10.21037/jtd-22-1824

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Supplementary

Table S1 Policies or measures for epidemic prevention and control against Omicron BA.5 in Macao, China

Date	Policies or measures
June 19th, 2022	Entering real-time precautionary status and activating the zoned and graded epidemic prevention program
June 20th, 2022	(I) Conducting universal nucleic acid testing
	(II) Government departments closed
	(III) Shut down public facilities
	(IV) Schools closed
June 21st, 2022	Fangcang shelter hospital completes preparations
June 22nd, 2022	Conducting universal antigen detection
June 23rd, 2022	Conducting second-round universal antigen detection
June 24th, 2022	Activation of Pavilion C of the Fangcang shelter hospital to enlarge the admission capacity

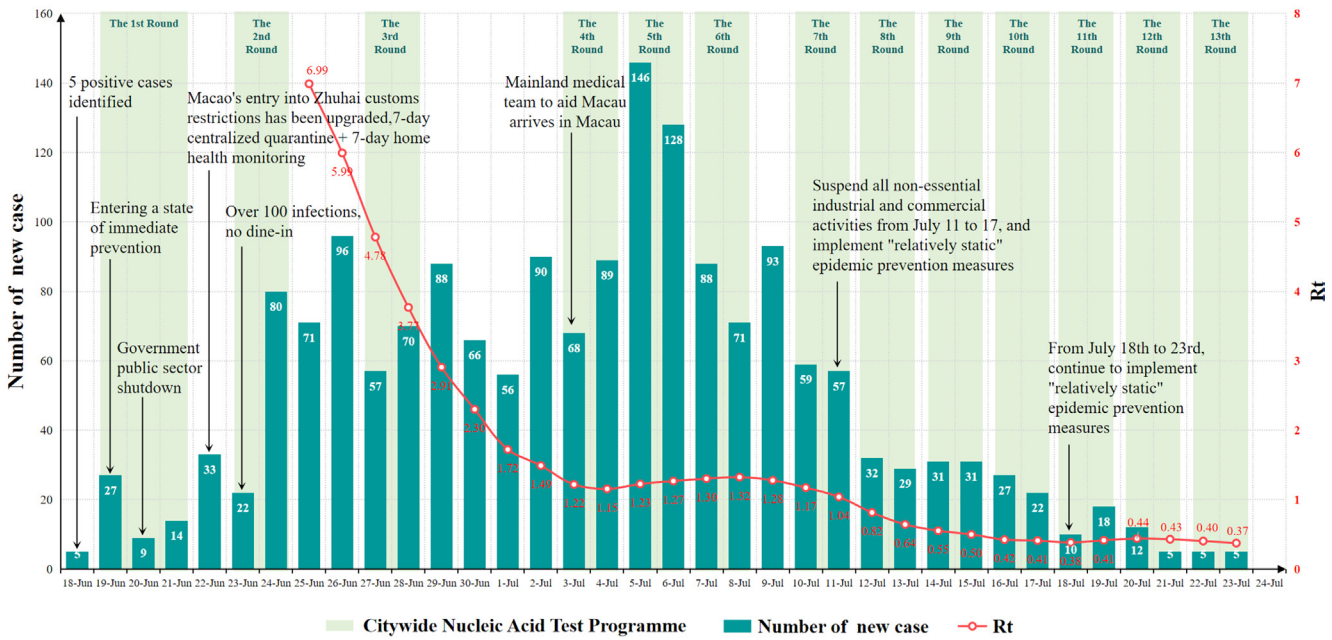

Figure S1 The timeline of epidemic prevention and control work in Macao, China. Rt means the time-varying effective reproductive numbers. The detailed epidemic prevention and control efforts are marked at the beginning of the arrow.

https://dx.doi.org/10.21037/jtd-22-1824