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Preplanned Studies

Effectiveness of Inactivated COVID-19 Vaccines Against Symptomatic, Pneumonia, and Severe Disease Caused by the Delta Variant: Real World Study and Evidence — China, 2021

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Summary

What is already known about this topic?

Effectiveness of China's 2 inactivated vaccines (BBIBP-CorV and CoronaVac) against pre-Delta severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) variants ranged from 47% to over 90%, depending on the clinical endpoint, and with greater effectiveness against more severe coronavirus disease 2019 (COVID-19). During an outbreak in Guangdong, inactivated vaccine effectiveness (VE) against the Delta variant was 70% for symptomatic infection and 100% for severe COVID-19. However, separate or combined VE estimates for the two inactivated vaccines against Delta are not available.

What is added by this report?

In an outbreak that started in a hospital, VEs of completed primary vaccination with inactivated COVID-19 vaccines against symptomatic COVID-19, COVID-19 pneumonia, and severe COVID-19 caused by the Delta variant were 51%, 61%, and 82%. Completed primary vaccination reduced the risk of progressing from mild to moderate or severe COVID-19 by 74%. VE estimates for BBIBP-CorV and CoronaVac or combined vaccination were similar, and partial vaccination was ineffective.

What are the implications for public health practice?

Completed primary vaccination with either of the 2 inactivated COVID-19 vaccines reduces risk of symptomatic COVID-19, COVID-19 pneumonia, and severe COVID-19 caused by the Delta variant. Completion of the completed primary vaccination with two doses is necessary for protection from Delta.

INTRODUCTION

Knowledge of real-world performance of coronavirus disease 2019 (COVID-19) vaccines is critically important for informing pandemic vaccination strategy and policy. As severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) evolves and variants emerge that vary in severity of illness, transmissibility, and immune escape potential, every opportunity must be taken to measure vaccine effectiveness (VE) in real-world studies so that policy can be adjusted to keep up-to-date with variants, duration of vaccine-induced protection, and implementation of booster doses. Currently in China, outbreaks offer the only opportunities to measure VE. At the end of July and August 2021 there was a 167-case, hospital-centered, Delta-variant outbreak in Henan Province. We conducted a retrospective cohort study among 1,462 close contacts of SARS-CoV-2-infected individuals in the outbreak who were quarantined and systematically tested for infection over a 2-week interval. Vaccination status was verified by the national vaccine information system. We found that completed primary series vaccination VE with 2 doses of inactivated vaccines was 51% against symptomatic infection, 61% against COVID-19 pneumonia, and 82% against severe COVID-19. Completed primary vaccination reduced the risk of progressing from mild to moderate or severe COVID-19 by 74%. VE levels were similar for BBIBP-CorV and CoronaVac vaccines. We concluded that both inactivated vaccines retained effectiveness against the Delta variant, consistent with efficacy clinical trials, and that these vaccines can continue to be used to protect individuals and prevent or control disease during the pandemic.

COVID-19 vaccines are important tools for COVID-19 pandemic management. Five vaccine development techniques are being used to develop and produce COVID-19 vaccines in China: whole-virus

inactivated, adenovirus vectored, recombinant protein subunit, nucleic acid, and attenuated influenza virus vectored vaccines. Inactivated vaccines are in the most widespread use in China (over 85% all COVID-19 vaccine doses administered), with two manufacturers — Sinopharm (BBIBP-CorV) and Sinovac (CoronaVac) — providing the largest share. These two vaccines have been listed by the World Health Organization (WHO) for emergency use and are in widespread use globally.

China initiated a large domestic COVID-19 vaccination campaign on December 15, 2020. In June and July 2021, the Delta (B.1.617.2) variant began to cause outbreaks in China. BBIBP-CorV and CoronaVac vaccines are frequently used in the same population at the same time during the campaign, providing opportunity for single-study estimates of VE against the Delta variant by vaccine brand. Taking advantage of a Delta variant outbreak in Zhengzhou city of Henan Province, we evaluated VE against symptomatic COVID-19, COVID-19 pneumonia, and severe COVID-19 by time since vaccination and vaccine brand.

METHODS

We evaluated VE using a retrospective cohort study among close contacts of individuals who were polymerase chain reaction (PCR)-confirmed to have been infected with SARS-CoV-2 in an outbreak that started in a hospital in Zhengzhou and spread to the community. We estimated the effectiveness of vaccination to prevent progression of illness by comparing the odds of vaccination of asymptomatic and mild cases versus the odds of vaccination in moderate and severe cases using an age-stratified analysis.

Setting and Subjects

The study setting was Zhengzhou, the capital city of Henan Province. As of July 17, 2021, 74.8% of Zhengzhou's 18–59-year-old residents were completed vaccinated and 46.4% of residents ≥60 years old were completed vaccinated. Over 98% of all adults who were vaccinated received an inactivated COVID-19 vaccine. We drew our subjects from close contacts of people with laboratory-confirmed SARS-CoV-2 infection.

For VE evaluation, we included only close contacts, 18 years and older, who had documented contact or exposure opportunities (contact with one or more confirmed cases or asymptomatic infections in the same public space, without protection, within close distance, within up to five days before illness onset for symptomatic cases or were identified by the first positive specimen for asymptomatic cases), and no history of COVID-19 infection. We excluded individuals vaccinated with vaccines other than BBIBP-CorV or CoronaVac. For analysis of impact of vaccination on risk of severe COVID-19, we included all infected individuals who were 18 years of age and older.

Vaccination Status

We considered vaccinations to be valid only if they were documented in the national or the provincial Immunization Information System. Subjects were categorized into an unvaccinated group, a partially-completed vaccinated group, and a completed primary vaccinated group based in part on compliance with technical guidelines from China CDC's COVID-19 Vaccines Technical Working Group (*1*). The unvaccinated group consisted of individuals who did not receive any COVID-19 vaccines before their last known contact with a confirmed case. The partially-completed vaccination group consisted of individuals who had received either 1 dose of a COVID-19 inactivated vaccine or had received 2 doses of inactivated vaccines with receipt of the second dose less than 14 days before exposure to an infected individual. The completed primary vaccination group consisted of individuals who completed 2 doses of inactivated vaccine 14 days or more before exposure to an infected individual.

Outcomes

We evaluated 3 outcomes: symptomatic COVID-19, COVID-19 pneumonia, and severe COVID-19. Case classifications were based on the *COVID-19 Prevention and Control Protocol (eighth edition)* (*2*), and *COVID-19 Diagnosis and Treatment Protocol (Trial eighth edition)* (*3*): asymptomatic, mild, moderate, severe, and critically severe. Symptomatic illness included mild, moderate, severe, and critically-severe cases. COVID-19 pneumonia included moderate, severe, and critically severe cases with evidence of pneumonia. Severe COVID-19 included severe and critically-severe cases.

Statistical Analyses

To calculate unadjusted VE, the relative risk (RR) of each outcome was calculated in reference to the unvaccinated group; VE was 1-RR. Gender, age grouping (18–59 years old and ≥60 years old), and presence of underlying disease(s) were considered potentially confounding variables in multivariate analyses. We used a generalized linear model with a binomial distribution and log link function to calculate adjusted risk ratios (aRR) which were used to calculate adjusted VE (aVE).

To estimate the effectiveness of vaccination for preventing severe COVID-19, we determined the odds of vaccination for subjects with asymptomatic or mild infections (combined) and for subjects with moderate or worse severity infections (combined); effectiveness to prevent severe infection was one minus the ratio of these odds. All data analyses were performed with SAS software (version 9.4, SAS Institute Inc., Cary, NC, USA).

Ethical Review

COVID-19 is considered a Level 2 infectious disease and is managed as a Level 1 infectious disease. Investigations into outbreaks of COVID-19, including estimating effectiveness of vaccination, are considered public health responsibilities and are exempt from ethical committee review.

RESULTS

Outbreak, Cases, and Subjects

On July 31, 2021, a local cluster of COVID-19 cases was identified through PCR screening in a hospital. The virus was isolated and sequenced, showing that the cluster was caused by the Delta variant. The epidemic was managed in accordance with the Protocol for Prevention and Control of COVID-19; the last case occurred on August 24. The epidemic consisted of 167 infections, 166 were symptomatic and 1 was asymptomatic; 139 cases were in Zhengzhou. A total of 14 infections were among children below 18 years of age, and 8 were among individuals vaccinated with a vaccine other than BBIBP-CorV or CoronaVac.

For VE evaluation, 1,462 close-contacts were identified including 107 cases that were ultimately diagnosed with PCR-confirmed SARS-CoV-2 infection; 473 close contacts were unvaccinated, and 288, 455, and 246 were vaccinated with BBIBP-CorV, CoronaVac, or both vaccines (one dose of each, in either order), respectively. Table 1 shows the breakdown of the close contacts by vaccination status (unvaccinated, full, or partial vaccination), vaccine brand, age group, presence of comorbidities, and infection status with clinical outcome. Among the close contacts, 42 were HIV-positive (10 individuals) or had tuberculosis (32 individuals); 33 of these 42 close contacts had not been vaccinated, 5 had been partially vaccinated, and 4 completed 2-dose vaccination series; 35 developed infection (11 mild, 17 moderate, 6 severe, and 1 critically severe).

Vaccine Effectiveness and Severity

Table 2 shows univariate (unadjusted) analyses of VE by vaccination status, age group, and brand of vaccine against three clinical outcomes — symptomatic COVID-19, COVID-19 pneumonia, and severe COVID-19. For adjusted vaccine effectiveness, multivariable regression analyses controlled for gender, presence of underlying conditions (comorbidities), and age group (18–59 and 60+ years).

Table 3 shows adjusted and unadjusted VE by vaccine brand and vaccination status against the 3 clinical outcomes. Completed primary vaccination VEs for adults 18 years and over were 50.54% against symptomatic COVID-19, 61.4% against COVID-19 pneumonia, and 82.41% against severe COVID-19. Partial vaccination had non-statistically-significant VEs against the clinical outcomes.

Table 4 shows adjusted and unadjusted VE by time between vaccination and exposure to SARS-CoV-2. Of the 784 people who completed primary vaccination, the average time from completing full vaccination (plus 14 days) to becoming a close contact was 76 days (range, 14–193 days); 572 (72.96%) completed primary vaccination three months or less before becoming a close contact, and 212 people (27.04%) had intervals 4 to 6 months following full vaccination. The adjusted VE of full vaccination against symptomatic COVID-19 was 52.32% for ≤3-month intervals and 49.95% for 4–6-month intervals (both statistically significant); against COVID-19 pneumonia, VEs were 67.08% for 4–6-month intervals; and against severe COVID-19, VEs were 80.64% for ≤3-month intervals. There were no severe cases for longer intervals.

Table 5 shows severity of COVID-19 by vaccination status. The 145 infected individuals aged ≥18 years were categorized as having mild (asymptomatic and mild cases together) or pneumonia/severe (moderate, severe, and critically severe combined together)

TABLE 1. Characteristics of the study population.

Type of study population	Characteristics	No. of unvaccinated (%)	Vaccinated with BBIBP-CorV (%)		Vaccinated with CoronaVac (%)		Vaccinated with BBIBP-CorV and CoronaVac (%)		Total (%)	
			Partially	Completely primary	Partially	Completely primary	Partially	Completely primary	Partially	Completely primary
Close contacts	Gender									
	Male	232 (49.05)	51 (66.23)	97 (45.97)	59 (49.58)	135 (40.18)	5 (55.56)	122 (51.48)	115 (56.10)	354 (45.15)
	Female	241 (50.95)	26 (33.77)	114 (54.03)	60 (50.42)	201 (59.82)	4 (44.44)	115 (48.52)	90 (43.90)	430 (54.85)
	Age group (years)									
	18–59	408 (86.26)	69 (89.61)	199 (94.31)	106 (89.08)	329 (97.92)	9 (100)	212 (89.45)	184 (89.76)	740 (94.39)
	≥60	65 (13.74)	8 (10.39)	12 (5.69)	13 (10.92)	7 (2.08)	0	25 (10.55)	21 (10.24)	44 (5.61)
	Comorbidities									
	None	360 (76.11)	72 (93.51)	191 (90.52)	105 (88.24)	309 (91.96)	9 (100)	213 (89.87)	186 (90.73)	713 (90.94)
	Yes	113 (23.89)	5 (6.49)	20 (9.48)	14 (11.76)	27 (8.04)	0	24 (10.13)	19 (9.27)	71 (9.06)
	Total	473	77	211	119	336	9	237	205	784
People with infection	Clinical outcome									
	Asymptomatic	0	0	0	0	1 (5.55)	0	0	0	1 (2.86)
	Mild	13 (21.31)	1 (25.00)	3 (33.33)	3 (42.86)	10 (55.56)	0	2 (25.00)	4 (36.36)	15 (42.86)
	Moderate	33 (54.10)	2 (50.00)	6 (66.67)	3 (42.86)	7 (38.89)	0	4 (50.00)	5 (45.46)	17 (48.57)
	Severe	9 (14.75)	1 (25.00)	0	1 (14.28)	0	0	2 (25.00)	2 (18.18)	2 (5.71)
	Critical severe	6 (9.84)	0	0	0	0	0	0	0	0
	Total	61	4	9	7	18	0	8	11	35

TABLE 2. Inactivated vaccine effectiveness against clinical outcomes by age group.

Outcome	Vaccination history	18 to 59 years old		≥60 years old		Total (≥18 years old)	
		Percentage/% (case/total infection)	Unadjusted VE/% (95% CI)	Percentage/% (case/total infection)	Unadjusted VE/% (95% CI)	Percentage/% (case/total infection)	Unadjusted VE/% (95% CI)
Symptomatic disease	Unvaccinated	10.29 (42/408)	Ref	29.23 (19/65)	Ref	12.90 (61/473)	Ref
	Partially	4.89 (9/184)	52.48 (4.45 to 76.37)	9.52 (2/21)	67.42 (−28.41 to 91.73)	5.37 (11/205)	58.39 (22.60 to 77.63)
	Completely primary	4.32 (32/740)	57.99 (34.53 to 73.05)	4.55 (2/44)	84.45 (36.57 to 89.63)	4.34 (34/784)	66.37 (49.65 to 77.54)
	BBIBP-CorV	4.52 (9/199)	56.07 (11.55 to 78.18)	0 (0/12)	—	4.27 (9/211)	66.93 (34.66 to 83.26)
	CoronaVac	5.17 (18/329)	49.80 (13.49 to 70.88)	0 (0/7)	—	5.06 (17/336)	60.77 (34.07 to 76.65)
	Combined	2.83 (6/212)	72.51 (36.37 to 88.12)	8.00 (2/25)	72.63 (−9.01 to 93.13)	3.38 (8/237)	73.83 (46.21 to 87.26)
Pneumonia	Unvaccinated	7.84 (32/408)	Ref	24.62 (16/65)	Ref	10.15 (48/473)	Ref
	Partially	3.26 (6/184)	58.42 (47.91 to 83.53)	4.76 (1/21)	80.65 (−37.27 to 97.27)	3.41 (7/205)	66.35 (26.90 to 84.51)
	Completely primary	2.30 (17/740)	70.71 (47.91 to 83.53)	4.55 (2/44)	81.53 (23.66 to 95.53)	2.42 (19/784)	76.12 (59.88 to 85.79)
	BBIBP-CorV	3.02 (6/199)	61.56 (9.58 to 83.66)	0 (0/12)	—	2.84 (6/211)	71.98 (35.54 to 87.82)
	CoronaVac	5.77 (17/329)	72.87 (39.33 to 87.87)	0 (0/7)	—	2.08 (7/336)	79.47 (55.19 to 90.59)
	Combined	1.89 (4/212)	75.94 (32.88 to 91.38)	8.0 (2/25)	67.50 (−31.23 to 91.95)	2.53 (6/237)	75.05 (42.55 to 89.17)
Severe case	Unvaccinated	1.47 (6/408)	Ref	13.85 (9/65)	Ref	3.17 (15/473)	Ref
	Partially	0.54 (1/184)	63.04 (−204.78 to 95.52)	4.76 (1/21)	65.61 (−155.79 to 95.38)	0.98 (2/205)	69.24 (−33.30 to 92.90)
	Completely primary	0 (0/740)	—	4.55 (2/44)	67.17 (−44.74 to 92.55)	0.26 (2/784)	91.96 (64.98 to 98.15)
	BBIBP-CorV	0 (0/199)	—	0 (0/12)	—	0 (0/211)	—
	CoronaVac	0 (0/329)	—	0 (0/7)	—	0 (0/336)	—
	Combined	0 (0/212)	—	8.0 (2/25)	42.22 (−149.05 to 86.60)	0.84 (2/237)	73.39 (−15.41 to 93.86)

Note: "—" Means no data were available.
Abbreviations: CI=Confidence interval; VE=vaccine effectiveness.

TABLE 3. Vaccine effectiveness by brand of COVID-19 vaccine.

Outcome	Vaccination history	Completely primary vaccination			Partially vaccination		
		Percentage/% (case/total infection)	Unadjusted VE/% (95% CI)	Adjusted VE/% (95% CI)	Percentage/% (case/total infection)	Unadjusted VE/% (95% CI)	Adjusted VE/% (95% CI)
Symptomatic disease	Unvaccinated	12.90 (61/473)	Ref	Ref	12.90 (61/473)	Ref	Ref
	Vaccinated	4.34 (34/784)	66.37 (49.65 to 77.54)	50.54 (27.59 to 66.21)	5.37 (11/205)	58.39 (22.60 to 77.63)	33.76 (−17.53 to 62.67)
	BBIBP-CorV	4.27 (9/211)	66.93 (34.66 to 83.26)	50.56 (3.79 to 74.59)	5.19 (4/77)	59.72 (−7.59 to 84.92)	24.72 (−98.83 to 71.49)
	CoronaVac	5.06 (17/336)	60.77 (34.07 to 76.65)	39.12 (−0.91 to 63.27)	5.88 (7/119)	54.39 (2.87 to 78.58)	29.95 (−44.33 to 66.00)
	Combined	3.38 (8/237)	73.83 (46.21 to 87.26)	59.94 (19.09 to 80.17)	0 (0/9)	—	—
Pneumonia	Unvaccinated	10.15 (48/473)	Ref	Ref	10.15 (48/473)	Ref	Ref
	Vaccinated	2.42 (19/784)	76.12 (59.88 to 85.79)	61.40 (36.05 to 76.70)	3.41 (7/205)	66.35(26.90 to 84.51)	45.92 (−15.82 to 74.75)
	BBIBP-CorV	2.84 (6/211)	71.98 (35.54 to 87.82)	54.71 (−3.42 to 80.16)	3.90 (3/77)	61.61(−20.2 to 87.74)	16.33 (−164.3 to 73.52)
	CoronaVac	2.08 (7/336)	79.47 (55.19 to 90.59)	64.90 (22.88 to 84.02)	3.36 (4/119)	66.88(9.96 to 87.81)	52.65 (−25.19 to 82.09)
	Combined	2.53 (6/237)	75.05 (42.55 to 89.17)	62.15 (13.95 to 83.35)	0 (0/9)	—	—
Severe case	Unvaccinated	3.17 (15/473)	Ref	Ref	3.17 (15/473)	Ref	Ref
	Vaccinated	0.26 (2/784)	91.96 (64.98 to 98.15)	82.41 (21.03 to 96.08)	0.98 (2/205)	69.24 (−33.30 to 92.90)	44.48 (−162.62 to 88.26)
	BBIBP-CorV	0 (0/211)	—	—	1.30 (1/77)	59.05 (−205.6 to 94.51)	7.49 (−655.64 to 88.68)
	CoronaVac	0 (0/336)	—	—	0.84 (1/119)	73.5 (−98.62 to 96.46)	59.75 (−209.91 to 94.77)
	Combined	0.84 (2/237)	73.39 (−15.41 to 93.86)	61.35 (−71.62 to 91.30)	0 (0/9)	—	—

Note: "—" Means no data were available.
Abbreviations: CI=Confidence interval; VE=vaccine effectiveness.

TABLE 4. Vaccine effectiveness by time since vaccination.

Outcome	Vaccination history	Duration ≤ 3 months			Duration 4−6 months		
		Percentage/% (case/total infection)	Unadjusted VE/% (95% CI)	Adjusted VE/% (95% CI)	Percentage/% (case/total infection)	Unadjusted VE/% (95% CI)	Adjusted VE/% (95% CI)
Symptomatic disease	Unvaccinated	12.90 (61/473)	Ref	Ref	12.90 (61/473)	Ref	Ref
	Completely primary	4.34 (34/784)	66.11 (46.89 to 78.37)	52.32 (25.73 to 69.39)	5.37 (11/205)	67.08 (34.97 to 83.34)	49.95 (1.20 to 74.64)
	BBIBP-CorV	5.48 (8/146)	57.51 (13.30 to 79.18)	39.37 (−20.41 to 69.46)	1.54 (1/65)	88.07 (15.41 to 98.32)	82.00 (−25.73 to 97.42)
	CoronaVac	4.64 (9/194)	64.03 (29.02 to 81.77)	45.50 (−5.98 to 71.97)	5.63 (8/142)	56.32 (10.90 to 78.58)	29.83 (−41.09 to 65.11)
	Combined	3.45 (8/232)	73.26 (45.06 to 86.99)	59.50 (18.31 to 79.92)	0 (0/5)	—	—
Pneumonia	Unvaccinated	10.15 (48/473)	Ref	Ref	10.15 (48/473)	Ref	Ref
	Completely primary	2.42 (19/784)	74.16 (54.45 to 85.34)	60.31 (31.31 to 77.07)	3.41 (7/205)	81.41 (49.10 to 93.21)	67.08 (9.33 to 88.05)
	BBIBP-CorV	4.11 (6/146)	59.51 (7.30 to 82.31)	39.63 (−35.46 to 73.10)	0 (0/65)	—	—
	CoronaVac	1.55 (3/194)	84.76 (51.66 to 95.20)	73.85 (17.91 to 91.67)	2.82 (4/142)	72.24 (24.35 to 89.81)	47.41 (−44.35 to 80.84)
	Combined	2.59 (6/232)	74.52 (41.32 to 88.93)	61.79 (13.21 to 83.18)	0 (0/5)	—	—
Severe case	Unvaccinated	3.17 (15/473)	Ref	Ref	3.17 (15/473)	Ref	Ref
	Completely primary	0.26 (2/784)	88.97 (52.03 to 97.47)	80.64 (13.16 to 95.68)	0.98 (2/205)	—	—
	BBIBP-CorV	0 (0/146)	—	—	0 (0/65)	—	—
	CoronaVac	0 (0/194)	—	—	0 (0/142)	—	—
	Combined	0.86 (2/232)	72.81 (−17.88 to 93.73)	61.11 (−72.65 to 91.24)	0 (0/5)	—	—

Note: "—" Means no data were available.
Abbreviations: CI=Confidence interval; VE=vaccine effectiveness.

TABLE 5. Severity of illness by vaccination status.

Age groups	Vaccination history	Mild cases (asymptomatic+mild)		Pneumonia (moderate+severe)		OR	95% CI
		n	%	n	%		
18–59 years old	Unvaccinated	13	30.95	40	55.56	Ref	Ref
	Partially	6	14.29	10	13.89	0.54	0.16 to 1.78
	Completely primary	23	54.76	22	30.56	0.31	0.13 to 0.73
	Sub-total	42	100	72	100		
≥60 years old	Unvaccinated	3	50.00	21	84.00	Ref	Ref
	Partially	1	16.67	1	4.00	0.16	0.002 to 14.92
	Completely primary	2	33.33	3	12.00	0.23	0.017 to 3.81
	Sub-total	6	100	25	100		
Total	Unvaccinated	16	33.33	61	62.89	Ref	Ref
	Partially	7	14.58	11	11.34	0.41	0.14 to 1.23
	Completely primary	25	52.08	25	25.77	0.26	0.12 to 0.57
	Sub-total	48	100	97	100		

Abbreviations: OR=odds ratio; CI=confidential interval.

COVID-19. Compared with the unvaccinated, completed primary vaccination reduced the risk of pneumonia/severe COVID-19 by 74% [95% confidence interval (CI): 43% to 88%]. By age grouping, pneumonia/severe risk was reduced by 69% (95% CI: 27% to 87%) among 18–59-year-olds and by 77% (95% CI: –281% to 98%, not statistically significant) among people over 60 years old.

DISCUSSION

To our knowledge, this is the first single-study evaluation of brand-specific vaccine effectiveness of the two China-produced inactivated COVID-19 vaccines approved for emergency use by WHO. Our study showed that completed primary vaccination with BBIBP-CorV and CoronaVac inactivated vaccines separately or combined had similar effectiveness against the Delta variant as was seen in the Phase 3 placebo-controlled licensure clinical trials that were conducted when the ancestral SARS-CoV-2 strain circulated (*4*–*5*). In this outbreak, centered in a hospital, inactivated VE levels against symptomatic COVID-19, COVID-19 pneumonia, and severe COVID-19 caused by the Delta variant were 51%, 61%, and 82%. Completed primary vaccination reduced the risk of progressing from mild to moderate or severe COVID-19 by 74%.

VE of the inactivated vaccine against symptomatic COVID-19 caused by the Delta variant in this outbreak was similar to VE estimates in other real-world studies against ancestral or earlier variants, also shown in other types of vaccines. A cohort study in Peru showed BBIBP-CorV VE against infection and death from pre-Delta variants of concern were 50% and 94%, respectively (*6*). A cohort study in Hungary estimated BBIBP-CorV effectiveness to be 87% against symptomatic COVID-19 and 88% against COVID-19 death caused by pre-Delta variants. A cohort study in Chile investigated the VE of CoronaVac found that the adjusted VE of completely primary vaccination was 65.9% against COVID-19, 87.4% against hospitalization, 90.3% against ICU admission, and 86.3% against COVID-19-related death (*7*). Inactivated vaccine effectiveness against COVID-19 pneumonia was similar to what was observed in a Delta-variant outbreak in Guangdong Province (61.4% *vs.* 69.5%) (*8*). Other COVID-19 vaccines, including mRNA and adenovirus-vectored retain effectiveness against the Delta variant (*9*).

VEs for BBIBP-CorV and CoronaVac or combined vaccination were similar, and partial vaccination was not effective. We used a case-control design to determine the ability of inactivated vaccines to prevent progression from mild to moderate or severe COVID-19, finding that complete primary vaccination reduced the risk of progression by 74%, thus demonstrating good effectiveness in this real world study, although there were differences for the point estimates of VE against symptomatic disease and against pneumonia.

We used a case-control design to determine the

ability of inactivated vaccines to prevent progression from mild to moderate or severe illness, finding that complete primary vaccination reduced the risk of progression by 74%, thus demonstrating good effectiveness in this real world study.

Our study has program and policy implications. First, evidence of effectiveness of both inactivated vaccines against the Delta variant, when given separately or together, supports continuation of the vaccination campaign to ensure that entire target populations are reached with full-series vaccination. Although completed primary series in the same brand are preferred, our study shows that interchangeable schedules are also effective. Our findings of brand-specific VE are new findings that were made possible by the widespread use of both vaccines in China and worldwide. Second, VEs were effective against pneumonia and severe cases caused by Delta variant compared with another ancestral variant.

This study was subject to some limitations. Because 90% of people living with HIV or who had tuberculosis had not been vaccinated, our study could not estimate VE in these special populations. Since these two special populations were high-risk groups for infection, their presence in the close-contact subjects may potentially impact the effectiveness of the vaccine. As an observational study, there may have been unmeasured confounding variables that could affect VE estimates. The study was conducted in a limited area in small-scale outbreak, which limited its sample size and therefore the ability to perform subgroup analyses. Also, rigorous non-pharmaceutical interventions may have affected VE in unknown directions. Finally, the durations from last dose to exposure were all less than 6 months, and most were concentrated in length around 2–3 months; although we found no decline in VE over time, none of the close contacts in our study had been vaccinated more than 6 months prior to becoming a close contact. Therefore, longer duration of effectiveness could not be shown in our study.

In conclusion, completed primary vaccination with 2 doses of the inactivated COVID-19 vaccines was effective against symptomatic COVID-19, COVID-19 pneumonia, and severe COVID-19 caused by the Delta variant of SARS-CoV-2 within 6 months. There were no significant differences in effectiveness of the 2 inactivated COVID-19 vaccines we evaluated. Although completed primary series with the same brand is recommended, combined primary series appear to be as effective. COVID-19 vaccine coverage of people over 60 years of age and potentially immunocompromised individuals needs to be improved.

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Preplanned Studies

Willingness of the General Public to Receive A COVID-19 Vaccine Booster — China, April–May 2021

Xiaoxiao Wang[1,&]; Leyuan Liu[2,&]; Minyue Pei[1]; Xiaoguang Li[2,#]; Nan Li[1,#]

Summary

What is already known about this topic?

A coronavirus disease 2019 (COVID-19) vaccine booster is planned for administration to eligible individuals. Understanding the factors that influence attitudes towards the booster shot will help to identify groups that will most readily accept a booster dose.

What is added by this report?

Of the individuals polled, 75.2% reported they would receive a booster shot. Sociodemographic characteristics influencing booster vaccine acceptance included age, gender, occupation, and education. Moreover, those who had been vaccinated against influenza, who believed herd immunity would be effective against severe acute respiratory syndrome coronavirus 2, and who reported reduced anxiety after vaccination were more likely to accept a booster dose.

What are the implications for public health practice?

A booster shot of the COVID-19 vaccine could be widely accepted. Communicating about the effectiveness of the COVID-19 vaccine and the impact of infection on people's health could help increase public willingness to get a booster dose.

On October 11, 2021, the strategic advisory group of experts (SAGE) of the World Health Organization (WHO) recommended that an additional dose of coronavirus disease 2019 (COVID-19) vaccine should be offered to moderately and severely immunocompromised people and to those aged 60 and over who were previously immunized with Sinovac or Sinopharm inactivated vaccines (*1*). The National Health Commission of the People's Republic of China (NHC) and the United States Centers for Disease Control Advisory Committee on Immunization Practices (ACIP) are planning a COVID-19 vaccine booster so that vaccinated people can maintain protection over the coming months (*2–3*). Numerous studies have shown that vaccination willingness is influenced by a variety of factors and that it changes over time (*4–5*). It is necessary to understand the public's willingness to receive a COVID-19 vaccine booster. Identifying factors that influence booster vaccine acceptance will aid in determining who is most likely to accept a booster dose.

Online questionnaires were completed by 2,047 vaccinated Chinese adults in April and May 2021. Respondents' sociodemographic characteristics, attitudes towards vaccination, and attitudes towards a COVID-19 vaccine booster were collected. All data were analyzed using R statistical software (version 4.0.3, R Core Team, Vienna, Austria). Logistic regression models were built to identify factors associated with respondents' acceptance of a COVID-19 vaccine booster. The odds ratio (OR) and its corresponding 95% confidence interval (CI) were calculated.

Of the respondents, 75.2% reported they planned to receive a booster shot. Respondents who expressed significantly higher acceptance of a booster dose tended to be aged 25–54 years old, male, non-healthcare workers, and less educated. Moreover, those who had been vaccinated against influenza (OR=1.26, 95% CI: 1.01–1.57), who believed herd immunity would be effective against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (OR=3.58, 95% CI: 2.69–4.77), or who reported reduced anxiety after vaccination (OR=1.27, 95% CI: 1.02–1.59) were more likely to report planning to receive a booster dose.

Based on these results, it seems that a booster shot of the COVID-19 vaccine could be widely accepted in China. Communicating to the public the effectiveness of COVID-19 vaccines and the impact of COVID-19 infection on one's health could increase individuals' willingness to receive a booster dose.

In April and May 2021, an online questionnaire was disseminated via WeChat, a Chinese multipurpose social media app. Using WeChat moments, which spread questionnaires by snowballing, 1,656 respondents were recruited. To reduce the risk of bias due to starting with a single sample source, 403

additional respondents were recruited via the Tencent questionnaire sample database. This database contains over 1 million people with verified personal information, and we used the recruitment service to recruit subjects aged ≥18. Incomplete questionnaires were excluded. The final sample consisted of 2,047 respondents. Respondents' sociodemographic characteristics, flu vaccination history, attitudes towards herd immunity, anxiety levels after initial vaccination, acceptance of a booster shot, and antibody tests were collected. The study was approved by Peking University Third Hospital Medical Science Research Ethics Committee (No. 2021-184-01).

The age- and gender-standardized acceptance rate of a COVID-19 vaccine booster was calculated using the 2010 population census of China as the reference (*6*). Logistic regression models were built to identify factors influencing COVID-19 vaccine booster acceptance (event: receiving COVID-19 vaccine booster when available). All data were analyzed using R statistical software. A *P*-value <0.05 was considered statistically significant.

Of the 2,047 vaccinated respondents (Table 1), 1,540 (75.2%) reported that they planned to receive a COVID-19 vaccine booster shot when it was available. The age- and gender-standardized acceptance rate was 75.8% (Table 2). In addition, 1,257 (81.6% of those who planned to receive the booster shot) reported that they would receive antibody tests, which could help to determine the effectiveness of the booster dose.

COVID-19 vaccine booster acceptance rate was highest among adults aged 45–54 years (81.2%) and lowest among adults aged ≥65 years (69.6%). Male respondents were more likely than female respondents to accept a COVID-19 vaccine booster (80.2% *vs.* 72.2%), and those who were not healthcare workers were more likely to accept a booster dose than healthcare workers (79.3% *vs.* 67.0%). Respondents who held a bachelor's degree or below were more likely to accept a booster dose (68.9%, 74.5%, 83.3%, *vs.* 85.4%). Vaccine booster acceptance was slightly higher among respondents who earned <5,000 CNY per month (77.7% *vs.* 73.6%). Respondents who lived in rural areas were more likely to accept a booster dose (83.1% *vs.* 74.1%). Moreover, those who had been vaccinated against influenza (77.7% *vs.* 73.4% who had not been), who believed herd immunity would be effective against SARS-CoV-2 (78.9% *vs.* 47.5% who did not believe this), and who reported reduced anxiety after vaccination (77.0% *vs.* 71.7% who did not report this) were more likely to accept a booster dose.

TABLE 1. Characteristics of the study population.

Characteristics	WeChat sample (n=1,644)	Tencent sample (n=403)
Age group, years		
18–24	184 (11.3)	14 (3.5)
25–34	614 (37.6)	18 (4.5)
35–44	451 (27.6)	43 (10.7)
45–54	254 (15.5)	245 (60.8)
55–64	91 (5.6)	68 (16.9)
≥65	41 (2.5)	15 (3.7)
Gender		
Male	613 (37.3)	164 (40.7)
Female	1,031 (62.7)	239 (59.3)
Non-healthcare staff		
Yes	973 (59.2)	398 (98.8)
No	671 (40.8)	5 (1.2)
Education		
Junior high school and below	105 (6.4)	135 (33.5)
Senior high school	78 (4.7)	216 (53.6)
Associate or bachelor	809 (49.2)	49 (12.2)
Master and above	652 (39.7)	3 (0.7)
Income (CNY per month)		
0–2,000	201 (12.2)	106 (26.3)
2,000–5,000	300 (18.3)	221 (54.8)
5,000–10,000	459 (27.9)	66 (16.4)
10,000 and above	684 (41.6)	10 (2.5)
Area type		
Rural	1,498 (91.6)	285 (70.9)
Urban	138 (8.4)	117 (29.1)
Flu vaccination history		
Yes	680 (41.4)	189 (46.9)
No/unsure	964 (58.6)	214 (53.1)
Whether herd immunity works		
Yes	1,423 (86.6)	382 (94.8)
No/unsure	221 (13.4)	21 (5.2)
Whether vaccination help reduce anxiety		
Yes	1,098 (66.8)	268 (66.5)
No	546 (33.2)	135 (33.5)

Note: All data are described in term of "Number (%) of participants".
Abbreviation: CNY=China Yuan.

The multiple logistic regression model identified the people most likely to get the booster dose as soon as it was available (Table 3). Those who expressed significantly higher acceptance of a booster dose included respondents who were: 25–34 years old

TABLE 2. The process of calculating age- and gender- standardized acceptance rate of a COVID-19 vaccine booster.

Age (year)	Gender	Observed acceptance rates (%)	Population according to census 2016	Expected number
18–24	Female	71.0	83,878,762	59,553,921
	Male	77.0	85,832,496	66,091,022
25–34	Female	69.0	97,793,195	67,477,305
	Male	76.4	100,358,860	76,674,169
35–44	Female	73.1	118,780,141	86,828,283
	Male	80.5	123,999,782	99,819,825
45–54	Female	78.3	90,208,072	70,632,920
	Male	86.2	94,139,652	81,148,380
55–64	Female	67.7	69,062,392	46,755,239
	Male	81.8	70,917,364	58,010,404
≥65	Female	60.6	49,507,029	30,001,260
	Male	82.6	48,430,783	40,003,827
Total		75.2	1,032,908,528	782,996,554

Note: The age- and gender- standardized acceptance rate of a COVID-19 vaccine booster equals 75.8%.
Abbreviation: COVID-19=coronavirus disease 2019.

(OR=2.06, 95% CI: 1.09–3.91); 35–44 years old (OR=2.24, 95% CI: 1.18–4.28); 45–54 years old (OR=2.07, 95% CI: 1.09–3.94); male (OR=1.33, 95% CI: 1.05–1.67); and non-healthcare workers (OR=1.50, 95% CI: 1.17–1.92). Booster shot acceptance was also higher among those who had: a junior high school level of education or below (OR=2.64, 95% CI: 1.50–4.62); a high school level of education (OR=2.12, 95% CI: 1.34–3.35); and who had been vaccinated against influenza (OR=1.26, 95% CI: 1.01–1.57). Finally, those who believed herd immunity would be effective against SARS-CoV-2 or who reported reduced anxiety after vaccination were more likely to accept a booster dose (OR=3.58, 95% CI: 2.69–4.77 and OR=1.27, 95% CI: 1.02–1.59, respectively).

DISCUSSION

This survey demonstrated that most of the vaccinated respondents (75.2%) would accept a COVID-19 vaccine booster shot when it became available. Although data on the efficacy and safety of the booster shot are still lacking, booster shots have a higher level of acceptance now than earlier doses of the vaccines did (*4*). Multiple studies have shown that vaccine acceptance changes over time, and the proportion of people who accept a vaccine may rise as the pandemic continues to fluctuate and the safety of vaccines is properly reported (*4–5*). Sociodemographic characteristics were important factors affecting the acceptability of the COVID-19 vaccine booster. Respondents who were aged 25–54 years old, male, non-healthcare workers, and less educated expressed significantly higher acceptance of the booster dose. According to WHO recommendations, people aged 60 or older who received inactivated vaccines should receive booster shots. The relatively low acceptance among people over 60 is therefore of great concern.

Moreover, those who had been vaccinated against influenza (OR=1.26, 95% CI: 1.01–1.57), who believed herd immunity would be effective against SARS-COV-2 (OR=3.58, 95% CI: 2.69–4.77) or who reported reduced anxiety after vaccination (OR=1.27, 95% CI: 1.02–1.59) were more likely to accept a booster dose. These results suggest that strong confidence in the vaccines would lead to more people getting vaccinated, which is consistent with previous studies (*7–8*). Therefore, efforts focused on clearly communicating to the public the effectiveness and safety of the COVID-19 booster vaccination and the risk of getting sick and dying from COVID-19 could help increase public willingness to get vaccinated.

This is the first study to address public acceptance of a booster shot of COVID-19 vaccines, and we find that they are likely to be widely accepted. This survey identifies priority groups to target for COVID-19 vaccine booster shots, which is of crucial importance in public health policy implementation (*9*).

This study was subject to some limitations. First is that convenience sampling was used, which may affect the representativeness of the individuals sampled compared to the population as a whole. The epidemic

TABLE 3. Influencing factors on COVID-19 vaccine booster preference.

Characteristics	COVID-19 vaccinebooster preference		Univariate analysis		Multivariate analysis	
	No (percentage %)	Yes (percentage %)	Crude OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Age group, years						
18–24	53 (26.8)	145 (73.2)	1.19 (0.62, 2.29)	0.596	1.99 (0.97, 4.10)	0.062
25–34	178 (28.2)	454 (71.8)	1.11 (0.61, 2.02)	0.727	2.06 (1.09, 3.91)	0.026
35–44	119 (24.1)	375 (75.9)	1.37 (0.75, 2.52)	0.304	2.24 (1.18, 4.28)	0.014
45–54	94 (18.8)	405 (81.2)	1.88 (1.02, 3.46)	0.044	2.07 (1.09, 3.94)	0.026
55–64	42 (26.4)	117 (73.6)	1.21 (0.62, 2.37)	0.570	1.14 (0.56, 2.30)	0.719
≥65	17 (30.4)	39 (69.6)	Ref.		Ref.	
Gender				<0.001		0.016
Male	154 (19.8)	623 (80.2)	1.56 (1.26, 1.93)		1.33 (1.05, 1.67)	
Female	353 (27.8)	917 (72.2)	Ref.		Ref.	
Non-healthcare staff				<0.001		0.002
Yes	284 (20.7)	1,087 (79.3)	1.88 (1.53, 2.32)		1.50 (1.17, 1.92)	
No	223 (33.0)	453 (67.0)	Ref.		Ref.	
Education						
Junior high school and below	35 (14.6)	205 (85.4)	2.65 (1.79, 3.93)	<0.001	2.64 (1.50, 4.62)	0.001
Senior high school	49 (16.7)	245 (83.3)	2.26 (1.60, 3.20)	<0.001	2.12 (1.34, 3.35)	0.001
Associate or bachelor	219 (25.5)	639 (74.5)	1.32 (1.05, 1.65)	0.016	1.26 (0.98,1.63)	0.070
Master and above	204 (31.1)	451 (68.9)	Ref.		Ref.	
Income (CNY per month)						
0–2,000	71 (23.1)	236 (76.9)	1.22 (0.89, 1.67)	0.220	0.64 (0.40, 1.01)	0.054
2,000–5,000	114 (21.9)	407 (78.1)	1.31 (1.00, 1.71)	0.049	0.83 (0.59, 1.16)	0.269
5,000–10,000	136 (25.9)	389 (74.1)	1.05 (0.81, 1.36)	0.725	0.86 (0.65, 1.15)	0.309
10,000 and above	186 (26.8)	508 (73.2)	Ref.		Ref.	
Residence				0.002		0.553
Rural	43 (16.9)	212 (83.1)	1.72 (1.22, 2.43)		1.14 (0.74, 1.76)	
Urban	461 (25.9)	1,322 (74.1)	Ref.		Ref.	
Flu vaccination history				0.028		0.039
Yes	194 (22.3)	675 (77.7)	1.26 (1.03, 1.55)		1.26 (1.01, 1.57)	
No/unsure	313 (26.6)	865 (73.4)	Ref.		Ref.	
Whether herd immunity works				<0.001		<0.001
Yes	380 (21.1)	1,425 (78.9)	4.14 (3.14, 5.46)		3.58 (2.69, 4.77)	
No/unsure	127 (52.5)	115 (47.5)	Ref.		Ref.	
Whether vaccination help reduce anxiety				0.008		0.035
Yes	314 (23.0)	1,052 (77.0)	1.33 (1.08, 1.63)		1.27 (1.02, 1.59)	
No	193 (28.3)	488 (71.7)	Ref.		Ref.	

Abbreviations: COVID-19=coronavirus disease 2019; OR=odds ratio; CI=confidence interval; CNY=China Yuan; Ref.=reference.

was relatively stable when the survey was conducted and therefore not causing a great amount of panic among members of the public, which suggests that this sample provided some insight to public willingness to get a booster dose. Second, acceptance of a COVID-19 vaccine booster could also be influenced by information spread in the media and on social networks, including the local number of daily confirmed cases, the capacity of healthcare services, and relevant policies in different areas. However, we are

unable to consider these issues in this study due to unavailability of the data. Further investigation is therefore needed in the future.

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Perspectives

Bubble Strategy — A Practical Solution to Return to Regular Life in the Intertwined Era of Vaccine Rollouts and Virus Mutation

Ying Shen[1]; Da Huo[1]; Tong Yu[1]; Quanyi Wang[1,#]

ABSTRACT

For a long time, vaccination and herd immunity were considered to be the magic solution for controlling coronavirus disease 2019 (COVID-19). However, the emergence of new variants altered people's expectations and prolonged the pandemic duration, especially the Omicron strain with substantially increased transmissibility and decreased vaccine efficacy. Therefore, we are in urgent need of a practical solution to resume regular life to some extent, while mitigating COVID-19 risks in the tight race between vaccine rollouts and virus variation. This commentary proposed that bubble strategy (or closed loop management), utilized in Tokyo 2020 Olympic Games and to be implemented in Beijing 2022 Winter Games, could serve as a novel technique of non-pharmaceutical interventions in coping with such a situation.

The second and final version of the Playbooks for the Olympic and Paralympic Winter Games Beijing 2022 were jointly released on December 13, 2021 by the International Olympic Committee (IOC), International Paralympic Committee (IPC), and Beijing 2022 (*1*). With a "closed-loop management" strategy to be strictly implemented from before the Games to the end of the Paralympic Winter Games, the playbooks exhibited the resolution and confidence of IOC, IPC, and Beijing 2022 to deliver safe and successful Games. Based upon the dynamic of the COVID-Zero strategy towards COVID-19 currently in place in China and considering that local cases only occasionally emerged, the closed loop management implemented for Beijing 2022 is rather comprehensive and rigorous. Once an individual enters the loop, all his/her activities will be subject to closed loop management of the same standard covering accommodation, transport, catering, training, competitions, and arrival and departure, regardless of his/her identity as foreign nationals or domestic workers. A dedicated transport system will be established for the Games, through which the Games participants will be allowed to move between permitted destinations. Based on the current requirements outlined in the Playbooks, the closed loop is sophisticated and rigorous, and will undoubtedly serve as a model for bubble strategies in global mass gathering events in the context of heterogeneous COVID-19 risk potentials between countries.

In the intertwined era of vaccine rollouts and virus variations, bubble strategy has its special implications. For a long time, vaccination and herd immunity are considered to be the solution for COVID-19. Most studies have estimated the threshold for herd immunity as 60%–70% of total population vaccinated or infected (*2*). However, the emergence of virus variants, especially the newly emerged Omicron strain, altered people's expectation and may prolong the pandemic duration. The resurgence of COVID-19 in Manaus, Brazil was a recent example, where the Gamma strain severely hit the city that was already presumed as herd immunized by October 2020, infecting over 70% of the population (*3*). Similarly, a recent study in Massachusetts, the United State reported that almost 75% of infections (346 cases) in this study occurred in fully vaccinated individuals and the vaccination coverage among eligible Massachusetts residents had already reached 69% (*4*). In the context of measles, whose R_0 is as high as 12 to 18, 95% vaccination coverage is sufficient to prevent local transmission (*5*). However, this might not be true for COVID-19 due to various reasons, although its R_0 is much lower at 1.9 to 6.5 (*6*–*7*). Constant virus mutations in COVID-19 hotspots along with vaccination hesitancy, uneven vaccine rollout status, breakthrough infections, and waning immunity make it possible that we will hardly achieve herd immunity in the foreseeable future. Therefore, we are in urgent need of a practical solution to resume regular life to some extent while mitigating COVID-19 risks in the tight race between vaccine

rollouts and virus variation. The bubble strategy, or more accurately, the closed loop management to be implemented in the Beijing 2022 Games happens to be one.

There were already some successful bubble strategies in practice, such as the bubble to bubble management utilized in the Tokyo 2020 Games, which was held in a special circumstance where community transmission of COVID-19 was still rampant, and Japan was trapped in a state of emergency. On the day of the opening ceremony (July 23, 2021) alone, Tokyo reported 1,359 positive cases (*8*). Against such background, Figure 1 suggested that although there might have been some haphazard enforcement that may have caused leaking

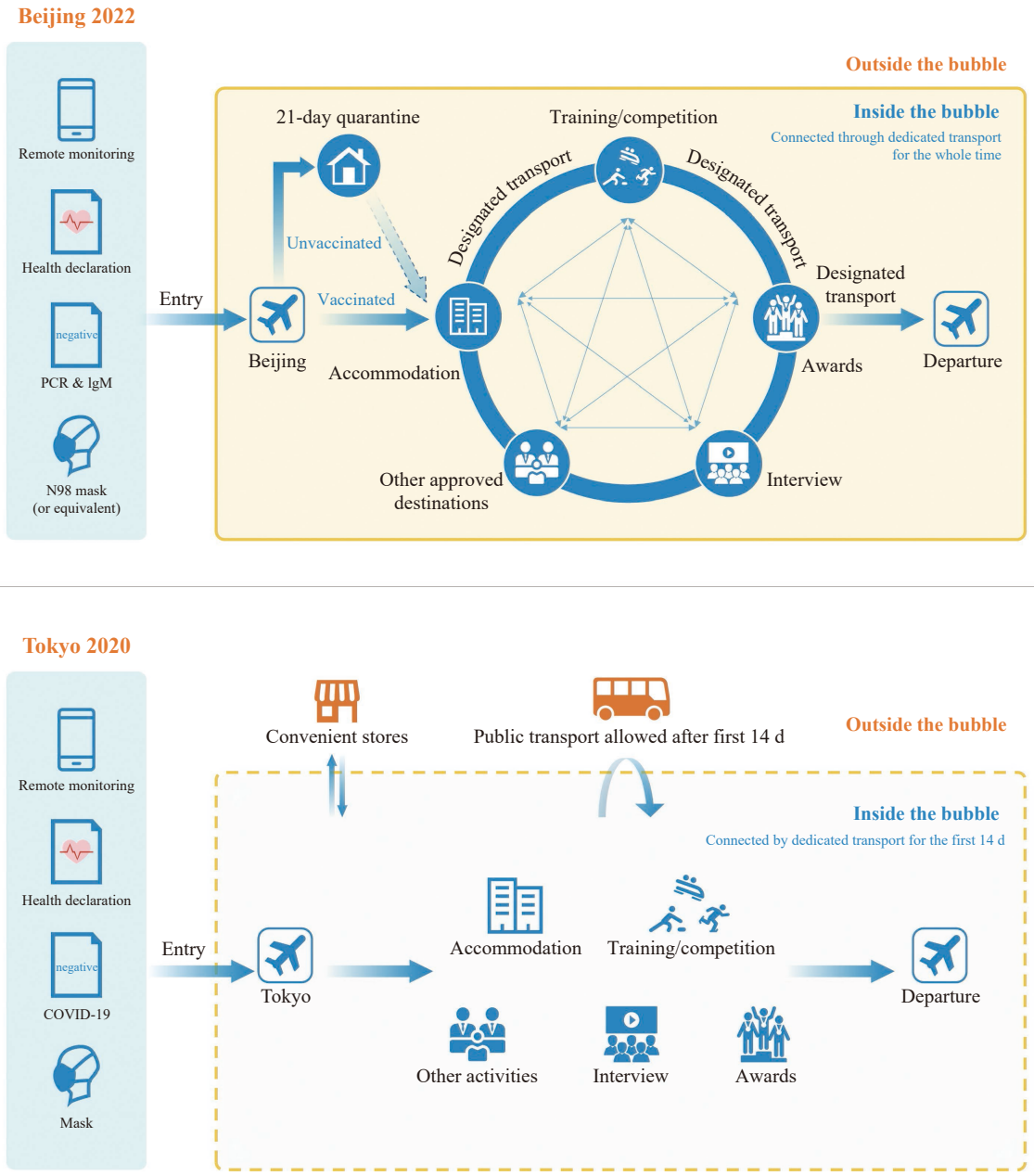

FIGURE 1. The figure depicted different bubble strategy used for Beijing 2022 Games and Tokyo 2020 Games.
Note: A rigorous closed-loop management system (or bubble strategy) will be applied for the Olympic and Paralympic Winter Games Beijing 2022 to all stakeholders from their pre-arrival days all the way to their departure from China. Within the bubble, stakeholders can only travel between pre-approved destinations via well-organized dedicated vehicles and interactions between those inside and outside of the bubble are strictly prohibited. The Tokyo 2020 Games, on the other hand, implemented a more compromised version of bubble strategy where stakeholders could temporarily leave the bubble for convenient stores, and were able to take public transport after 14 days in the bubble.

out (*9*), the bubble strategy, along with other measures including vaccination and restricted social interactions, helped to effectively deliver a successful summer Olympic Games and offered an option to hold global major sporting events in the middle of a pandemic. Some might argue that compared to the bubble strategy for the Beijing 2022 Games, the Tokyo 2020 strategy was more penetrable as those in the bubble could easily get out and move around. However, the contexts of COVID-19 influenced the strategy employed in Beijing to that in Tokyo — Beijing is coping with sporadic and clusters of cases whereas Tokyo was in a state of emergency. Therefore, it is quite understandable that Beijing 2022 chooses to contain the virus with meticulous effort while Tokyo 2020 embraces a more compromised approach, which might be its best choice given its background.

From the two bubbles above, we can see that the bubble strategy is resilient in nature and each model of it could offer some potential to restore regular life while mitigating COVID-19 risks. Apart from the global mass gathering events such as sports competitions and business/academic conferences, the bubble strategy could also offer some opportunities for bilateral collaborations between international organizations or even between countries. For instance, to our knowledge, the most considerably successful bubble strategy implemented in record is the travel bubble (or travel corridors) between 2 or more countries at low risks for COVID-19. This is the case for New Zealand and Australia; through an exclusive partnership represented by travel bubbles, countries can re-establish connections and revive businesses by allowing people to travel freely with no requirements for upon-arrival quarantine. Furthermore, there are always some special occasions where low-risk individuals have to enter high risk regions. In this case, individuals of low-risk could intentionally establish a "protective bubble," through which they can restrict interactions with those outside of the bubble, minimizing the risk of infection. Furthermore, the bubble strategy could also be utilized in people's daily life in the world divided by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As pointed out by researchers, COVID-19 has substantially affected people's mental health and quality of life. By establishing social bubbles (or "social pods" or "quaranteams") between limited households, individuals are able to expand their social circles and carry out leisure activities, therefore restoring regular life to some extent and maintaining good mental health.

To conclude, bubble management is promising as a feasible strategy and a novel technique of non-pharmaceutical interventions when coping with emerging infectious diseases in the Olympic Games.

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Perspectives

The Dynamic COVID-Zero Strategy in China

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

Since its outbreak in late 2019, coronavirus disease 2019 (COVID-19) has remained a global pandemic for nearly two years, which poses a huge test on the resilience of global public health system (*1*). After experiencing the large-scale epidemic in February 2020, China has entered a normalization stage of prevention and control since May 2020 (*2*). In response to the spread of the highly transmissible Delta variant, China adopted a new strategy called "Dynamic COVID-zero" from August 2021. This strategy is a summary of China's experience in dealing with the spread of the Delta variant, considering how to control the epidemic at a higher level, at a lower cost, and in a shorter time (*3*). The most important purpose is to minimize the impact of the epidemic on the economy, society, production, and people's normal lives, and to balance the prevention and control of this disease with socioeconomic stability. For instance, multiple outbreaks occurred Beijing were controlled in 2 maximum incubation periods (within 28 days) by this strategy (Figure 1).

The "Dynamic COVID-zero" strategy is a transitional strategy to be adopted after a successful containment strategy, when the population immunity barrier is not yet established in the face of continued risk of foreign importation and high transmission of variants. This is different from the traditional containment and mitigation strategies (*4*). The core is to take effective and comprehensive measures to deal with localized COVID-19 cases precisely, to quickly cut off the transmission chain, and to end the epidemic in a timely manner (to "find one, end one"). In other words, China took precise prevention and control measures to quickly find, control, and cure infected people in each cluster outbreak within a specific geographic region to avoid affecting social and economic development in other regions, so as to achieve the maximum effect at the lowest cost. When there is a local recurrence, epidemic prevention staff will quickly find the close contacts using new technologies like big data analysis before the spread in the golden response time (within 24 hours after each outbreak). The aim is to find and control potential infected individuals in advance and try to end the outbreak within one or two maximum incubation periods (Figure 2). The formulation and

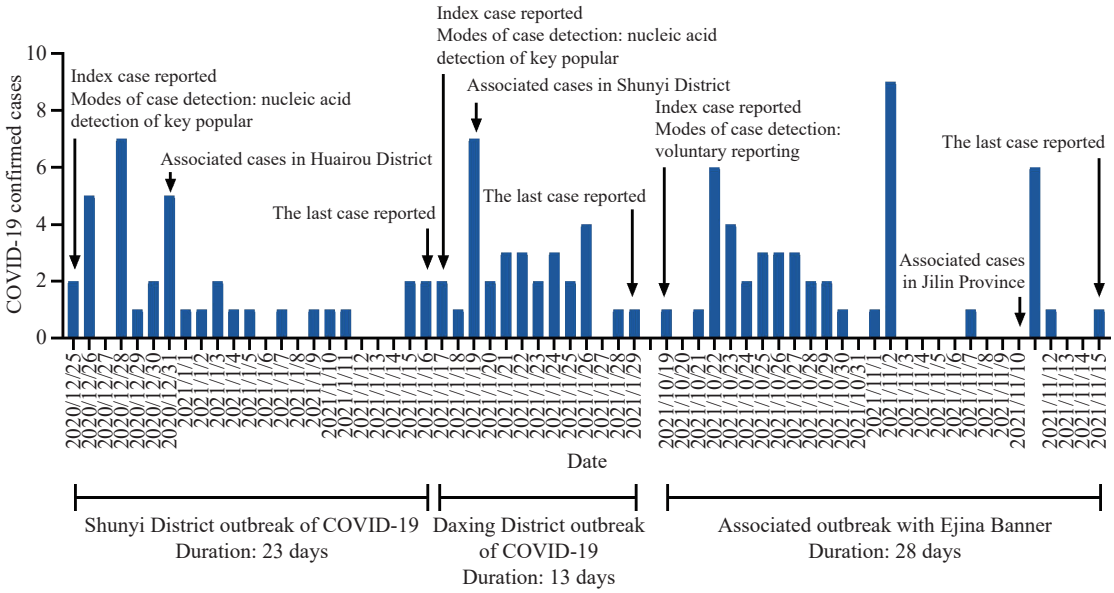

FIGURE 1. Outbreaks of COVID-19 in Beijing from December 2020 to December 2021.
Abbreviation: COVID-19=coronavirus disease 2019.

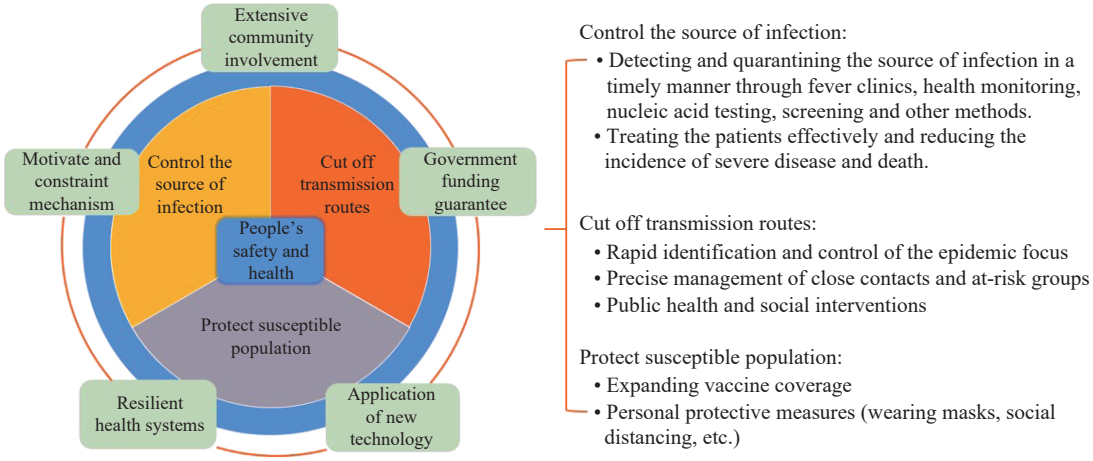

FIGURE 2. The theoretical framework of dynamic COVID-zero strategy.

implementation of this strategy requires extensive community involvement, government funding guarantees, application of new technology, motivating mechanisms, constraint mechanisms, and a resilient health system. Moreover, the scientific suggestions from multidisciplinary experts (for example, public health, clinical medicine, big data analysis, sociology, economics, management, and informatics discipline, etc.) are adopted in timely manner to support decision making.

With the rapid development of molecular biology technology and the wide use of big data analysis, nucleic acid screening can quickly find the source of infection hidden in the population (*5*). Strict quarantine and management measures can be subsequently implemented. Big data technology can quickly identify close contacts and risk groups, helping to implement precise prevention and control measures. Compared with severe acute respiratory syndromes (SARS) in 2003, the resilience of China's health system has been improved, and new technologies such as nucleic acid testing and big data analysis have effectively ensured the implementation of the "Dynamic COVID-zero" strategy.

"Dynamic COVID-zero" strategy sums up China's experience in dealing with Delta, Omicron, and other variants, which has advantages in reducing infection. In general, governments adopt country-specific prevention and control strategies based on their COVID-19 situation, health resources, response capacity and final goals (*6*). No matter what kind of strategy a country takes, concerted and sustained efforts are needed to end the COVID-19 pandemic globally, especially for curbing the rapid spread of the Omicron variant.

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Notes from the Field

The First Two Imported Cases of SARS-CoV-2 Omicron Variant — Tianjin Municipality, China, December 13, 2021

Zhaolin Tan[1,&]; Zhixiao Chen[2,&]; Aiping Yu[1]; Xiaoyan Li[1]; Yenan Feng[2]; Xiang Zhao[2]; Wenbo Xu[2,#]; Xu Su[1,#]

On December 9, 2021, 2 international passengers arrived in Tianjin Binhai International Airport from Warsaw, Poland via airplane and tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), using nucleic acid tests. The first case (Patient A) was a flight crew member, a 35-year-old male, who had returned to Warsaw with the same flight on December 10, 2021. The second case (Patient B) was a 17-year-old female student, who has been transferred to Haihe Hospital for isolation. Both cases are Polish nationality that had recently lived in Warsaw, Poland. According to the investigation, neither patient had disease symptoms nor medication history. Patient B received the Pfizer/BNT162b2 vaccine on September 27, 2021. Patient A was vaccinated on May 25, 2021, but no further vaccine information was collected as Patient A had left China. No other infections from this flight have been detected.

On December 10, 2021, Tianjin CDC received specimens from the 2 cases, sequenced using Illumina iSeq platform (Illumina, San Diego, CA, USA), and obtained the sequencing results on December 13. Compared with the Wuhan reference (EPI_ISL_402125) (*1*–*2*), the viral nucleotide sequence from Patient A displayed 58 substitutions, 39 deletions, and 9 insertions (genomic coverage 99.62%) and belonged to Pango lineage BA.1 (alias of B.1.1.529.1, GISAID ID: EPI_ISL_7734647) (Figure 1). Due to low viral load, the coverage of the viral genome from Patient B was only 92.62%. Based on the characteristics of the detected 50 substitutions and 3 deletions, the strain from Patient B belonged to lineage B.1.1.529. The lineage B.1.1.529 and its descendants (BA.1 and BA.2) were designated as the fifth SARS-CoV-2 Variant of Concern (VOC) by World Health Organization (WHO), named Omicron, following the designation of the Alpha, Beta, Gamma, and Delta variants. This variant was first reported to the WHO by South Africa on November 24, 2021. As of December 14, 2021, 55 counties shared 4,265 Omicron genome sequences in the GISAID database (*3*).

A total of 40 amino acid mutation sites (A67V, T95I, Y145D, L212I, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, A701V, N764K, D796Y, N856K, Q954H, N969K, L981F, H69del, V70del, G142del, V143del, Y144del, N211del, and 214insEPE) and at least 26 amino acid mutation sites (T19R, G142D, C361R, K424I, N439I, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, F497Y, Q498R, N501Y, Y505H, N679K, P681H, A701V, N764K, D796Y, N856K, Q954H, N969K, L981F, and P1069S) were detected in the spike protein of the strains from Patient A and B, respectively. Some of the mutations in the receptor binding domain and near the furin cleavage were concerning and may be associated with immune escape potency and higher transmissibility (*4*).

Nowadays, Omicron is displaying a growth advantage over other circulating variants in many countries of the world (*5*–*6*). In addition, preliminary laboratory data have shown that Omicron displayed a reduction of immune protection against infection and vaccine (*7*). The strains from two cases in Tianjin were the first detected cases of the imported Omicron variant in the mainland of China and pose a great potential threat to the prevention and control of COVID-19 in China. The transmissibility, pathogenicity, and immune evasion of Omicron urgently needs to be further studied.

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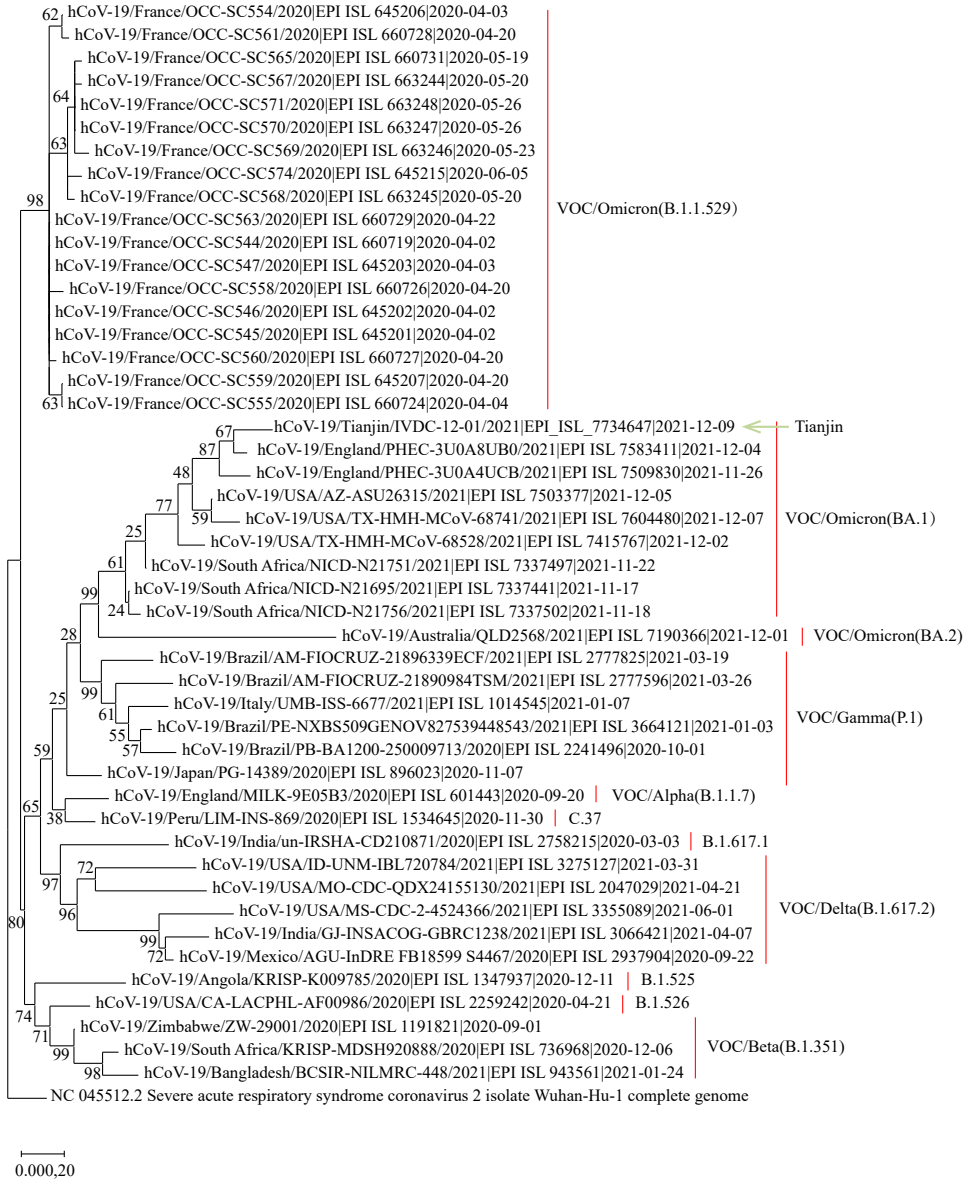

FIGURE 1. Phylogenetic tree based on the full-length genome sequences of SARS-CoV-2.
Notes: The Tianjin imported Omicron variant is marked with a green arrow. The three lineages of the Omicron variant (GISAID ID: EPI_ISL_7734647) and other seven distinguished SARS-CoV-2 variants are marked and colored on the right. The Wuhan reference strain is on the bottom. The nucleotide sequence from Patient B is not included as its genomic sequence is incomplete.
Abbreviations: SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; VOC=variant of concern.

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