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Cover Photo: Sampling packages of garments originating from the Republic of Korea for COVID-19, several of which have tested positive in multiple places in China recently.

Perspectives

The "Wolf" Is Indeed Coming: Recombinant "Deltacron" SARS-CoV-2 Detected

Liang Wang[1]; George F. Gao[1,2,#]

The Emergence of "Deltacron"

On March 9, 2022, researchers from the Institut Pasteur used the global data science initiative GISAID (*1–3*) to release a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) genome (ID: EPI_ISL_10819657) from an isolated virus and announced that it was the first solid evidence for a recombinant strain from 2 types of variants of concern (VOCs) of SARS-CoV-2 (lineage AY.4 and BA.1, belonging to Delta and Omicron, respectively). Complementary to the original data submitters' full analysis, we would like to comment on this case in context of our experience in coronavirus evolution and the further perspective of this finding on the course of the pandemic. As announced, this novel strain has high genomic similarity to viruses belonging to lineage AY.4, except for the region encoding the spike (S) gene, which is more similar to those from lineage BA.1 (Figure 1A). Therefore, this novel strain uses Delta as its genomic backbone and then replaces a large portion of original S gene with the ortholog from Omicron. A total of 36 amino acid changes were found in the S protein compared to the prototype of SARS-CoV-2 (Figure 1B). Among 36 amino acid mutations, 27 were found in BA.1, 5 mutations were found in AY.4, and 4 mutations were found in both AY.4 and BA.1. However, it was not the first case of a recombination event identified in SARS-CoV-2. A previous study has documented that inter-lineage recombination events have been found in SARS-CoV-2 and then some recombinants caused further community transmission (*4*). However, these inter-lineage recombination events only occurred in some loci of the genome. No recombination events involving large genomic fragments (like "Deltacron") have been found in SARS-CoV-2 before.

Genetic Recombination Frequently Occurs in Coronaviruses

Coronaviruses (CoVs) belong to a highly diverse family *Coronaviridae*, which could infect numerous types of species (like those from Aves and mammalian). Therefore, CoVs will pose a potential risk to public health and economy. As a hallmark of CoVs, genetic recombination events occur frequently in natural reservoir hosts due to co-infection of different types of CoVs in a single individual host and/or other reasons. Genetic recombination could arise at both the intra-species and inter-species level. For intra-species recombination, some genetic materials could be exchanged between strains of different subtypes of the same species. For example, an isolate of the Middle East respiratory syndrome coronavirus (MERS-CoV), imported to China from the Republic of Korea, has been documented as a recombinant virus from group 3 and group 5 (*5*). On the other hand, inter-species recombination occurs when two different species exchange their partial genetic materials and are also common in nature (including several types of human CoVs) (*6*). Despite most recombination events occurring among species belonging to *Coronaviridae*, cross-family genetic recombination events had also been found in nature (between *Coronaviridae* and *Reoviridae*) (*7*). The frequent genetic recombination of CoVs could lead to the emergence of novel viruses. Further, the most important threat of the emergence of these novel recombinant viruses is the possibility of cross-species transmission (*8*). The most recent example was two canine-feline recombinant alphacoronaviruses with extremely high genomic similarity (99.4%) were isolated from humans by two independent research groups in different countries (*9–10*).

A "Grey Rhino" Event for "Deltacron"

Before the emergence of "Deltacron," most scientific efforts were focused on assessing and responding to the effects of point mutations in the genome of SARS-CoV-2 during its global spread and evolution. Until now, 5 types of SARS-CoV-2 VOCs had been found

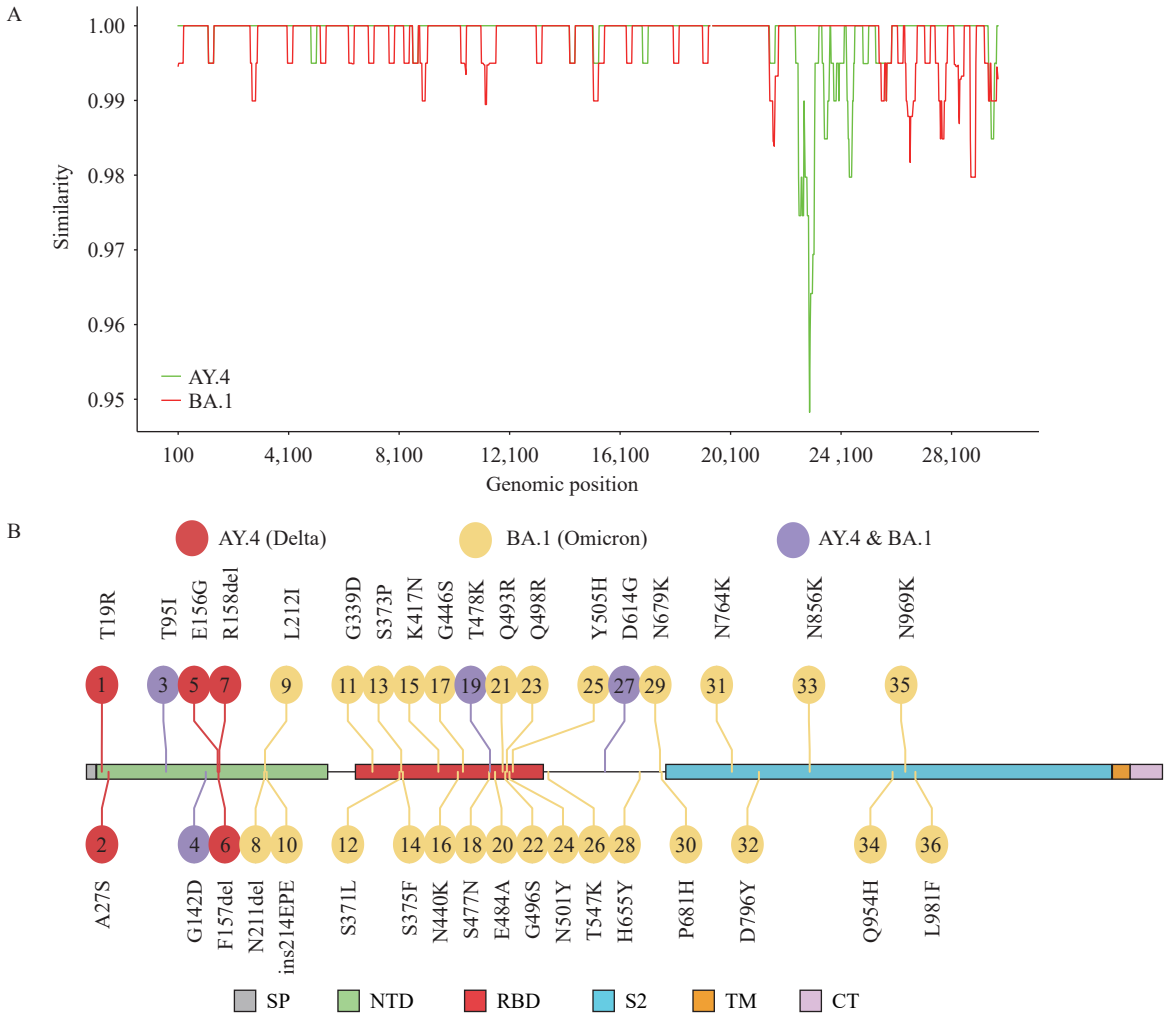

FIGURE 1. Genetic variation of "Deltacron." (A) The nucleotide similarity of "Deltacron" compared to AY.4 and BA.1; (B) The mutation profile of the S protein encoded by "Deltacron."
Note: Mutations in only AY.4, BA.1, both AY.4 and BA.1, and "Deltacron" were assigned to different colors.
Abbreviations: SP=signal peptide; NTD=N terminal domain; RBD=receptor binding domain; TM=transmembrane domain; CT=C terminal.

circulating globally (Alpha, Beta, Gamma, Delta, and Omicron). They all exhibited increased transmissibility and varying degrees of immune escape (*11–12*). Although the emergence and subsequent spread of these VOCs has had a huge impact on global health and economy, it may not have been the worst case until now, as recombination (a major mechanism bringing genetic diversity to coronaviruses) had not really emerged on a large scale and shown its power before the emergence of "Deltacron." The emergence of "Deltacron" is therefore a "grey rhino" event rather than a "black swan" event.

"Deltacron" Is Just the Beginning

With the advent of "Deltacron," further concerns are coming. According to our preliminary analysis on the first "Deltacron" genome, recombination event only occurs in S gene. However, recombination events involving all types of genes encoded by CoVs have been found in nature (*13*). Consequently, the genetic recombination events involving other genes and/or the combination of other genes would also occur with high probability. Furthermore, the genetic recombination event of "Deltacron" occurs at the inter-lineage level, that is the parents of the "Deltacron" came from different lineages of the same species (AY.4 and BA.1), respectively. We could speculate that cross-species recombination events would also appear in future for the following reasons. First, the variety of host types of CoVs has resulted in its wide distribution throughout the world (*14*) and SARS-CoV-2 has spread all over the world. Second, several species of mammals other

than humans have been infected by SARS-CoV-2 in nature, and many more species have been shown to be susceptible to SARS-CoV-2 (*15*). In addition, the spillover events of SARS-CoV-2 between humans and animals in both directions (for example transmission of SARS-CoV-2 from humans to minks and then back to humans and further community transmission) (*16–17*) have been found in nature. Taken together, the probability of co-infection with SARS-CoV-2 and other types of CoVs or even other viruses in a single host would be high, leading to the occurrence of cross-species recombination with high probability. Therefore, it is difficult to predict which viral species SARS-CoV-2 will recombine with, and on which genes future recombination will occur. This kind of uncertainty is doomed to increase the likelihood of generating a novel recombinant virus with unknown risk to humans.

Concluding Remarks

Although the emergence of a recombinant SARS-CoV-2 isolate was expected by scientists, it still attracted great attention. In addition to the need to conduct in-depth evaluation and research on the various properties of this novel recombinant virus, and adjust in prevention and control strategies based on the results, it is more important to be alert to the generation of other types of recombinant viruses produced by SARS-CoV-2 and other viruses. Therefore, it is particularly important to implement large-scale virome study in both domesticated and wild animals.

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Preplanned Studies

COVID-19 Mortality and Vaccine Coverage — Hong Kong Special Administrative Region, China, January 6, 2022–March 21, 2022

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Editorial This report is being published simultaneously in the *Weekly Epidemiological Record* (https://www.who.int/publications/journals/weekly-epidemiological-record) and *Morbidity and Mortality Weekly Report* (https://www.cdc.gov/mmwr/volumes/71/wr/mm7115e1.htm?s_cid=mm7115e1_w).

Summary

What is already known about this topic?

COVID-19 vaccines are important tools to protect populations from severe disease and death.

What is added by this report?

Among persons aged ≥60 years in Hong Kong, 49%, had received ≥2 doses of a COVID-19 vaccine, and vaccination coverage declined with age. During January–March 2022, reported COVID-19–associated deaths rose rapidly in Hong Kong. Among these deaths, 96% occurred in persons aged ≥60 years; within this age group, the risk for death was 20 times lower among those who were fully vaccinated compared with those who were unvaccinated.

What are the implications for public health practice?

Efforts to identify and address gaps in age-specific vaccination coverage can help prevent high mortality from COVID-19, especially in older adults.

On January 6, 2022, a cluster of COVID-19 cases[*] caused by the Omicron variant of SARS-CoV-2, the virus that causes COVID-19, was detected in Hong Kong Special Administrative Region, China (Hong Kong), resulting in the territory's fifth wave of COVID-19 cases (*1*). This wave peaked on March 4, 2022, with 8,764 COVID-19 cases per million population (*2*), resulting in a total of 1,049,959 cases and 5,906 COVID-19–associated deaths reported to the Hong Kong Department of Health during January 6–March 21, 2022.[†] Throughout this period, the COVID-19 mortality rate in Hong Kong (37.7 per million population) was among the highest reported worldwide since the COVID-19 pandemic began (*3*). Publicly available data on age-specific vaccination coverage in Hong Kong with a 2-dose primary vaccination series (with either Sinovac-CoronaVac [Sinovac], an inactivated COVID-19 viral vaccine, recommended for persons aged ≥3 years or BNT162b2 [Pfizer-BioNTech], an mRNA vaccine, for persons aged ≥5 years), as of December 23, 2021,[§,¶] and COVID-19 mortality during January 6–March 21, 2022, were analyzed. By December 23, 2021, 67% of vaccine-eligible persons in Hong Kong had received ≥1 dose of a COVID-19 vaccine, 64% had received ≥2 doses, and 5% had received a booster dose. Among persons aged ≥60 years, these proportions were 52%, 49%, and 7%, respectively. Among those aged ≥60 years, vaccination coverage declined with age: 48% of

[*] A hotel cluster of COVID-19 cases on January 6, 2022, is thought to have been the origin of the fifth wave of cases, based on genomic surveillance data from sequences uploaded to GISAID. Before January 6, previous Omicron cases with different sequences were detected from sporadic introduction and community transmission (https://www.ceo.gov.hk/eng/pdf/article20220128.pdf); 50 cases were detected as of December 28, 2021 (https://www.ceo.gov.hk/eng/pdf/article20211228.pdf).

[†] Daily new confirmed COVID-19 cases and deaths per million persons listed are 7-day rolling averages.

[§] Vaccination rates and vaccine-derived immunity were calculated 14 days before the introduction of the Omicron variants leading to Hong Kong's fifth wave.

[¶] Sinovac is recommended in persons aged ≥3 years. For persons aged ≥18 years, a 28-day interval between the first and second dose, a 28-day interval for immunocompromised persons, and a 90-day interval for the general population (priority for those aged ≥60 years) between the second and third dose is recommended; a fourth dose is recommended 90 days after the third dose for immunocompromised persons. Pfizer BioNTech vaccine is recommended for persons aged ≥5 years. For persons aged ≥18 years, a 56-day interval is recommended between the first and second doses; a 28-day interval for those who are immunocompromised, and a 90-day interval for the general population (priority to those aged ≥60 years) between the second and third dose; a fourth dose with an interval of 90 days after the third dose is recommended for immunocompromised persons. https://www.covidvaccine.gov.hk/en/vaccine.

persons aged 70–79 years had received ≥1 dose, 45% received ≥2 doses, and 7% had received a booster, and among those aged ≥80 years, 20%, 18%, and 2% had received ≥1 dose, ≥2 doses, and a booster dose, respectively. Among 5,906 COVID-19 deaths reported, 5,655 (96%) occurred in persons aged ≥60 years[**]; among these decedents, 3,970 (70%) were unvaccinated, 18% (1,023) had received 1 vaccine dose, and 12% (662) had received ≥2 doses. The overall rates of COVID-19–associated mortality among persons aged ≥60 years who were unvaccinated, who had received 1 COVID-19 vaccine dose, and who had received ≥2 vaccine doses were 10,076, 1,099, and 473 per million population, respectively; the risk for COVID-19–associated death among unvaccinated persons was 21.3 times that among recipients of 2–3 doses in this age group. The high overall mortality rate during the ongoing 2022 Hong Kong Omicron COVID-19 outbreak is being driven by deaths among unvaccinated persons aged ≥60 years. Efforts to identify and address gaps in age-specific vaccination coverage can help prevent high mortality from COVID-19, especially among persons aged ≥60 years.

The Chinese Center for Disease Control and Prevention and the U.S. CDC conducted a descriptive analysis of COVID-19 incidence, mortality, age-specific vaccination coverage, and booster dose coverage after introduction of the Omicron variant in Hong Kong.[††] Relative risks were calculated using mortality rates (deaths per million persons) by vaccination status and age, with the referent groups being ≥2-dose recipients; persons aged <30 years; or, within specific age groups, receipt of ≥2 vaccine doses. Data were obtained from publicly available sources, primarily the Hong Kong Department of Health (*2*) and Our World in Data (*3*). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[§§]

During February 2020–December 2021, Hong Kong reported 12,649 COVID-19 cases and 213 associated deaths. On January 6, 2022, the first cluster of COVID-19 cases attributable to the Omicron variant were identified in guests in a hotel for compulsory quarantine after arrival in Hong Kong from abroad (*1*). Daily COVID-19 incidence increased sharply, from 1.7 per million population on January 6 to a peak of 8,764.2 per million on March 4, before declining to 2,716.0 by March 21, 2022. By February 14, 2022, 100% of sequenced isolates were Omicron variant, BA.2 lineage.

As of December 23, 2021, two thirds (67%) of vaccine-eligible persons overall in Hong Kong had received ≥1 COVID-19 vaccine dose, 64% had received ≥2 doses, and 5% had received a booster dose (Table 1). Vaccination coverage varied by age; among persons aged 30–59 years, 82%, 80%, and 5% had received ≥1 dose, ≥2 doses, and a booster dose, respectively. Among persons aged ≥60 years, approximately one half (52% and 49%) had received ≥1 and ≥2 vaccine doses, respectively, and 7% had received a booster dose. Coverage declined with increasing age: 48% of persons aged 70–79 years and 20% of those aged ≥80 years had received ≥1 vaccine dose, 45% and 18% had received ≥2 doses, and 7% and 2% had received a booster dose.

A total of 5,906 COVID-19–related deaths were reported in Hong Kong during January 6–March 21, 2022 (Table 2). The daily mortality rate increased from zero on January 6 to 34.8 per million on March 21 and peaked at 37.7 on March 14. Among all deaths, 4,118 (70%) occurred in unvaccinated persons and 5,655 (96%) occurred in persons aged ≥60 years. Unvaccinated decedents aged ≥60 years (3,970) accounted for 67% of total deaths, and among the 5,655 deaths in persons aged ≥60 years, 70% were in unvaccinated persons. Unvaccinated decedents aged ≥70 years (3,661) and ≥80 years (3,036) accounted for 62% and 51% of all deaths, respectively.

Overall, the relative risk of dying from COVID-19 among unvaccinated persons in Hong Kong was 33.2 times the risk among persons who received ≥2 doses (Table 3). Compared with persons aged <30 years, mortality risk among those aged ≥60 years was 252.7 times as high, and among persons aged ≥80 years was 946.2 times as high. Among persons aged ≥60 years, the relative risk for death among those who were unvaccinated was 21.3 times the risk among persons who had received ≥2 doses and 2.3 times the risk among those who had received 1 vaccine dose.

[**] Age was unknown for two unvaccinated decedents.

[††] Death counts were obtained from the Hong Kong Department of Health, which provides the most up-to-date mortality data, but these data might differ slightly from other sources because of differences in completeness. The government of Hong Kong has established processes for linking case and vaccination data. COVID-19–associated death is defined as a death in a person who received a positive SARS-CoV-2 test result who died within 28 days of the collection date of the first positive specimen. The underlying cause of death might have been unrelated to COVID-19.

[§§] 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

TABLE 1. COVID-19 vaccination coverage, by age group — Hong Kong Special Administrative Region, China, December 23, 2021.

Age group, years	No. of doses received/vaccination coverage*		
	≥1 dose no./total no. (%)	≥2 doses no./total no. (%)	Booster† no./total no. (%)
3–29	980,945/1,784,800 (55)	869,096/1,784,800 (49)	14,471/1,784,800 (0.8)
3–19	345,393/976,100 (35)	255,510/976,100 (26)	730/976,100 (0.1)
20–29	635,552/808,700 (79)	613,586/808,700 (76)	13,741/808,700 (2.0)
30–59	2,817,846/3,443,000 (82)	2,751,916/3,443,000 (80)	171,899/3,443,000 (5.0)
30–39	889,354/1,126,300 (79)	864,294/1,126,300 (77)	32,943/1,126,300 (3.0)
40–49	983,239/1,142,500 (86)	963,035/1,142,500 (84)	63,356/1,142,500 (6.0)
50–59	945,253/1,174,200 (81)	924,587/1,174,200 (79)	75,600/1,174,200 (6.0)
≥60	1,049,110/2,034,100 (52)	1,004,606/2,034,100 (49)	145,989/2,034,100 (7.0)
60–69	701,148/1,071,800 (65)	679,592/1,071,800 (63)	96,451/1,071,800 (9.0)
70–79	266,706/560,500 (48)	253,378/560,500 (45)	39,761/560,500 (7.0)
≥80	81,256/401,800 (20)	71,635/401,800 (18)	9,777/401,800 (2.0)
Total	**4,847,901/7,261,900 (67)**	**4,625,618/7,261,900 (64)**	**332,359/7,261,900 (5.0)**

Source: COVID-19 Vaccination Programme. https://www.covidvaccine.gov.hk
* Total persons vaccinated divided by total population in the age group.
† In Hong Kong, booster doses are considered third and fourth doses after the 2-dose primary COVID-19 vaccination series vaccines.

TABLE 2. COVID-19–associated mortality,* by age group and vaccination status — Hong Kong Special Administrative Region, China, January 6–March 21, 2022.

Age group, years	Total no. of deaths (% of total)	Age-specific mortality*	No. of deaths, by no. of vaccine doses			Mortality,* by no. of vaccine doses		
			None	1	≥2	None	1	≥2
Total	**5,906 (100)**	**799**	**4,118**	**1,068**	**720**	**4,277**	**317**	**129**
<30	21 (0.4)	11	13	4	4	29	6	4
<3	1 (0.0)	8	1	0	0	8	0	0
3–11	5 (0.1)	9	3	2	0	13	8	0
12–19	5 (0.1)	11	3	1	1	158	7	3
20–29	10 (0.2)	12	6	1	3	92	4	4
30–59	228 (4.0)	66	133	41	54	1,039	23	17
30–39	15 (0.3)	13	8	3	4	140	6	4
40–49	43 (0.7)	38	30	4	9	1,000	6	8
50–59	170 (2.9)	145	95	34	41	2,317	52	39
≥60	5,655 (95.9)	2,780	3,970	1,023	662	10,076	1,099	473
60–69	496 (8.4)	463	309	94	93	2,784	168	108
70–79	977 (16.5)	1,743	625	201	151	5,841	786	396
≥70	5,159 (87.4)	5,363	3,661	929	569	12,936	2,490	1,061
≥80	4,182 (70.8)	10,408	3,036	728	418	17,250	6,207	2,696

* Deaths per million population.

DISCUSSION

After the emergence of the Omicron variant in Hong Kong in early January 2022, COVID-19 cases increased rapidly, resulting in 5,906 deaths as of March 21, 2022. At the start of this outbreak, immunity in Hong Kong was presumed to be predominantly vaccine-derived as a result of a dynamic COVID-Zero strategy, whereby after successful containment, every case is investigated, and measures are implemented to interrupt onward transmission (*4*). Although overall 2-dose vaccination coverage was 64%, rates varied between age groups and were lower among older

TABLE 3. COVID-19 mortality* and relative mortality risk† among persons aged <30 years, 30–59 years, and ≥60 years, overall and by age and vaccination status — Hong Kong Special Administrative Region, China, January 6–March 21, 2022.

Characteristic	Mortality rate*	Relative mortality risk†
Overall no. of COVID-19 vaccine doses received		
≥2	129	Ref
1	317	2.5
0	4,277	33.2
All vaccination groups, by age group, years		
<30	11	Ref
30–59	66	6
≥60	2,780	252.7
60–69	463	42.1
70–79	1,743	158.5
≥80	10,408	946.2
No. of doses received, by age group, years		
<30		
≥2	4	Ref
1	6	1.5
0	29	7.3
30–59		
≥2	17	Ref
1	23	1.4
0	1,039	61.1
≥60		
≥2	473	Ref
1	1,099	2.3
0	10,076	21.3
60–69		
≥2	108	Ref
1	168	1.6
0	2,784	25.8
70–79		
≥2	396	Ref
1	786	2.0
0	5,841	14.7
≥80		
≥2	2,696	Ref
1	6,207	2.3
0	17,250	6.4

Abbreviation: Ref=referent group.
* Deaths per million population.
† Compared with referent group of ≥2 doses.

adults: 2-dose vaccination coverage was 63% among persons aged 60–69 years, 45% among those aged 70–79 years, and 18% among those aged ≥80 years. New Zealand, a country with a much lower population density than Hong Kong, China, also had largely vaccine-derived immunity. Although New Zealand's 2-dose COVID-19 vaccination coverage was 95% among persons aged ≥60 years, the country experienced a similar increase in incidence after introduction of Omicron; however, mortality in New Zealand peaked at 2.1 per million population per day compared with 38.0 in Hong Kong, China (*5*). These findings align with data from existing studies indicating that the risk for death from COVID-19 increases with age and reinforce the effectiveness of vaccination in preventing death from the Omicron variant in older adults (*6*–*7*).

COVID-19 vaccine-induced immunity wanes over time, but booster vaccinations can elicit a strong immune response and restore vaccine effectiveness (*7*). At the beginning of the Omicron wave in Hong Kong, only 7% of persons aged ≥60 years had received a booster dose, including just 2% of those aged ≥80 years. The primary series of COVID-19 vaccines plus a booster dose is more effective at preventing severe outcomes caused by the Omicron variant than a primary series alone (*8*). In addition to the low vaccination coverage among persons aged ≥60 years, waning immunity since the last vaccine dose could have contributed to COVID-19–associated mortality in Hong Kong.

The reasons for low COVID-19 vaccination coverage among older persons in Hong Kong are not clear. Low vaccine confidence has presented major hurdles for governments aiming to reduce COVID-19 transmission and mortality. A June 2021 survey in Hong Kong found that 56.8% of participants were hesitant about or resistant to receiving a COVID-19 vaccine (*9*). The dynamic COVID-Zero strategy, successful until the emergence of the Omicron variant, might have resulted in further complacency, particularly among older persons. A survey conducted during November 2020–January 2021 in China found that older adults were more likely to accept a COVID-19 vaccine if they perceived themselves to be at high risk for infection or had trust in the government (*10*). Experience with the COVID-19 pandemic can motivate public health officials to increase vaccine distribution and coverage. Hong Kong targeted older persons for vaccination during the outbreak. As of March 21, 2022, 2-dose COVID-19 vaccination coverage in Hong Kong has increased substantially, to 81% among persons aged 60–69 years, 69% among persons aged 70–79 years, and 39% among persons

aged ≥80 years (*3*).

The findings in this report are subject to at least four limitations. First, summary-level data were analyzed, and other risk factors for death, including comorbidities, could not be examined. Second, completeness of reporting of COVID-19–attributed deaths is unknown. Third, immunity due to previous infection could not be assessed; however, such immunity was likely low given that few cases had been reported during previous waves (*4*). Finally, vaccine effectiveness can vary by type and timing of vaccination, which were not accounted for in this analysis.

During January–March 2022, data from Hong Kong suggest that higher mortality rates were driven by low vaccination coverage among older adults. These data underscore the importance of monitoring age-specific vaccination coverage and implementing strategies that increase COVID-19 vaccination coverage among all population groups, especially those most at risk for severe illness. Efforts to identify disparities in age-specific vaccination rates and address gaps in vaccination coverage among groups at high risk can help prevent high mortality from COVID-19, especially in older adults.

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Preplanned Studies

Association of COVID-19 Vaccination and Clinical Severity of Patients Infected with Delta or Omicron Variants — China, May 21, 2021–February 28, 2022

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Summary

What is already known about this topic?

Compared with the international mRNA and adenovirus-vectored coronavirus disease 2019 (COVID-19) vaccines, there is less real-world research data about breakthrough cases in people vaccinated with China-made COVID-19 vaccines. Analyses of clinical outcomes of breakthrough cases will be an important supplement to the clinical trial efficacy and observational effectiveness data of China-made COVID-19 vaccines.

What is added by this report?

COVID-19 vaccine age-eligible individuals (≥3 years old) who received full primary series and a booster dose of China-made COVID-19 vaccines had good protection from pneumonia caused by Delta variant infection. There was only one serious Delta case in children (unvaccinated), but among adults 18 years and older, there was good protection from serious illness with primary vaccination and booster vaccination. Among people ≥60 years, full vaccination and booster vaccination were associated with protection from pneumonia and risk of serious COVID-19 caused by Omicron variant infection. There were few serious Omicron cases.

What are the implications for public health practice?

Everyone 3 years and older without contraindications should be fully vaccinated against COVID-19; schedule-eligible adults should receive booster doses. The pace of booster dose administration, especially among the elderly, should be accelerated.

The coronavirus disease 2019 (COVID-19) pandemic remains a global public health crisis, with nearly half a billion cases and over six million deaths reported to the World Health Organization (WHO). Vaccines are one of the most effective tools against COVID-19. More than 11 billion doses have been administered globally, and 64% of the world's population has received at least 1 dose of a COVID-19 vaccine (*1*). On December 15, 2020, China initiated a COVID-19 vaccination campaign. More than 3.2 billion doses have been administered, the vast majority of which have been inactivated vaccines.

Studies have demonstrated good effectiveness of COVID-19 vaccines made using different technical platforms on prevention of severe illness and death, effectiveness at preventing infection is much less. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been evolving, and the variants seen in China have paralleled strains seen globally. Omicron has now replaced Delta to become the predominant strain in China.

Protective effectiveness of vaccines produced and used in China against different variants must be monitored carefully. Using individual-level matched data from two databases — the National Notifiable Disease Reporting System (NNDRS) that records clinical information on COVID-19 patients and the National Immunization Program Information System (NIPIS) that record vaccination histories — we analyzed clinical outcomes of Delta and Omicron infections by vaccination status to estimate protective effectiveness of COVID-19 vaccines used in China.

This was a retrospective, descriptive analysis based on all cases of COVID-19 diagnosed nationwide in China between May 21, 2021 and February 28, 2022. We estimated the effectiveness of vaccination to prevent progression of illness by comparing the odds of vaccination in different outcomes using an age-stratified analysis.

This study included all individuals diagnosed with COVID-19 in the mainland of China reported to NNDRS between May 21, 2021 and February 28, 2022. Cases in NNDRS were matched by national identification number to vaccination histories in NIPIS.

Vaccination status was categorized into four groups:

unvaccinated, partially vaccinated, full vaccination, and booster vaccination. The unvaccinated group consisted of individuals who did not receive any COVID-19 vaccines before becoming infected or received COVID-19 vaccines on the day of infection. The partially vaccinated group consisted of individuals who had not completed full primary vaccination or who completed primary vaccination less than 14 days before becoming infected. The full vaccination group consisted of individuals who completed 2 doses of inactivated vaccine, 1 dose of adenovirus-vectored vaccine, or 3 doses of recombinant-subunit vaccine 14 or more days before becoming infected. The booster dose group consisted of individuals who received a booster dose 7 or more days before becoming infected. Breakthrough cases were individuals who completed full vaccination or booster vaccination before becoming infected.

According to the Protocol for Prevention and Control of COVID-19 (Eighth Version) (*2*), cases are classified by clinical symptoms as asymptomatic, mild, moderate, serious, or severe. We categorized cases into one of two outcomes: pneumonia, which includes moderate, serious, and severe cases; and serious COVID-19, which included only serious and severe cases.

The study used SPSS software (version 25.0, IBM Crop., Armonk, NY, US) to perform the following tasks: (a) descriptive analysis of the distributions of clinical outcomes by age group, vaccination status, and variant, (b) variant-specific, age-stratified, univariate logistic regression analyses of COVID-19 pneumonia cases and exact logistic regression of serious COVID-19 cases by vaccination category among cases ≥3 years old to determine odds ratios (OR) and their 95% confidence intervals (CI). We calculated effectiveness of vaccination to prevent COVID-19 pneumonia or serious COVID-19 as one minus the ORs times 100%. Statistical significance was considered as $P<0.05$.

A total of 10,829 domestic COVID-19 cases were reported between May 21, 2021 and February 28, 2022 in the mainland of China. Among those, 8,675 were caused by the Delta variant and 2,154 were caused by Omicron. Vaccination status by age group and variant is shown in Figure 1. Among cases ≥3 years, 15.1% were unvaccinated, 7.3% were partially vaccinated, 63.6% were fully vaccinated, and 14.0% received a booster dose.

Among cases with full vaccination, 95.1% (7,849) received inactivated vaccine, 2.2% (183) received adenovirus-vectored vaccine and 2.7% (223) received recombinant-subunit vaccine. Among Delta cases, the proportions of fully vaccinated cases with COVID-19 pneumonia in inactivated vaccine, adenovirus-vectored vaccine, and recombinant-subunit vaccine groups were 95.9% (3,197), 1.5% (50), and 2.6% (85), while the proportions of serious cases were 97.5% (157), 0 (0), and 2.5% (4), respectively. Among Omicron cases, the proportions of fully vaccinated cases with COVID-19 pneumonia in inactivated vaccine, adenovirus-vectored vaccine, and recombinant-subunit vaccine groups were 90.9% (497), 6.2% (34), and 2.9% (16) respectively, and only the inactivated vaccine group had 9 serious cases.

Table 1 shows outcomes by variant and age group among the 1,793 unvaccinated cases (1,631 Delta and 162 Omicron); 59.0% of unvaccinated Delta cases had pneumonia and 37.7% of unvaccinated Omicron cases

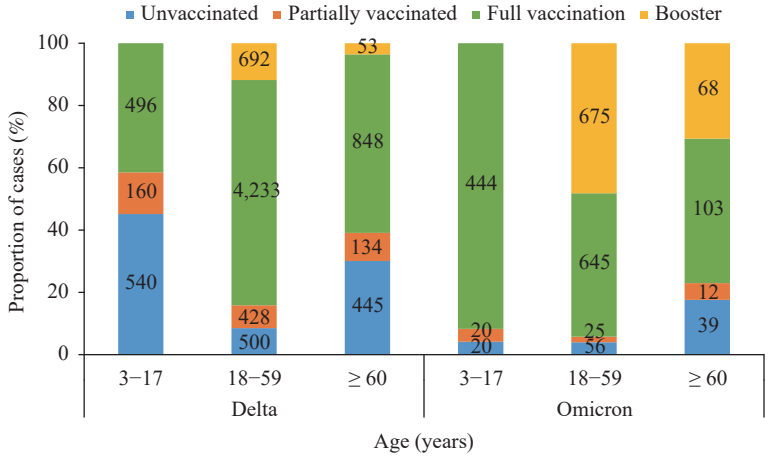

FIGURE 1. Age-specific COVID-19 vaccination status among Delta- and Omicron-infected cases, China, May 21, 2021–February 28, 2022.

TABLE 1. Age- and variant-specific clinical outcomes among unvaccinated cases, China, May 21, 2021–February 28, 2022.

Age (years)	Variants	Number of cases (N)	COVID-19 pneumonia cases			Serious COVID-19 cases		
			n (%)	*P* value	OR (95% CI)	n (%)	*P* value	OR (95% CI)
<3	Delta	146	28(19.2)	Ref	Ref	0(0)	–	–
	Omicron	47	10(21.3)	0.75	1.14(0.51–2.56)	0(0)	–	–
	Subtotal	193	38(19.7)			0(0)		
3–17	Delta	540	169(31.3)	Ref	Ref	1(0.2)	Ref	Ref
	Omicron	20	2(10.0)	0.06	0.24(0.06-1.06)	0(0)	0.96	–
	Subtotal	560	171(30.5)			1(0.2)		
18–59	Delta	500	363(72.6)	Ref	Ref	39(7.8)	Ref	Ref
	Omicron	56	18(32.1)	<0.01	0.18(0.10–0.32)	0(0)	0.03	0.15(0–0.68)
	Subtotal	556	381(68.5)			39(7.0)		
≥60	Delta	445	402(90.3)	Ref	Ref	133(29.9)	Ref	Ref
	Omicron	39	31(79.5)	0.04	0.41(0.18–0.96)	4(10.3)	<0.01	0.27(0.07–0.77)
	Subtotal	484	433(89.5)			137(28.3)		
Total	Delta	1,631	962(59.0)	Ref	Ref	173(10.6)	Ref	Ref
	Omicron	162	61(37.7)	<0.01	0.32(0.21–0.48)	4(2.5)	<0.01	0.20(0.06–0.57)
	Subtotal	1,793	1,023(57.1)			177(9.9)		

Note: –: data not applicable.
Abbreviations: Ref=reference; OR=odds ratio; CI=confidence interval.

had pneumonia; 10.6% of unvaccinated Delta cases were severe, and 2.5% of unvaccinated Omicron cases were severe (P<0.01). Overall, Omicron cases were 68% (95% CI: 52%–79%) less likely to develop pneumonia and 80% (95% CI: 43%–94%) less likely to become severe, a finding that held for both adult groups.

Table 2 shows age-stratified logistic regression analyses of the outcomes by vaccination status separately for Delta cases and Omicron cases. Among Delta cases, the proportions of fully vaccinated cases with COVID-19 pneumonia in the 3–17 year, 18–59 year, and ≥60 year groups were significantly lower than respective proportions in the unvaccinated groups. By age group, the risk of developing pneumonia was 58%, 51%, and 66% lower in the full vaccination age groups compared with no vaccination. The proportions of fully vaccinated serious cases in the 18–59 year and ≥ 60-year age groups were lower than age-group-respective unvaccinated cases; full vaccination was associated with 83% and 69% lower risk of becoming severe.

Among Omicron cases ≥60 years old, the risk of developing into pneumonia was 72% lower than among unvaccinated cases, and there were no statistically significant differences in serious infections by full vaccination status.

At the time of the study, booster doses were recommended only for adults. Among 18–59 year and ≥60-year Delta cases, the booster dose had 86% and 86% lower risk of developing pneumonia. Compared with no vaccination age groups, risk of serious COVID-19 in the 2 adult booster age groups was 98% and 91% lower, respectively.

Among Omicron cases ≥60 years old, the booster dose was associated with a 65% decrease in pneumonia. There were no severe Omicron cases in the booster group ≥60 years old, while 4 (10.3%) of the unvaccinated cases in this age group were severe, the risk of developing into serious COVID-19 was 90% lower than among unvaccinated cases.

DISCUSSION

This study used national COVID-19 surveillance and vaccination data from May 21, 2021 through February 28, 2022 to estimate effectiveness of the China-produced vaccines that are building population immunity against SARS-CoV-2 and its variants. Based on individual-level analysis of all Delta and Omicron infections in the mainland of China, we found that full primary vaccination was associated with a 50%–70% lower risk of Delta-variant COVID-19 pneumonia in the vaccine-eligible age range (≥3 years), a 70%–80% lower risk of developing into serious Delta-variant COVID-19 among adults ≥18 years, and a 70%–80%

TABLE 2. Logistic regression analysis on risk of developing into COVID-19 pneumonia and serious COVID-19 by vaccination status, China, May 21, 2021–February 28, 2022.

Variants	Age (years)	Vaccination	Number of cases	COVID-19 pneumonia cases			Serious COVID-19 cases		
			N	n (%)	*P* value	OR (95% CI)	n (%)	*P* value	OR (95% CI)
Delta	3–17	Unvaccinated	540	169(31.3)	Ref	Ref	1(0.2)	Ref	Ref
		Partially vaccinated	160	31(19.4)	<0.01	0.53(0.34–0.81)	0(0)	–	–
		Full vaccination	496	80(16.1)	<0.01	0.42(0.31–0.57)	0(0)	–	–
		Subtotal	1,196	280(23.4)			1(0.1)		
	18–59	Unvaccinated	500	363(72.6)	Ref	Ref	39(7.8)	Ref	Ref
		Partially vaccinated	428	286(66.8)	0.06	0.76(0.57–1.01)	12(2.8)	<0.01	0.34(0.16–0.68)
		Full vaccination	4,233	2,392(56.5)	<0.01	0.49(0.40–0.60)	59(1.4)	<0.01	0.17(0.11–0.26)
		Booster	692	185(26.7)	<0.01	0.14(0.11–0.18)	1(0.1)	<0.01	0.02(0.01–0.10)
		Subtotal	5,853	3226(55.1)			111(1.9)		
	≥60	Unvaccinated	445	402(90.3)	Ref	Ref	133(29.9)	Ref	Ref
		Partially vaccinated	134	126(94.0)	0.19	1.69(0.77–3.68)	22(16.4)	<0.01	0.46(0.27–0.77)
		Full vaccination	848	645(76.1)	<0.01	0.34(0.24–0.48)	99(11.7)	<0.01	0.31(0.23–0.42)
		Booster	53	30(56.6)	<0.01	0.14(0.07–0.26)	2(3.8)	<0.01	0.09(0.01–0.36)
		Subtotal	1,480	1,203(81.3)			256(17.3)		
Omicron	3–17	Unvaccinated	20	2(10.0)	Ref	Ref	0(0)	Ref	Ref
		Partially vaccinated	20	4(20.0)	0.36	2.34(0.38–14.57)	0(0)	–	–
		Full vaccination	444	59(13.3)	0.63	1.44(0.32–6.37)	0(0)	–	–
		Subtotal	484	65(13.4)			0(0)		
	18–59	Unvaccinated	56	18(32.1)	Ref	Ref	0(0)	Ref	Ref
		Partially vaccinated	25	3(12.0)	0.07	0.29(0.08–1.10)	0(0)	–	–
		Full vaccination	645	203(31.5)	0.91	0.97(0.54–1.74)	3(0.5)	0.78	–
		Booster	675	192(28.4)	0.57	0.84(0.47–1.52)	2(0.3)	0.83	–
		Subtotal	1,401	416(29.7)			5(0.4)		
	≥60	Unvaccinated	39	31(79.5)	Ref	Ref	4(10.3)	Ref	Ref
		Partially vaccinated	12	7(58.3)	0.15	0.36(0.09–1.46)	0(0)	0.66	0.58(0–3.66)
		Full vaccination	103	54(52.4)	0.01	0.28(0.12–0.68)	4(3.9)	0.29	0.36(0.06–2.02)
		Booster	68	39(57.4)	0.02	0.35(0.14–0.87)	0(0)	0.03	0.10(0–0.61)
		Subtotal	222	131(59.0)			8(3.6)		

Note: –: data not applicable.
Abbreviations: Ref=reference; OR=odds ratio; CI=confidence interval.

lower risk of developing Omicron-variant pneumonia among adults ≥60 years. Booster doses have been recommended since October 2021 for adults ≥18 years. Among Delta infections, receipt of a booster dose was associated with an 86% lower risk of pneumonia and a 91%–98% lower risk developing serious COVID-19. Among Omicron infections in people ≥60 years, receipt of a booster dose was associated with a 65% lower risk of pneumonia. There were no serious Omicron cases among ≥60-year-olds who received a booster dose. Delta infections were more severe on average than Omicron infections in an unvaccinated population.

Because of China's policy of "zero tolerance for local transmission", there have been few domestic cases of COVID-19 and virtually all of China's population immunity comes solely from vaccine, rather than hybrid immunity from infection and vaccine. The combination of increasing vaccination coverage and increased transmissibility of Delta and Omicron variants is causing a rapid increase of breakthrough cases of COVID-19. The degree to which vaccines maintain protection is critically important in the assessment of the strength of population immunity and is of great significance for adjustment of immunization strategies.

Compared with the international mRNA and adenovirus-vectored vaccines, there were fewer real-world data about breakthrough cases from China-produced COVID-19 vaccines. A case-control study in the US showed that full mRNA vaccination significantly reduced risk of hospitalization (OR=0.15) and death or invasive mechanical ventilation in hospitalized cases (OR=0.33) (*3*), findings consistent with ours. Our finding that China-made COVID-19 vaccines reduced risk of pneumonia by 72% among ≥ 60-year-olds infected with Omicron, with no serious boosted cases, was consistent with the results reported by the University of Hong Kong (*4*). Their study, which was also in an infection-naive population, showed that protective effectiveness of 2 doses of inactivated vaccine among people ≥ 60 years was 72% and protective effectiveness of a homologous booster dose was 98%. Although with a smaller number of serious cases, our study found a similar booster dose effect among ≥60-year-olds, with a 90% reduction of serious COVID-19 caused by the Omicron variant. We need to sustain monitoring and analysis of breakthrough cases for more refined assessments.

Existing evidence from neutralizing antibody testing shows that the Omicron variant has partial immune escape (*5*). A real-word study in South Africa found that the protective effect of BNT162b2 vaccine against Delta was 93% after full vaccination, but decreased to 70% against Omicron. Although effectiveness of COVID-19 vaccines against infection with Omicron is lower, protection against hospitalization and death remains high (*6*). Data from U.S. CDC compared unvaccinated, full primary vaccinated, and boosted individuals, and found significantly reduced morbidity (725.6/100,000, 254.8/100,000 and 148.6/100,000) and mortality (7.8/100,000, 0.6/100,000 and 0.1/100,000) by vaccination and boosting (*7*).

This study was subject to several limitations. First, the clinical outcomes (severity) of cases were based on the most severe clinical classification reported, which may cause some misclassification bias due to regional variation in classification. Second, the study could only analyze associations between vaccination and clinical outcomes, and we did not have data on underlying medical conditions and did not control for time interval after vaccination and other factors associated with protective effectiveness. Third, our study was a case-case study, a special kind of case-control study, so the results only reflected the association between vaccination and risk of disease development and were not direct measures of vaccine effectiveness. Moreover, in view of the vast majority of cases administered inactivated vaccines and the case sizes of the other two vaccines were not big enough to do statistical analysis, our study did not include the analysis of different technical platforms vaccines.

In conclusion, our study of Delta infections showed that China-made COVID-19 vaccines were associated with a 50% to 70% lower risk of developing into pneumonia among all ages and a 70% to 80% lower risk of severe COVID-19 among adults. Booster doses were associated with an 86% risk reduction for pneumonia and a 91% to 98% risk reduction of developing severe COVID-19. Our study of Omicron infections found that full vaccination and booster doses were associated with reduced risk of pneumonia among adults over 60 years, with the booster dose associated with reduced risk of developing serious COVID-19. In an unvaccinated population, Delta infections were more severe on average than Omicron infections.

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Preplanned Studies

Aerosol Transmission of SARS-CoV-2 in Two Dormitories — Hubei and Shandong Provinces, China, 2020

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Summary

What is already known about this topic?

Aerosol transmission is one route for the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, uncertainty remains on the threshold of ventilation rate in its occurrence.

What is added by this report?

Based on two cases in Shandong Province and Hubei Province, the effect of wearing masks and the minimum ventilation required to reduce coronavirus disease 2019 (COVID-19) aerosol transmission was determined.

What are the implications for public health practice?

No masking and low ventilation rates lead to a relatively high contribution of aerosols to COVID-19 transmission. Thus, public awareness of wearing masks should increase and the ventilation rate should be sufficiently higher than the minimum required ventilation.

Aerosol transmission of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been confirmed in many studies (*1*–*3*). Previous studies have shown that the highest concentration of outbreak cases outside of the Hubei Province came from indoor environments (*4*), especially ones with overcrowding and poor ventilation. A previous theoretical model predicted that a ventilation rate above 36 m^3/h per person can effectively reduce the risk of aerosol infection when people socially distance (*5*); however, this has not been confirmed by real-world data.

Overall, 2 COVID-19 outbreaks in the dormitory buildings in Hubei and Shandong Province — with different mask wearing habits and rates of indoor ventilation — were analyzed in February 2020. From June 5–13, 2020, an onsite investigation was conducted. The epidemiological data were collected and ventilation conditions were investigated at the time of occurrence. Preliminary information of the cases was obtained, including dates of symptom onset, mask wearing habits, and detailed infection data, such as the number of infected persons in each room and their distributions. The information collected also includes the building information, the opening of doors and windows, and the mechanical ventilation conditions.

Experiments were carried out according to whether doors or windows were open and ventilation equipment was on during the epidemic. The ventilation rate was measured by CO_2 tracer-concentration decay method. More than two concentration detectors and temperature recorders were arranged in each room. After releasing a certain concentration of CO_2, the change in indoor CO_2 concentration was continuously recorded for 2 hours with a sampling interval of 1 minute. A total of 54,848 experimental data points were obtained, including indoor CO_2 concentration, outdoor CO_2 concentration, indoor and outdoor temperature, etc.

For the dormitory building in Shandong Province, the main ventilation mode was mechanical ventilation. When the wind pressure and the window opening were both small, the difference in ventilation rate between winter and summer was not obvious. For the building in Hubei Province, there was no mechanical ventilation and it was located in the city center, densely surrounded by buildings; therefore, the wind ventilation was ignored and only buoyancy ventilation was considered. The natural ventilation rate was calculated by the following formula (*6*):

$$Q = \frac{1}{3} C_D A \sqrt{gH \frac{T_i - T_0}{T_i}}$$

$$Let\ k = \frac{1}{3} C_D A \sqrt{gH}$$

$$Q = k \sqrt{\frac{T_i - T_0}{T_i}}$$

where Q is the natural ventilation rate (m^3/h); C_D is the flow coefficient; A is the window opening area (m^2); g is the gravitational acceleration; H is the height

of the window (m); T_i is the indoor temperature (K); and T_0 is the outdoor temperature (K).

Through this field experiment, the room ventilation rate and the difference between indoor and outdoor temperature were measured, and the k value of each room was calculated. Outdoor temperatures during the disease outbreak period were obtained through a meteorological website and the average outdoor nighttime temperature was used for calculations.

According to our investigation, the transmission period for the Shandong Province was mainly from January 21 to February 12, 2020, and the infected people were concentrated in the north dormitory building.

The first case of infection was a dormitory supervisor who had been infected before January 21, due to contact with an asymptomatic infected person. There were 30 dormitory rooms in the building with an average number of 9 residents in each room. During the epidemic, internal personnel did not wear masks and they were in frequent contact. In this case, the infection rate in 30 rooms was between 29%–100%, of which 7 rooms had a 100% rate of infection. During the outbreak, the interior doors of the building were open, and the exterior windows were closed. The ventilation of rooms mainly depended on negative pressure generated by the four exhaust fans in the bathroom that were always on.

This case also occurred in Hubei Province due to infections of dormitory staff. The epidemic spread mainly from January 21 to February 11. There were 90 rooms in the building, and the average number of residents in each room was 21. Internal personnel used hand-stitched coarse cloth masks throughout the day. There was no mandatory mask wearing requirement at night; however, they were required to sleep on time. According to interviews conducted, a centralized area consisting of ten rooms (recorded as area M) had residents who were older and weak. During winter, they kept doors and windows closed all day to prevent catching a cold. Members in this area had a high awareness of self-protection and wore masks all day. Most of the residents in other areas (recorded as zone N) were young and middle-aged. They did not have a habit of wearing masks at night, and they opened windows or doors all day to enhance ventilation. The overall rate of infection was between 0% and 56%, of which 14 rooms had a 0% rate of infection.

According to the simulation results, the ventilation rate of each room in Shandong Province was 129–246 m^3/h. The range of ventilation rate per person was 12.9–32.4 m^3/h. The ventilation rate of each room in Hubei Province was between 169 and 1,790 m^3/h (Supplementary Table S1). The ventilation rate per person was between 6.9 and 56.4 m^3/h (Figure 1).

The average room ventilation in Hubei M Zone was 236 m^3/h and the average ventilation rate per person was 7.7 m^3/h. The average room ventilation in Hubei N Zone was 601 m^3/h and the average ventilation rate per person was 28 m^3/h. The room ventilation and ventilation rate per person in Zone M were significantly lower than those in Zone N. However, the average infection rate was 8% in Zone M and 16% in Zone N. Zone M achieved a lower infection rate with worse ventilation levels, reflecting how mask wearing habits reduce infection rates.

In comparing the Shandong case with zone N of the Hubei case, their ventilation rates were both between 12.9 and 32.4 m^3/h per person (Figure 2); however, the average infection rate for Zone N was 18% and 74% for the Shandong case. The difference in the likelihood of infection between the two regions also reflected the significant effect of mask wearing habits.

The data from the Zone N in Hubei case showed that there was an obvious threshold of ventilation rate (Figures 1 and 2). When the room ventilation rate was higher than 800 m^3/h or 40 m^3/h per person, the rate of infection was less than 25%. Therefore, it was concluded that the contribution of aerosol transmission was very low. When the room ventilation rate was lower than 800 m^3/h or 40 m^3/h per person, the highest infection rate reached 56%, indicating a high risk of aerosol transmission.

DISCUSSION

Previous studies have shown that SARS-CoV-2 can survive 3 hours in aerosols (*7*), and a number of cases have proven the possibility of aerosol transmission of COVID-19, especially in poorly ventilated and crowded spaces. Li Yuguo et al. discussed the possibility of aerosol transmission due to the poor ventilation below 3.2 L/s (11.5 m^3/h) per person through the analysis of the actual case. However, they did not determine the minimum ventilation requirement for mitigating airborne transmission of COVID-19 (*8–9*). By analyzing the ventilation rate and infection rate of the dormitories in Hubei and Shandong Province, the change of infection rate was obtained within a larger range of ventilation rates. Our

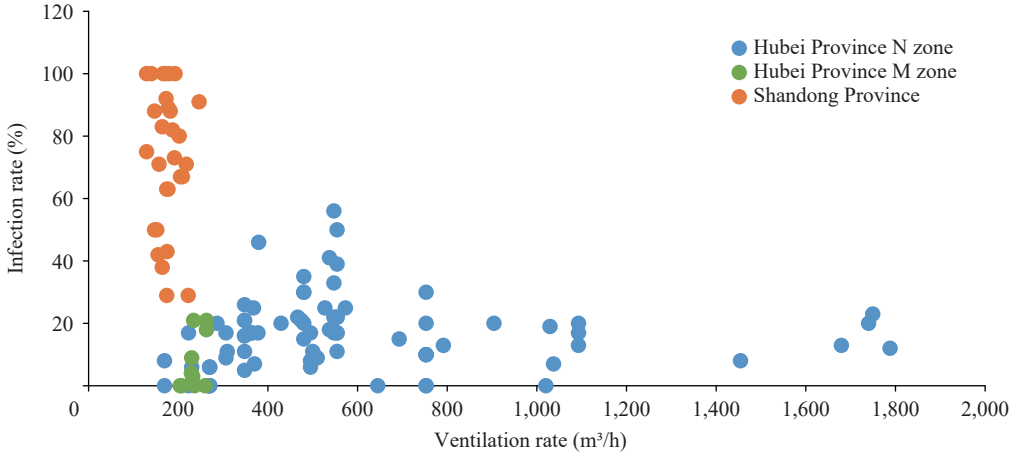

FIGURE 1. Relationship between room infection rate and room ventilation rate in two dormitory buildings in Hubei and Shandong Province.
Note: Each point in the figure represents a room, the abscissa axis represents the ventilation rate (m³/h), and the ordinate axis represents the infection rate (%).

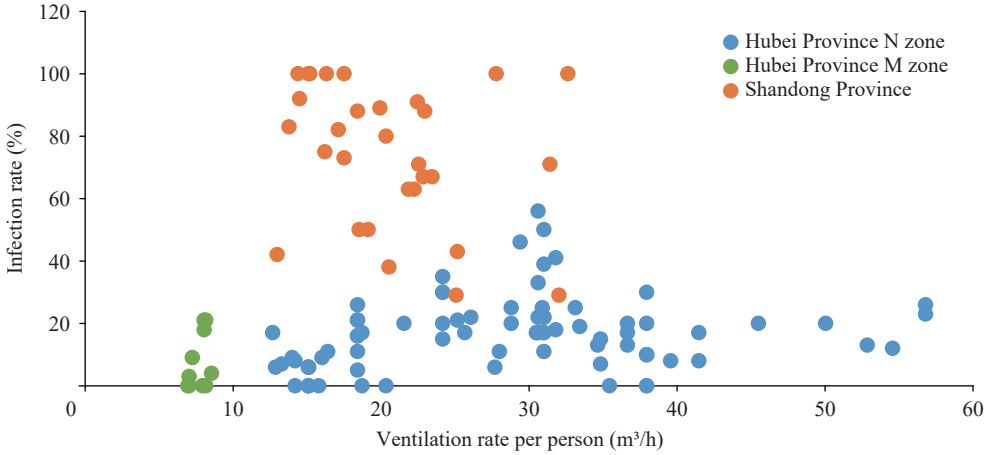

FIGURE 2. Relationship between room infection rate and room ventilation rate per person in two dormitory buildings in Hubei and Shandong Province.
Note: Each point in the figure represents a room, the abscissa axis represents the ventilation rate per person (m³/h), and the ordinate axis represents the infection rate (%).

results showed that if the ventilation rate per person was higher than 40 m³/h, the risk of aerosol transmission could be greatly reduced.

Through analyzing the actual data of two dormitory buildings with different mask wearing habits, it was found that even wearing hand-stitched coarse cloth masks can significantly reduce the risk of infection.

This study has some limitations. When analyzing the relationship between infection rate and ventilation rate, the statistics and comparison were carried out in the unit of room, and the difference of dormitory members in different bed positions were not discussed. Also, the indoor personnel's behavior could only rely on recollections from memory.

These results help guide COVID-19 prevention and control in dormitory spaces, suggesting that people should wear masks when entering or staying in a confined space and a sufficient ventilation rate above 40 m³/h per person should be maintained.

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SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. The location, ventilation rate, ventilation rate per person and infection rate of each room in two dormitories.

Zone	Room No.	Floor	Room ventilation (m^3/h)	Ventilation rate per person (m^3/h)	infection rate (%)
Hubei Province N zone	1	1	270	15	0
Hubei Province N zone	2	1	266	15.7	0
Hubei Province N zone	3	1	270	15	6
Hubei Province N zone	4	1	270	15	0
Hubei Province N zone	5	1	270	15	6
Hubei Province N zone	6	1	270	15	0
Hubei Province N zone	7	1	270	15	6
Hubei Province N zone	8	1	230	12.8	6
Hubei Province N zone	9	1	169	14.1	0
Hubei Province N zone	10	1	169	14.1	8
Hubei Province N zone	11	1	510	15.9	9
Hubei Province N zone	12	2	537	31.6	41
Hubei Province N zone	13	2	527	32.9	25
Hubei Province N zone	14	2	537	31.6	18
Hubei Province N zone	15	2	547	30.4	22
Hubei Province N zone	16	2	547	30.4	33
Hubei Province N zone	17	2	547	30.4	17
Hubei Province N zone	18	2	547	30.4	56
Hubei Province N zone	19	2	495	27.5	6
Hubei Province N zone	20	2	364	30.3	17
Hubei Province N zone	21	2	364	30.3	17
Hubei Province N zone	22	2	1,029	33.2	19
Hubei Province N zone	23	3	554	30.8	17
Hubei Province N zone	24	3	554	30.8	22
Hubei Province N zone	25	3	554	30.8	11
Hubei Province N zone	26	3	554	30.8	39
Hubei Province N zone	27	3	554	30.8	22
Hubei Province N zone	28	3	554	30.8	50
Hubei Province N zone	29	3	554	30.8	17
Hubei Province N zone	30	3	500	27.8	11
Hubei Province N zone	31	3	368	30.7	25
Hubei Province N zone	32	3	379	29.2	46
Hubei Province N zone	33	3	573	28.6	25
Hubei Province N zone	34	3	904	45.2	20
Hubei Province N zone	35	4	480	24	35
Hubei Province N zone	36	4	480	24	15
Hubei Province N zone	37	4	480	24	20
Hubei Province N zone	38	4	466	25.9	22
Hubei Province N zone	39	4	474	25	21
Hubei Province N zone	40	4	480	24	30

Continued

Zone	Room No.	Floor	Room ventilation (m^3/h)	Ventilation rate per person (m^3/h)	infection rate (%)
Hubei Province N zone	41	4	480	24	30
Hubei Province N zone	42	4	429	21.4	20
Hubei Province N zone	43	4	306	25.5	17
Hubei Province N zone	44	4	286	28.6	20
Hubei Province N zone	45	4	791	34.4	13
Hubei Province N zone	46	5	753	37.7	20
Hubei Province N zone	47	5	753	37.7	30
Hubei Province N zone	48	5	753	37.7	10
Hubei Province N zone	49	5	753	37.7	0
Hubei Province N zone	50	5	753	37.7	10
Hubei Province N zone	51	5	753	37.7	0
Hubei Province N zone	52	5	753	37.7	10
Hubei Province N zone	53	5	693	34.6	15
Hubei Province N zone	54	5	495	41.2	17
Hubei Province N zone	55	5	495	41.2	8
Hubei Province N zone	56	5	1,454	39.3	8
Hubei Province N zone	57	6	348	18.3	26
Hubei Province N zone	58	6	348	18.3	21
Hubei Province N zone	59	6	348	18.3	16
Hubei Province N zone	60	6	348	18.3	16
Hubei Province N zone	61	6	348	18.3	5
Hubei Province N zone	62	6	348	18.3	21
Hubei Province N zone	63	6	348	18.3	11
Hubei Province N zone	64	6	309	16.3	11
Hubei Province N zone	65	6	223	18.6	17
Hubei Province N zone	66	6	223	18.6	0
Hubei Province N zone	67	6	645	20.2	0
Hubei Province N zone	68	2	1,679	52.5	13
Hubei Province N zone	69	2	1,749	56.4	23
Hubei Province N zone	70	2	1,788	54.2	12
Hubei Province N zone	71	2	1,749	56.4	26
Hubei Province N zone	72	2	1,740	49.7	20
Hubei Province N zone	73	3	1,020	35.2	0
Hubei Province N zone	74	3	1,093	36.4	17
Hubei Province N zone	75	3	1093	36.4	13
Hubei Province N zone	76	3	1,093	36.4	20
Hubei Province N zone	77	3	1,037	34.6	7
Hubei Province N zone	78	4	306	13.9	9
Hubei Province N zone	79	4	378	12.6	17
Hubei Province N zone	80	4	370	13.2	7
Hubei Province M zone	1	2	207	6.9	0
Hubei Province M zone	2	2	234	8.1	21

Continued

Zone	Room No.	Floor	Room ventilation (m^3/h)	Ventilation rate per person (m^3/h)	infection rate (%)
Hubei Province M zone	3	2	229	8.5	4
Hubei Province M zone	4	2	236	7.9	0
Hubei Province M zone	5	2	204	7	0
Hubei Province M zone	6	3	230	7.2	9
Hubei Province M zone	7	3	263	8	18
Hubei Province M zone	8	3	260	8.1	0
Hubei Province M zone	9	3	263	8	21
Hubei Province M zone	10	3	232	7	3
Shandong Province	1	2	152	19	50
Shandong Province	2	2	147	18.3	88
Shandong Province	3	2	129	16.1	75
Shandong Province	4	2	147	18.4	50
Shandong Province	5	2	129	16.2	100
Shandong Province	6	2	140	17.4	100
Shandong Province	7	2	157	22.4	71
Shandong Province	8	2	202	20.2	80
Shandong Province	9	2	172	14.3	100
Shandong Province	10	2	191	17.4	73
Shandong Province	11	3	227	32.4	100
Shandong Province	12	3	182	22.8	88
Shandong Province	13	3	178	19.8	89
Shandong Province	14	3	174	24.9	29
Shandong Province	15	3	177	22.1	63
Shandong Province	16	3	174	21.7	63
Shandong Province	17	3	173	14.4	92
Shandong Province	18	3	180	15	100
Shandong Province	19	3	187	17	82
Shandong Province	20	3	164	13.7	83
Shandong Province	21	4	218	31.2	71
Shandong Province	22	4	175	25	43
Shandong Province	23	4	222	31.8	29
Shandong Province	24	4	193	27.6	100
Shandong Province	25	4	246	22.3	91
Shandong Province	26	4	164	20.4	38
Shandong Province	27	4	166	15.1	100
Shandong Province	28	4	209	23.3	67
Shandong Province	29	4	205	22.7	67
Shandong Province	30	4	155	12.9	42

Notes from the Field

A Local Cluster of Omicron Variant COVID-19 Likely Caused by Internationally Mailed Document — Beijing Municipality, China, January 2022

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On January 15, 2022, a 26 years old female (Case A) went to a sampling site for coronavirus disease 2019 (COVID-19) testing due to excessive fatigue and fever for two days. This patient preliminarily tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) using a quantitative real-time reverse transcription polymerase chain reaction (qRT-PCR) method. Beijing CDC subsequently verified the result. Furthermore, a rapid site mutation test based on qRT-PCR showed that the virus carried the Q498R mutations but lacked the L452R, T478K, and P681R mutations (ABT, Beijing, China and Bojie), indicating the case was infected by the Omicron variant.

In the following seven days, five close contacts tested positive in screenings, including her mother (Case B), a colleague of the index case (Case C), and three family members of Case C (Case D, E, and F).

The field investigation was performed to identify the source of infection. Case A lived and worked in Haidian District, Beijing, without travel history out of Beijing or close contact with local or imported high-risk populations. Further investigation indicated that the case sent and received international mail occasionally at no fixed interval, due to the need of her work. Notably, an internationally mailed document was received by the case on January 11 (2 days before onset of symptoms), which was delivered from abroad on January 7. The disinfection was carried out from the outer surface of the packaged document when it arrived in Beijing. A total of 1,054 environmental samples were collected, including 22 swabs for the package received by the case. The qRT-PCR showed that 12 of 22 samples were positive in the SARS-CoV-2 ORF1ab/N gene test, including 2 samples collected from the outer surface of the package, 2 from the inner package, and the other 8 from contained papers. Moreover, the rapid site mutation test suggested all 12 positive samples carried the Q498R mutation, which inferred infection with the Omicron variant.

The respiratory samples from all 6 cases and 12 environmental samples, including the inner package and contained papers that were untouched by the case, were used for next generation sequencing (NGS). The viral RNA was reverse transcribed and amplified using ULSEN® 2019-nCoV Whole-Genome Capture Kit (Beijing MicroFuture Technology Co., Ltd, Beijing, China). Then, the sequencing libraries were prepared using the Illumina Nextera® XT Library Prep Kit (Illumina, Inc., San Diego, CA, USA) and were conducted on Illumina MiniSeq platform. Six full genomes were collected from the cases. Overall, 1 full genome and 1 near-full-length genome with a coverage of 88.8% were obtained from environmental samples due to the low viral load. The sequencing analysis concluded that the whole virus belonged to lineage BA.1, Variants of Concern (VOC)/Omicron. In addition, 7 full genomes and 1 near-full-length genome shared a nucleotide similarity of 100%. Phylogenetic analysis indicated the virus located near the cluster of some strains collected in North American and Southeast Asia in mid-December, which had significant differences with local clusters in China in the same period (Figure 1).

This is the first local cluster caused by Omicron variant in Beijing. The Omicron variant was first reported on November 9, 2021 and was listed as a VOC by the World Health Organization (WHO) (*1–2*). As of February 1, 2022, this variant has been identified in more than 170 countries and has become the dominant strain worldwide (*3*). A remarkable finding of this study was the possible source of the infection for this cluster. We proposed the infection was induced by the internationally mailed document, mainly based on the following evidence. Field investigations showed no potential exposure of the case except the internationally mailed document, with an

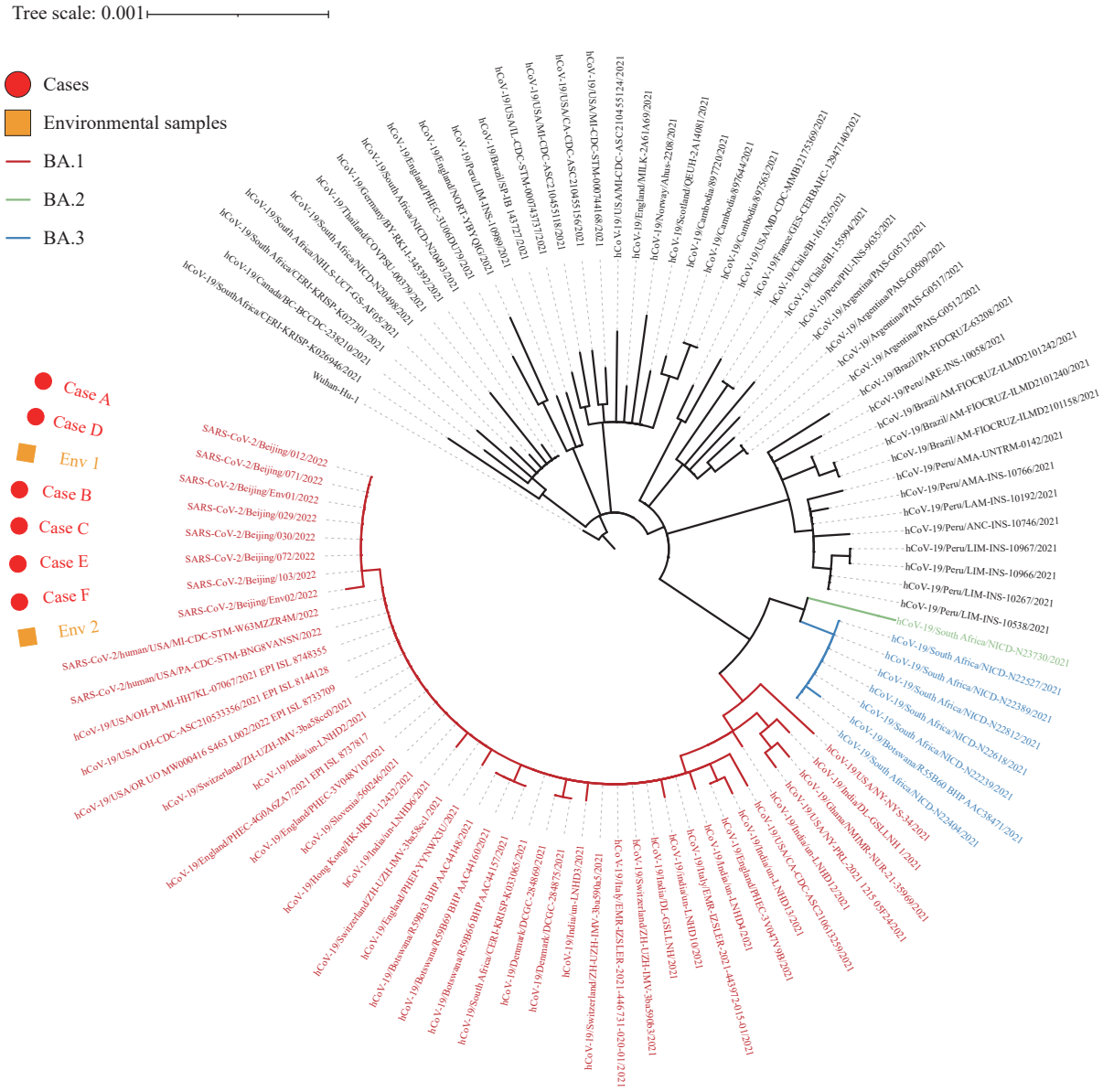

FIGURE 1. Neighbor-joining phylogenetic tree for the local cluster of Omicron Variant in Beijing, China, 2022.
Note: The six genomes from Case A to E were indicated by dots. The two genomes from environmental samples were indicated by squares. The major (VOC)/Omicron lineages were colored. The tree was rooted using strain Wuhan-Hu-1 (EPI_ISL_402125).
Abbreviations: VOC=variants of concern; Env 1=environmental sample 1; Env 2=environmental sample 2.

onset interval of 2 days. All identified cases showed epidemiological links with Case A. Environmental surveillance identified SARS-CoV-2 RNA positive samples from the package's contents, and parts of these positive contents were untouched by the case. More importantly, NGS showed that the genome of the case matched the samples collected from the mailed documents, which differed from other local strains in China.

Previous studies investigated the virus survival under various conditions. Chin et al. showed SARS-CoV-2 could only survive on printed papers and tissue papers for 3 hours; while on treated smooth papers (such as banknote), it could survive for 4 days (*4*). Van Doremalen et al. found that no viable SARS-CoV-2 could be measured after 24 hours on cardboard (*5*). In general, SARS-CoV-2 was less stable on papers than on plastic and stainless steel. However, the temperature should not be neglected during the assessment for viral survival. The low temperatures in winter and in some countries located at high latitudes might lead to an extended viral survival period (*4*) and should be

considered as an essential factor in this cluster.

In summary, we reported the first local cluster caused by Omicron variant in Beijing and showed this cluster was likely caused by a contaminated internationally mailed document, which has not been reported before. Our data emphasized the surveillance and disinfection of imported express cargo in COVID-19 control, especially in certain seasons and regions in China.

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Finland Celebrates the 50th Anniversary of North Karelia Project

April 6, 2022 in Joensuu, Finland marked 50 years since the start of the North Karelia project — the first population-based program for prevention and control of cardiovascular diseases. The decline in heart disease mortality over the last 50 years in Finland has been one of the most rapid in the world and the overall health of the adult population has greatly improved. Population-based prevention through changes in lifestyle and environment was the most cost-effective and sustainable way of controlling cardiovascular and other major chronic diseases.

During the 1960's, Finland grew painfully aware of its massive burden of ischemic heart disease. The Seven Countries Study showed that Finnish men had higher serum cholesterol level than any other population in the world. Mean blood pressure was also high and almost 60% of men were smokers. Coronary mortality, especially among middle age men, was extremely high across Finland at about 500/100,000 and in North Karelia, the most eastern province of the country, at 700/100,000.

The high cardiovascular mortality in an eastern province North Karelia in Finland caused great concern among the local population. A petition for action to the Finnish government was signed by local representatives of the population. In response, the North Karelia project was launched in 1972 to carry out a comprehensive community based prevention program. After the first five years, prevention activities were launced nationally. The main aim was to reduce the extremely high serum cholesterol, blood pressure and smoking levels with lifestyle changes and improved drug treatment, especially for hypertension. Major declines were seen in serum cholesterol, blood pressure, and smoking levels. Coronary mortality decreased in the middle age population by 84% from 1972 to 2014. About 2/3 of the mortality decline was explained by risk factor changes and 1/3 by improvement of new treatments developed since 1980s.

The North Karelia experience, from epidemiology to public health action, is a demonstration of how an epidemic of cardiovascular diseases — and more general major non-communicable diseases — can be drastically reduced when population risk factors and determinants change. The experiences and results of the North Karelia Project in Finland supported the idea that a well-planned and determined population-based program can have a major impact, reducing cardiovascular rates in the community.

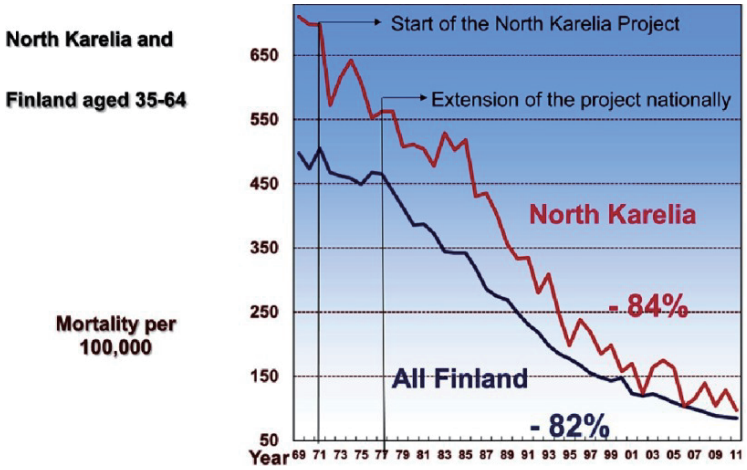

Figure 1. Coronary heart disease mortality in men 1969–2011 in Finland and North Karelia.

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