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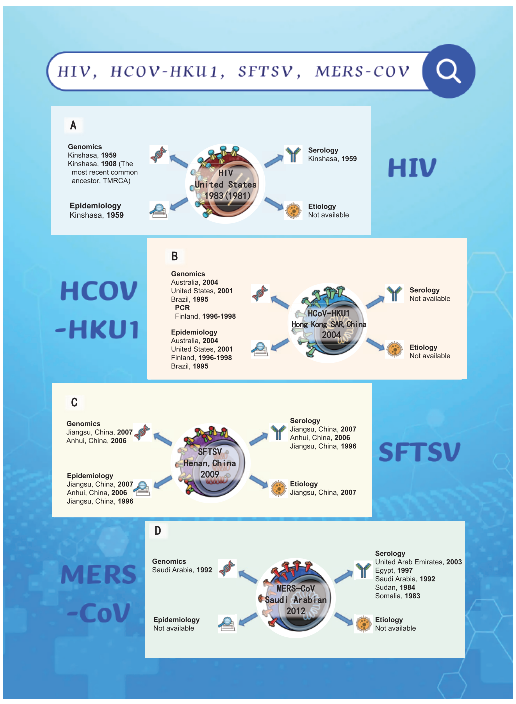

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Preplanned Studies

COVID-19 Vaccination Rates of People Who Use Drugs — Chengdu City, Sichuan Province, China, November 2021 – February 2022

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Summary

What is already known about this topic?

Few studies have reported that people who use drugs (PWUDs) have much lower coronavirus disease 2019 (COVID-19) vaccination rates than the general population, especially with no relative information reported in China specifically.

What is added by this report?

This study seminally uncovers that the vaccination rate among PWUDs was about 79.34% in one district of Chengdu City, Sichuan Province, China. Assuming that unvaccinated PWUDs with disease records were really not eligible for vaccination, the vaccination rate goes up to 87.25% among the studied PWUDs. The study implies that PWUDs were not left behind in the vaccination drive for COVID-19 in China.

What are the implications for public health practice?

In pandemics like COVID-19, government leadership and the overall planning and distribution of public health products are critical in achieving national health equity. However, in order to do this as well as avoid discrimination or exclusion among specific portions of the general population, it's necessary to understand the vaccination rates and behaviors of at-risk groups such as PWUD's.

Vaccination is expected as the most effective tool for protecting people from getting seriously ill or dying of COVID-19 in the absence of specialized treatment drugs (*1*). By June 10, 2022, the data of the World Health Organization (WHO) reported that about 11.83 billion doses had been administered globally and an average of 65.7% of the worldwide population have received at least 1 dose of a COVID-19 vaccine (*2*). However, vaccination coverage was significantly uneven across populations and geographically. Previous studies have already shown that people who use drugs (PWUDs) in particular are vulnerable and easily neglected by public health infrastructure, and have lower vaccination coverage in comparison with the general population (*3*–*8*).

One reason is that, in many countries, PWUDs were not included in initial priority groups for vaccination of COVID-19. In addition, they are more likely to face barriers to vaccination on the basis of insufficient vaccine supplies (*4*). Third, PWUDs often possess lower vaccination acceptance rates compared to the general population (*5*). One study on patients with substance use disorders in the United States showed that nearly half of the patients expressed unwillingness to get a COVID-19 vaccine, even though they — particularly those with opioid use disorders — had been told they were at a higher risk of being infected and getting severally ill as a result of chronic lung or liver diseases (*6*). Two studies further reported that only 10% (*vs.* 60% of the general population) and 57% (*vs.* 77% of the general population) of people who inject drugs received COVID-19 vaccines during the early phase of COVID-19 in the United States and Australia, respectively (*7*–*8*).

China was one of the first countries to initiate nationwide vaccinations for COVID-19 and achieved a coverage rate of 87.85% by March 18, 2022 (*9*). However, it was not clear prior to this study how high COVID-19 vaccination rates might have been among PWUDs in China. As such, this study endeavored to investigate PWUD vaccination coverage rates by analyzing data from the Management and Control Database for Persons Who Use Drugs in one particular Sichuan district.

This research analyzed anonymous data in the Management and Control Database for Persons Who Use Drugs in one district of Chengdu City, Sichuan Province, China, from November 2021 to February 2022, which is part of National Dynamic Management and Control Database for Persons Who Use Drugs (*10*). The data included age, sex, drug categories, last treatment approaches, drug use history, drug use modes, disease history, dosage of vaccine (single dose, double doses, and three doses), time of vaccination, and self-reported reasons of non-vaccination. All the data were updated in February 2022 to reflect participants' latest vaccination status. There were two reasons for this study to select this district in Sichuan Province in particular. One reason is that it is difficult to access the PWUD data necessary for this type of research in other districts. Second, Sichuan ranked 5th in drug users, 6th in terms of GDP, and 8th in the service industry nationally. Therefore, it has a fair degree of representativeness for PWUDs nationwide.

The PWUDs were divided into groups based on their vaccination information (i.e. presence of vaccination, type of vaccine, and time of vaccination). The vaccination rate was calculated by the number of fully vaccinated persons divided by the total of PWUDs who had clear vaccine information. The drugs that PWUDs used were divided into opioid drugs (ex. heroin), synthetic drugs (ex. methamphetamine), psychoactive substances (ex. marijuana, LSD), and polydrug use (ex. heroin and methamphetamine together) based on international classifications.

All data were double-checked by Erri Du and Pengyu Jiang. The chi-square test was used to compare the above characteristics between the two groups (vaccinated and unvaccinated); the odds ratios (ORs) and their 95% Confidence Intervals (CIs) for the multivariable binary logistic regression were used to estimate factors associated with the vaccination of PWUDs.

A two-sided *P* value of 0.05 or less was regarded as significant. All the data cleaning was done using Excel (version 2017, Microsoft Corp., Redmond, WA, US) and WPS Office (version 3.9.6, Kingsoft Office Corp., Beijing, China). All analysis was done using IBM SPSS (version 24.0, IBM Corp., Armonk, NY, US). The data were anonymized without participant identifiers so that this research does not require additional regulation by the Institutional Review Board.

Among a total of 1,671 available records of PWUDs in the region, 310 PWUDs did not have vaccination information, 192 PWUDs could not specify their vaccination situation by type of vaccine and/or time of vaccine, 56 PWUDs had not finished vaccination, and 1,113 PWUDs with clear vaccinating information were included in the final analysis (Figure 1). The fully vaccinated PWUDs with single dose, double doses, and triple doses were 2, 869, and 12, respectively (Figure 1).

86.79% of the PWUDs were 30–59 years old. Men accounted for 74.39% of the sampled PWUDs. About 47.80% of the PWUDs had jobs, while 36.30% PWUDs reported being unemployed (Table 1).

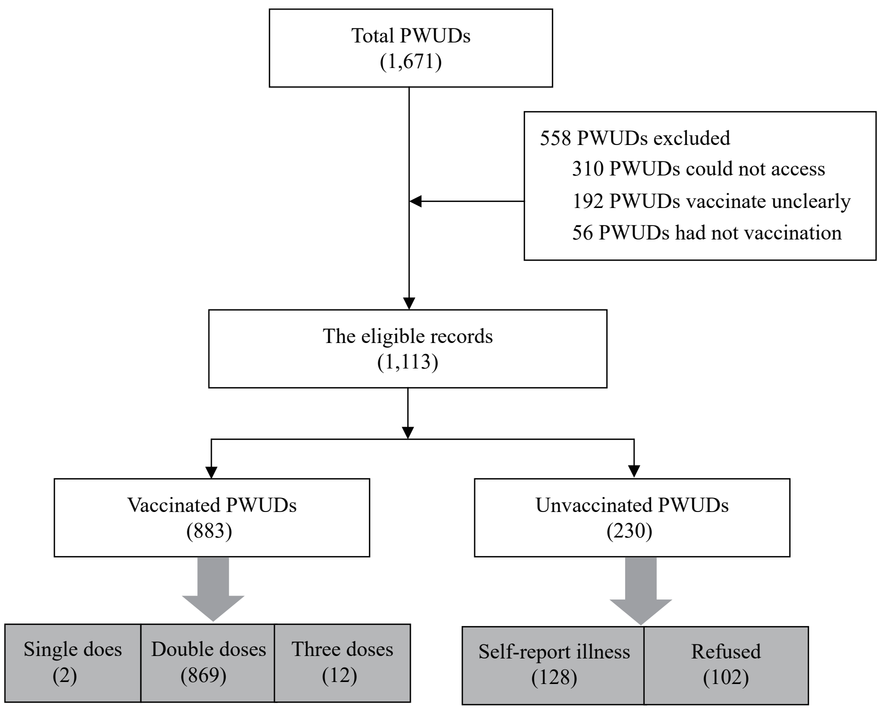

FIGURE 1. The management of data for PWUDs
Abbreviation: PWUDs=people who use drugs.

TABLE 1. The basic characteristics of people who use drugs.

Characteristic	Total, n (%)	Fully vaccinated, n (%)	Not vaccinated, n (%)	Vaccination rate (%)
Total	1,113	883	230	79.34
Sex				
Men	828 (74.39)	654 (74.07)	174 (75.65)	78.99
Women	285 (25.61)	229 (25.93)	56 (24.35)	80.35
Age (years)				
19–29	96 (8.63)	74 (8.38)	22 (9.57)	77.08
30–39	393 (35.31)	345 (39.07)	48 (20.87)	87.79
40–49	299 (26.86)	252 (28.54)	47 (20.43)	84.28
50–59	274 (24.62)	184 (20.84)	90 (39.13)	67.15
≥60	51 (4.58)	28 (3.17)	23 (10.00)	54.90
Occupation				
Public institution & enterprise	172 (15.45)	155 (17.55)	17 (7.39)	90.12
Service industry	360 (32.35)	297 (33.64)	63 (27.39)	82.50
Unemployed	404 (36.30)	292 (33.07)	112 (48.70)	72.28
Missing	177 (15.90)	139 (15.74)	38 (16.52)	78.53
Type of drugs used				
Only opioid	221 (19.86)	142 (16.08)	79 (34.35)	64.25
Only synthetic	745 (66.94)	630 (71.35)	115 (50.00)	84.56
New psychoactive substance	35 (3.14)	30 (3.40)	5 (2.17)	85.71
Polydrug	103 (9.25)	75 (8.49)	28 (12.17)	72.82
Missing	9 (0.81)	6 (0.68)	3 (1.30)	66.67
Status of last treatment				
Completed	218 (19.59)	189 (21.40)	29 (12.61)	86.70
Drug maintenance therapy	10 (0.90)	7 (0.79)	3 (1.30)	70.00
Compulsory isolated detoxication	75 (6.74)	58 (6.57)	17 (7.39)	77.33
Administrative detention	179 (16.08)	154 (17.44)	25 (10.87)	86.03
Community-based detoxification	240 (21.56)	176 (19.93)	64 (27.83)	73.33
Community-based rehabilitation	181 (16.26)	153 (17.33)	28 (12.17)	84.53
Missing	210 (18.87)	146 (16.53)	64 (27.83)	69.52
Years of using drugs				
≤5	624 (56.06)	520 (58.89)	104 (45.22)	83.33
6–10	170 (15.27)	139 (15.74)	31 (13.48)	81.76
11–15	186 (16.71)	135 (15.29)	51 (22.17)	72.58
≥16	32 (2.88)	18 (2.04)	14 (6.09)	56.25
Missing	101 (9.07)	71 (8.04)	30 (13.04)	70.30
Mode of using drugs				
Oral	907 (81.49)	742 (84.03)	165 (71.74)	81.81
Injection	89 (8.00)	57 (6.46)	32 (13.91)	64.04
Oral & injection	66 (5.93)	41 (4.64)	25 (10.87)	62.12
Missing	51 (4.58)	43 (4.87)	8 (3.48)	84.31
Diseases records				
No diseases	944 (84.82)	815 (92.30)	129 (56.09)	86.33
Only IDs	25 (2.25)	9 (1.02)	16 (6.96)	36.00
Only CDs	130 (11.68)	52 (5.89)	78 (33.91)	40.00
IDs & CDs	14 (1.26)	7 (0.79)	7 (3.04)	50.00

Abbreviation: IDs=infectious diseases; CDs=chronic diseases.

Synthetic drugs and opioids were the main drugs used by sampled PWUDs (66.94% and 19.84%, respectively). Oral use was the most popular reported drug use mode (81.49%). About 56.06% of the PWUDs started using drugs less than 5 years ago, and 84.82% had no disease records. More than 61.54% of the PWUDs were still in treatment (Table 1).

By February 2022, 883 PWUDs were fully vaccinated, and the vaccination rate reached 79.34% among all PWUDs included in this analysis (Table 1). However, 101 of the 230 unvaccinated PWUDs had illness records, so the vaccination rate could be calculated as 87.25% if this study excluded these 101 PWUDs (Table 1). Occupation and diseases were significant risk factors related to the vaccination rate of PWUDs (Table 2, Supplementary Table S1, available in http://weekly.chinacdc.cn). The finding indicated that the PWUDs unemployed and employed in service sectors were less likely to be vaccinated than those in public institutions and enterprises (the reference group), the risk of unvaccination were about 3 times [2.52 (1.33–4.77)] and 4 times [3.81 (2.03–7.14)] that of the reference group, respectively (Table 2). The PWUDs with infectious diseases, chronical diseases, or both infectious and chronical diseases were 9 times [9.49 (3.67–24.59)], 8 times [8.22 (5.19–13.03)], and 4 times [3.73 (1.12–12.41)] the risk of unvaccination compared to those who did not report any diseases, respectively (Table 2).

DISCUSSION

An unexpected finding is that the COVID-19 vaccination rate is about 79.34% among the studied PWUDs, which is much higher than that of many other regions globally (*7*–*8*,*11*). In fact, if 101 of the 230 unvaccinated PWUDs were not really eligible for the vaccine (Table 1, Supplementary Table S1, available in http://weekly.chinacdc.cn), the vaccination rate in the investigated PWUDs would increase to 87.25%, close to 87.85% in the whole population by March 18, 2022. This encouraging finding indicates that PWUDs have not been left behind in vaccination efforts for COVID-19 in China. Two phenomena might explain this result. First, China was one of the first countries to initiate nationwide COVID-19 vaccinations. Its national COVID-19 vaccination program provided free vaccines for all eligible people by June 16, 2022, China had provided a total of 3.39 billion vaccine doses (*12*). Second, it has benefited from the development of community services for PWUDs. In China, each community has a social worker assistance group to help people with various difficulties, including PWUDs. Since the implementation of the Narcotics Control Law of the People's Republic of China, China's rehabilitation strategy for PWUDs has been changing from the "judicial punishment" model, led by compulsory institutions, to the "physiological social comprehensive rehabilitation" model, led by communities, which has been integral in providing support for PWUDs (*13*).

Each community (or village) rehabilitation worker can ensure that PWUDs are not forgotten or neglected and can provide health education to PWUDs about COVID-19 prevention and the benefits of vaccination. This helps PWUDs share the same rights as other residents, such as voluntarily accepting or refusing to become vaccinated (*14*). This study finds no significant difference in the risk of non-vaccination among people receiving different drug detoxification treatments, which indicates a degree of fairness in COVID-19 vaccination rates across different PWUD sub-groups (Table 1).

It is worth noticing that it is disease that discourages most PWUDs from getting fully vaccinated (Table 2). Of the 230 non-vaccinated PWUDs, 43.91% have disease records and 55.65% self-report illness — though this study cannot judge whether those 55.65% are really not eligible for vaccination (Table 1, Figure 1, Supplementary Table S1, available in http://weekly.chinacdc.cn/). This evidence can also be supported by occupation. The unvaccinated rate in unemployed PWUDs is four times higher than those in public institutions & enterprise; the obvious reason is most of the former have illnesses (Supplementary Table S1, available in http://weekly.chinacdc.cn/). But, this research cannot explain why PWUDs working in the service industry have a lower vaccination rate (Table 2).

Sex, age, type of drugs, years of use, and mode of usage are not uniquely associated with vaccination status in this study's findings. This is slightly different from a previous study in China, which indicated that vaccination rates were uneven across age groups, and that the vaccination coverage in older age groups was lower than that of younger age groups (*15*). However, evidence of other impact factors of COVID-19 vaccination among PWUDs is lacking worldwide, which prevents further comparison with this study.

The study had limitations. First, data were collected from a specific area (a district of Sichuan Province);

TABLE 2. The factors associated with unvaccination among people who use drugs by the characteristics.

Characteristic	OR (95% CI)	*P* value
Sex		
Men	1.00	
Women	0.82 (0.56–1.22)	0.336
Age (years)		
≥60	1.00	
50–59	0.68 (0.33–1.40)	0.297
40–49	0.45 (0.21–0.97)	0.040
30–39	0.57 (0.26–1.25)	0.160
19–29	1.31 (0.54–3.16)	0.547
Occupation		
Public institution&enterprise	1.00	
Service industry	2.52 (1.33–4.77)	0.040
Unemployed	3.81 (2.03–7.14)	<0.001
Missing	2.70 (1.33–5.46)	0.006
Type of drugs used		
Only opioid	1.00	
Only synthetic	0.61 (0.36–1.04)	0.071
New psychoactive substance	0.87 (0.27–2.84)	0.817
Polydrug use	0.68 (0.33–1.41)	0.300
Missing	4.01 (0.59–27.35)	0.156
Status of last treatment		
Completed	1.00	
Drug maintenance therapy	1.55 (0.31–7.87)	0.594
Compulsory isolated detoxication	1.10 (0.48–2.51)	0.820
Administrative detention	0.94 (0.49–1.79)	0.847
Community-based detoxification treatment	1.85 (1.06–3.23)	0.031
Community-based rehabilitation treatment	0.70 (0.35–1.37)	0.296
Missing	3.31 (1.83–5.96)	<0.001
Years of using drugs		
≤5	1.00	
6–10	1.14 (0.68–1.91)	0.608
11–5	1.16 (0.70–1.93)	0.565
≥16	2.05 (0.81–5.15)	0.129
Missing	1.50 (0.80–2.80)	0.203
Mode of using drugs		
Oral	1.00	
Injection	1.05 (0.51–2.15)	0.904
Oral & injection	1.96 (0.91–4.20)	0.086
Missing	0.33 (0.11–0.99)	0.048
Diseases records		
No diseases	1.00	
Only IDs	9.49 (3.67–24.59)	<0.001
Only CDs	8.22 (5.19–13.03)	<0.001
IDs & CDs	3.73 (1.12–12.41)	0.032

Abbreviation: OR=odds ratio; IDs=infectious diseases; CDs=chronic diseases.

Sichuan was chosen because it is culturally and socioeconomically representative, especially for the situation of PWUDs across most parts of China. Second, because it is an analysis of secondary data, this study cannot estimate whether the 101 of the 230 unvaccinated PWUDs are really ineligible for vaccination: the adjusted vaccination rate of 87.25% might be an optimistic assumption. Third, similarly to the above, this research could not get more details about why 102 of the PWUDs refused to be vaccinated, even though the real reasons for hesitation on vaccination are helpful to improve new vaccination policy. However, learning COVID-19 vaccination rates among PWUDs in this district in Sichuan is a strong basis for further study. The findings in this study have certain implications in a pandemic like COVID-19 for the government's leadership, overall planning, and as a prerequisite for the equitable distribution of public health products like COVID-19 vaccines across the general population (including across both subgroups as well as geographically).

Conflicts of interest: No conflicts of interest.

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Supplementary

SUPPLEMENTARY TABLE S1. The basic characteristics of the PWUDs by record of disease history.

Characteristic	Total	Diseases (%)	No diseases (%)
	1,113	169	944
Vaccinated			
Yes	883 (79.34)	68 (40.24)	815 (86.33)
No	230 (20.66)	101 (59.76)	129 (13.67)
Sex			
Men	828	133 (78.70)	695 (73.62)
Women	285	36 (21. 30)	249 (26.38)
Age (years)			
19–29	96	4 (2.37)	92 (9.75)
30–39	393	16 (9.47)	377 (39.93)
40–49	299	42 (24.85)	257 (27.22)
50–59	274	89 (52.66)	185 (19.60)
≥60	51	18 (10.65)	33 (3.50)
Occupation			
Public institution / enterprise	172	20 (11.83)	152 (16.10)
Service industry	360	41 (24.26)	319 (33.79)
Unemployed	404	87 (51.48)	317 (33.58)
Missing	177	21 (12.43)	156 (16.53)
Type of drugs			
Only opioid	221	69 (40.83)	152 (16.10)
Only synthetic	745	67 (39.64)	678 (71.82)
New psychoactive substance	35	3 (1.78)	32 (3.39)
Polydrug use	103	30 (17.75)	73 (7.74)
Missing	9	0 (0.00)	9 (0.95)
Status of last treatment			
Completed	218	19 (11.24)	199 (21.08)
Drug maintenance therapy	10	2 (1.18)	8 (0.85)
Compulsory isolated detoxication	75	19 (11.24)	56 (5.93)
Administrative detention	179	21 (12.44)	158 (16.74)
Community-based detoxification	240	54 (31.95)	186 (19.70)
Community-based rehabilitation	181	29 (17.16)	152 (16.10)
Missing	210	25 (14.79)	185 (19.60)
Years of using drugs			
≤5	624	75 (44.38)	549 (58.16)
6–10	170	21 (12.43)	149 (15.78)
11–15	186	37 (21.89)	149 (15.78)
≥16	32	10 (5.92)	22 (2.34)
Missing	101	26 (15.38)	75 (7.94)
Mode of using drugs			
Oral	907	110 (65.09)	797 (84.43)
Injection	89	32 (18.93)	57 (6.04)
Oral & injection	66	24 (14.20)	42 (4.45)
Missing	51	3 (1.78)	48 (5.08)

Perspectives

Origins of HIV, HCoV-HKU1, SFTSV, and MERS-CoV and Beyond

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Tales of tracing the origins of human immunodeficiency virus (HIV), human coronavirus HKU1 (HCoV-HKU1), severe fever with thrombocytopenia syndrome virus (SFTSV), and Middle East respiratory syndrome coronavirus (MERS-CoV) can enlighten the scientific search for the origins of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Here, we detail key research studies on the origins of these four viruses.

On June 5, 1981, US CDC reported five cases of now-called acquired immunodeficiency syndrome (AIDS) in the *Morbidity and Mortality Weekly Report (MMWR)* — the first official report of AIDS in the world (*1*). Two years later, scientists at the Pasteur Institute in France isolated the pathogen, HIV, from lymphoid ganglions (*2*). Last year was the 40th anniversary of the initial report of AIDS, but we still lack a successful vaccine for its prevention. In 1986, Nahmias and colleagues conducted serological studies of 1,213 plasma samples that were obtained as early as 1959 from various parts of Africa, and confirmed with indirect immunofluorescence assay (IFA), Western blot, and radioimmunoprecipitation that one of the samples was positive for HIV-1 (*3*). The positive sample had been collected in early 1959 from an adult Bantu member who had glucose-6-phosphate dehydrogenase deficiency and was living in Léopoldville, now Kinshasa, Democratic Republic of Congo (*4*). In 1998, Zhu and colleagues reported the HIV-1 nucleotide sequence from this 1959 sample. Phylogenetic analysis confirmed HIV-1 infection, and the phylogenetic position of the virus was near the ancestor node of HIV-1 subtypes B, D, and F, suggesting that these HIV-1 subtypes may have evolved from an introduction into the African population prior to 1959 (*5*). A 2008 report further pushed back the putative origins of HIV by several decades. Worobey and colleagues performed viral genome sequencing on a Bouin's-fixed, paraffin-embedded lymph node biopsy specimen obtained in 1960 from an adult female in Léopoldville. Evolutionary analysis of the virus sequence in the specimen dates the most recent common ancestor (TMRCA) of HIV-1 M group to 1908 (95% confidence interval: 1884–1924) — about a hundred years before recognition of the AIDS epidemic (*6*) (Figure 1A).

Coronavirus HCoV-HKU1, which causes human respiratory tract infections, was first identified in 2004 in a 71-year-old male returning to Hong Kong SAR, China from Shenzhen City, Guangdong Province. The virus was named after the University of Hong Kong, where it had been discovered (*7*). In 2006, researchers detected HCoV-HKU1 positive polymerase chain reaction (PCR) signals in specimens from Australian children suffering from upper or lower respiratory tract illnesses in autumn or winter of 2004 (*8*). Also in 2006, using reverse transcription-PCR (RT-PCR), American researchers identified HCoV-HKU1 in children's respiratory specimens collected in Connecticut, USA during 2001 and 2002 — the first identification of HCoV-HKU1 in the Western Hemisphere (*9*). In 2009, Finnish researchers discovered HCoV-HKU1 using RT-PCR in nasopharyngeal aspirates collected from Finnish children between 1996 and 1998 (*10*). In a retrospective study in Brazil, scientists used a universal coronavirus PCR assay and identified HCoV-HKU1 in children's nasopharyngeal swab samples that were frozen and stored in 1995, thus pushing back HCoV-HKU1 identification to 1995 (*11*). Together, these results show that HCoV-HKU1 was present in Europe and the Americas before its discovery in 2004 in Hong Kong SAR, China (Figure 1B).

In 2009, scientists in Henan Province, China made the initial discovery of SFTSV in patients with severe fever with thrombocytopenia syndrome (SFTS) (*12*). This discovery prompted researchers in Jiangsu Province to perform SFTSV testing on samples obtained in 2007 from patients with similar clinical manifestations and elusive etiologies (*13*). Six blood specimens tested positive for SFTSV RNA by real-time RT-PCR and positive for SFTSV antibody by microneutralization assay (MNA) and IFA. In addition, SFTSV was isolated from one serum specimen. In 2012, researchers performed SFTSV IFA

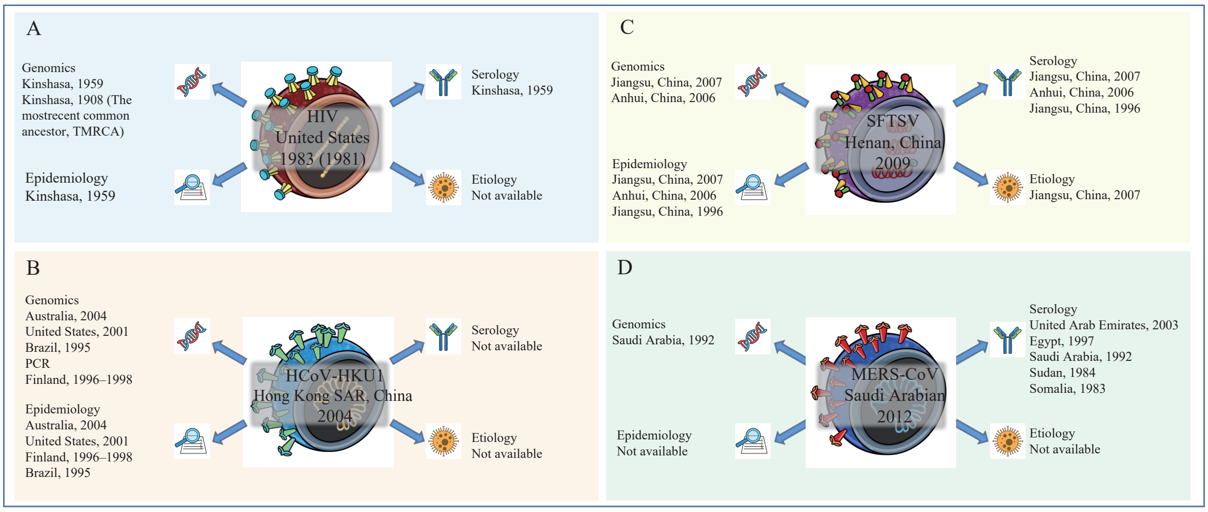

FIGURE 1. The origins-tracing of (A) HIV, (B) HCoV-HKU1, SFTSV, and MERS-CoV.
Note: Graphs illustrate the time and place of the first discovery of HIV, HCoV-HKU1, SFTSV and MERS-CoV, as well as the tracing history of these viruses from four aspects: genomics (i.e., with nucleic acid sequencing or specific PCR products), epidemiology, serology, and etiology (virus isolation). (A) HIV was first reported in the United States in 1981 and the virus was isolated in 1983; it has been traced back to Kinshasa in 1908. Except for etiology, all genomics, serology, and epidemiology could be traced back to 1959. (B) HCoV-HKU1 was first identified in Hong Kong, China in 2004 and has been traced back to Brazil in 1995. Other evidence of genomics and epidemiology was observed in other countries before 2004, as shown. (C) SFTSV was first discovered in Henan Province, China in 2009 and has been traced back to Jiangsu Province, China, as early as in 1996. Some additional evidence in 2006 and 2007 was seen. (D) MERS-CoV was first reported in Saudi Arabia in 2012 and has been traced back to Somalia as early as 1983. Other evidence between 1983 and 2012 is shown in the figure.
Abbreviation: HIV=human immunodeficiency virus; HCoV-HKU1=human coronavirus HKU1; SFTSV=severe fever with thrombocytopenia syndrome virus; MERS-CoV=Middle East respiratory syndrome coronavirus; PCR=polymerase chain reaction.

and RT-PCR tests on sera collected in 2006 from 13 patients suffering from infections of unknown etiology in Anhui Province, China. Tests for SFTSV were positive, and given that all secondary patients had contact with blood from the index patient or underwent endotracheal intubation, the test results suggested that the virus could spread from person to person through contact with blood (*14*). Another group of researchers performed SFTSV testing on sera obtained in 1996 from six patients with SFTS in Yixing County, Jiangsu Province (*15*). Enzyme-linked immunosorbent assays (ELISA) identified IgM antibodies against SFTSV in sera from all six patients, while IFA testing found IgG antibodies in one patient. This study demonstrated that SFTSV IgG antibodies could still be detected in the sera 14 years after disease onset. Based on epidemiological analyses, clinical symptoms, and serological studies, unexplained fever and thrombocytopenia were determined to have been caused by SFTSV. Taken together, these studies demonstrated that SFTSV was in China more than ten years before it was first discovered in 2009 (Figure 1C). Based on phylogenetic analyses of SFTSV genomics, the scientists concluded that SFTSV originated in the early 18th century from Zhejiang Province and that Genotype F was an early genotype, thus promoting a more comprehensive understanding of the origin of SFTSV (*16*). This experience also shows that the discovery of the emergence of a new pathogen in the human population and the origin tracing of a new pathogen can be separate scientific events.

MERS-CoV has spread from the Arabian Peninsula to over 20 countries in Europe, Africa, Asia, and North America since it was first reported in a 60-year-old Saudi Arabian man who died in 2012; these cases were all sporadic, unable to be linked into chains of transmission (*17*). Azhar and colleagues suggested that MERS-CoV can be transmitted from camels to humans through close contact, and that camels may act as intermediate hosts that transmit the virus from its reservoir to humans (*18*). Bats are proposed to be a reservoir host, as partial genomic sequences with 100% identity to MERS-CoV were discovered in bat samples dating back to 2012 (*19*). A study by Meyer and colleagues published in 2014 analyzed 651 dromedary camel serum samples from the United Arab Emirates using recombinant spike protein-specific IFA and virus neutralization tests. A total of 151 samples had been collected in 2003 (*20*). The study found that 97.1% of dromedaries (632 of 651 samples, including all of the dromedary sera collected in 2003) had antibodies against MERS-CoV, and that 59.8% of serum samples had high MERS-CoV neutralizing antibody titers — greater than 1,280. Antibodies discovered in the serum samples that were obtained in 2003 indicated that a high proportion of dromedaries in the region were infected with MERS-CoV or a conspecific virus long before the first human case was identified. In 2013, Lipkin and colleagues performed ELISA, Western blot, luciferase immunoprecipitation system (LIPS) assays, and nucleotide sequencing on freshly collected dromedary camels, sheep, and goat samples and on archived serum samples collected during 1992–2010 in the Kingdom of Saudi Arabia. Their results suggested that MERS-CoV had been circulating countrywide in camels for at least 2 decades, and that it had evolved into phylogenetic clades related to human infections (*21*). In 2014, Müller and colleagues used a highly specific MERS-CoV microneutralization assay to test 189 archived dromedary serum samples accumulated over the previous 30 years, including sera collected in Somalia during 1983–1984, in Sudan June–July 1984, and in Egypt June–July 1997. They found that 81.0% of samples were positive for MERS-CoV antibodies, indicating that the virus had been circulating in these animals for decades before its discovery in 2012 (*22*) (Figure 1D).

Similarly, multiple lines of evidence show that before the coronavirus disease 2019 (COVID-19) outbreak in Wuhan Huanan Seafood Wholesale Market, sporadic positive samples and cases of SARS-CoV-2 appeared in many countries and regions. In October 2021, researchers from IRCCS National Cancer Institute Foundation reported multiple SARS-CoV-2 antibody positive serum samples collected in Milan, Italy starting from September 2019 (*23*). In December 2020, researchers from the University of Milan reported a positive test for SARS-CoV-2 in an oropharyngeal swab sample collected on December 5, 2019 from a 4-year-old boy with no prior travel history (*24*). In January 2021, another group of researchers from the University of Milan reported that the SARS-CoV-2 gene sequence was detected in a biopsy sample collected from a 25-year-old female patient with skin disease in Italy on November 10, 2019 (*25*). In a preprint of *The Lancet* released on August 6, 2021, Amendola and colleagues collected 435 oropharyngeal swabs and urine and serum samples from 156 individuals with morbilliform rashes and tested them for SARS-CoV-2 infection by PCR, Sanger sequencing, ELISA, and SARS-CoV-2 plaque reduction neutralization assays. The first positive result of SARS-CoV-2 RNA was found in a sample that was collected in September 2019. Researchers estimated that SARS-CoV-2 progenitors emerged in late June to late August 2019 (*26*). These results confirmed that the virus had been prevalent in Italy before the official announcement of the first confirmed local COVID-19 case on February 21, 2020.

In April 2020, the mayor of Belleville, New Jersey, Michael Melham, announced that he had tested positive for antibodies against SARS-CoV-2 and believed that he had been infected with the virus in November 2019 (*27*), even though the first confirmed case of COVID-19 in the United States was identified on January 21, 2020. In November 2020, US CDC researchers reported that they tested 7,389 blood samples collected by the American Red Cross between December 13, 2019 and January 17, 2020 and found 106 blood samples containing antibodies against SARS-CoV-2 (*28*). In June 2021, US National Institutes of Health (NIH) (*29*) and ABC NEWS (*30*) both reported a study initiated by NIH in which scientists tested 24,000 blood samples that were collected in early 2020 across the United States. The study found that SARS-CoV-2 antibodies were detected in blood samples from at least 9 people, with the earliest positive sample collected on January 7, 2020. Since antibodies do not appear until about two weeks after human infection, this finding suggests that SARS-CoV-2 was circulating at a low level in the United States as early as December 2019 (*31*).

Researchers from Paris Seine Saint-Denis Hospital Group, Bobigny, France retrospectively tested a respiratory specimen obtained from a patient with hemoptysis in December 2019 and confirmed that the patient was infected by SARS-CoV-2. Judging from this result, the outbreak in France started earlier than the official notification of the first confirmed case on January 24, 2020 (*32*).

Worldwide, earlier SARS-CoV-2 infections have not only been found in human cases, but also, studies of wastewater have shown that SARS-CoV-2 infections may have existed much earlier than the first reported human cases. The Italian Istituto Superiore di Sanità announced that SARS-CoV-2 was identified in wastewater samples collected in northern Italian cities Milan and Turin on December 18, 2019 — more than two months before the first local case of COVID-19 in the country (*33*). The Federal University of Santa Catarina in Brazil published a paper in which researchers detected SARS-CoV-2 RNA in human sewage samples collected in Florianópolis, Brazil on November 27, 2019, about three months before the first case of COVID-19 was reported in Brazil (*34*). Similarly, an investigation in Spain found that SARS-CoV-2 was detected in a frozen wastewater sample collected from a wastewater treatment plant in Barcelona on January 15, 2020, which was 41 days before the first confirmed case was reported in Spain (*35*).

Tracing the origin of a virus is scientific work, and solid conclusions only result from an enormous amount of effort, patience, global cooperation, some luck, and possibly decades of continuous research (*36*). There are common phenomena seen during the process of back-tracing a virus, including that transmission of a new pathogen is often greater in dense populations than in sparse populations. Therefore, emergence of major, new infectious diseases correlate strongly with human population density. Disease emergence is driven by the diagnostic ability of local doctors, the research capacity of scientists, the surveillance capabilities of local government, and the willingness to share information.

HIV was first reported in the United States in 1981 and has been traced back to Kinshasa in 1908. HCoV-HKU1 was first identified in Hong Kong SAR, China in 2004 and has been traced back to Brazil in 1995. SFTSV was first discovered in Henan Province, China in 2009 and has been traced back to Jiangsu Province, China in 1996. MERS-CoV was first reported in Saudi Arabia in 2012 and has been traced back to Somalia in 1983. Now, there is a growing number of clues, reports, and studies indicating that COVID-19 outbreaks occurred in multiple locations around the world before 2020. We should be inspired by the origin studies of previous viruses and carry out global cooperation to test more samples from patients that had COVID-19 symptoms, more environmental samples, and more susceptible-animal samples on larger spans of time and space.

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Perspectives

Vaccinate with Confidence and Finish Strong

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China's sustained containment of the coronavirus disease 2019 (COVID-19) epidemic has spared over 99% of the mainland of China's 1.4 billion people from exposure to and infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its variants for an astonishing two and a half years. Although the whole-of-government, whole-of-society containment effort has its own socioeconomic costs, the now-called dynamic COVID-zero strategy purchased a rare commodity — tranquil time with relatively little suffering and death from COVID-19 to develop and deploy tools for escaping the pandemic: diagnostics, vaccines, antivirals, and knowledge (*1*).

During this two and a half years, China's vaccine industry developed, tested domestically, tested overseas, received regulatory approval, received the World Health Organization (WHO) emergency use listing, and produced over 5 billion doses of COVID-19 vaccines for domestic and international use. China's immunization programs have vaccinated over 1.3 billion people, most with boosted primary series vaccination, protecting more than 90% of the population with the China-produced vaccines.

With an overarching strategy of achieving broad and deep vaccine-induced population immunity strong enough to prevent suffering and death from COVID-19, there is precious little time left to finish the vaccination campaign (*2*). The last 10% in any vaccination campaign is the most difficult to reach, and in our case, the last 10% is also a critically important group to protect because the last 10% has an enrichment of people with comorbidities, many of whom are elderly and will suffer the most from COVID-19 if infected. A systematic review of the association of common comorbidities with severe or fatal COVID-19 shows that obesity, hypertension, diabetes, cardiovascular disease, cerebrovascular disease, respiratory disease, kidney disease, and malignancy are risk factors, with obesity being the most prevalent and respiratory disease being the most strongly predictive (*3*).

Because SARS-CoV-2 is not amenable to herd immunity from any of the current generation vaccines or from natural infection, everyone needs to be individually protected by vaccination (*4*). With little indirect protection, effective population immunity must be built one person at a time until all are protected — a daunting task for a large-population country.

China-produced COVID-19 vaccines have performance characteristics in common with all of the first-generation COVID-19 vaccines, regardless of technical platform. All approved COVID-19 vaccines are safe and effective; all are most protective against severe/critical/fatal COVID-19; none are highly effective at blocking infection and transmission; all have waning protection after a few months; all require one or more booster doses to maintain protection; booster doses restore protection and people with immunocompromising conditions need additional doses; and all are associated with some loss of protection from Omicron.

Real-world evidence shows that the vaccines produced and widely used in China are up to the job of protection. They have the greatest effectiveness where it is needed the most — prevention of serious, critical, and fatal COVID-19 among people of all ages and regardless of comorbidities. They are among the least reactogenic vaccines in existence, and after over 3.4 billion doses used in the mainland of China, they are associated with no serious safety concern other than the exceedingly rare serious allergic reactions that all vaccines are associated with. A population-based study of inactivated vaccine safety among people 60 years or older in Hong Kong Special Administrative Region (SAR), China found no increased risk of adverse events of special interest, regardless of whether the vaccinee is older or younger than 80 years, and regardless of the presence of comorbidities (*5*).

The first large-scale, real-world vaccine effectiveness (VE) study of China-produced inactivated vaccine was conducted in Chile and published in mid-2021. Dr. Jara and colleagues showed that among both working-age and elderly adults, primary-series, non-boosted inactivated vaccine was 86% to 88% effective against hospitalization, 89% to 90% effective against critical care unit admission, and 86% effective against fatal COVID-19 (*6*).

The most recently published overseas VE study of China-produced inactivated vaccine was in Abu Dhabi, where Dr. Al Kaabi and colleagues demonstrated primary-series, non-boosted inactivated VE against Delta and Omicron COVID-19 was 80% against hospitalization, 86% against critical care unit admission, and 84% against fatal COVID-19, and was slightly more effective in people with comorbidities compared with people without comorbidities. The Abu Dhabi team concluded that the inactivated vaccine "was effective in preventing and reducing COVID-19 related hospitalizations and critical care admissions, as well as mortality," and that waning protection "confirmed the need for booster doses (*7*)."

Now, the most relevant evidence on population immunity in China comes from domestic evidence because of China's nearly unique situation of having only vaccine-induced immunity — essentially no hybrid immunity. During the dynamic COVID-zero period, there have been numerous small-to-moderate COVID-19 importation outbreaks and two large importation outbreaks (Jilin and Shanghai). Each outbreak and every infection probes the adequacy of population immunity to prevent serious/critical/fatal COVID-19. It is the job of the immunization program to gather evidence with these immunity probes for updating vaccination and prevention and control strategies.

The 2021 Ruili Delta-variant outbreak happened early in the vaccination campaign and allowed measurement of VE for two inactivated and the Ad5-vectored vaccine. Careful analysis of 686 virus-exposed close contacts showed that primary-series, non-boosted VE of the three most used vaccines in China provided roughly equivalent and strong protection from serious and critical Delta COVID-19, with VEs of 68% to 77% against pneumonia and 100% against severe COVID-19, with no deaths (*8*). Analysis of the 2021 Guangdong Delta outbreak found vaccine effectiveness of 78% against pneumonia and 100% VE against severe/critical COVID-19 (*9*). Similarly, in the Henan Delta-variant outbreak, non-boosted primary-series VE against COVID-19 pneumonia and severe COVID-19 were 62% and 82%, respectively (*10*).

The Jilin Omicron BA.2 outbreak demonstrated that regardless of age group, primary series vaccination was associated with an impressive 9-fold reduction in severe COVID-19 and a 4-fold reduction in critical COVID-19, and that homologous boosting was associated with 44-fold and complete reductions in severe and critical COVID-19 (*11*). The relative impact of a booster dose of inactivated vaccine was further shown in a case-case study in an outbreak in Henan Province in early 2022 with 405 Delta infections and 421 Omicron infections. Compared with primary vaccination 6-months before infection, a homologous booster dose reduced Delta COVID-19 pneumonia by an additional 82%, primary series alone reduced Omicron pneumonia by 66%, and there were too few boosted Omicron pneumonia cases (2 cases) to estimate relative VE (*12*).

One of the most important and directly relevant assessments of China-produced inactivated COVID-19 vaccine effectiveness in an infection-naïve population is Dr. McMenamin and colleagues' evaluation of the serious and fatal COVID-19 cases in the 2022 Omicron BA.2 outbreak in Hong Kong SAR, China (*13*). She and her team found that homologous-boosted inactivated vaccine was 98% effective at preventing severe/fatal COVID-19 — on par with homologous boosted mRNA vaccine. Without boosting, inactivated primary series vaccination was 70% effective, showing that boosting is important for optimal protection. Three-dose inactivated vaccine effectiveness against severe/fatal COVID-19 was very high among the elderly, with three-dose VEs of 97%, 95%, and 97% for people in their 60s, 70s, and 80s or older.

Another study in Hong Kong that spanned the Delta and Omicron periods assessed VE and safety of inactivated COVID-19 vaccine in people with kidney diseases, including individuals on hemodialysis and kidney transplant recipients (*14*). In this study, Dr. Cheng and colleagues found identical two and three-dose vaccine effectiveness in renal disease patients as did Dr. McMenamin in the general population: two-dose VE of 70% and three-dose VE of 97%. Their safety analysis also found no concerns about the safety of the inactivated vaccine. Similarly, Dr. Wan and colleagues used a case-control study in the Hong Kong outbreak to estimate VE against hospitalization, intensive care admission, and fatal COVID-19 from Omicron BA.2 infection in people with diabetes. These scientists found that the VE of three doses of inactivated vaccine was 86% against hospitalization, 94% against ICU admission, and 96% against all-cause mortality (*15*).

The recent Shanghai outbreak provided a cogent test the effectiveness of the vaccines being used to build population immunity in the mainland of China. In this 650,000-person outbreak, there were 588 COVID-19 deaths, and only 5% of these fatal COVID-19 cases were vaccinated. An elegant, matched case-control study by Shanghai CDC and Fudan University scientists, led by Dr. Huang and colleagues, showed that boosted primary-series vaccine effectiveness was 93% against severe COVID-19 and 96% against fatal COVID-19 – results that are nearly identical to those of McMenamin and colleagues in Hong Kong, furthering our confidence in the vaccines being used in China and emphasizing the importance of the booster dose (*16*).

Population immunity created by the vaccination campaign is paying off by keeping the severity of illness low in the domestic importation outbreaks (*17*). In difficult-to-control large outbreaks, unvaccinated people with comorbidities and the elderly are at risk of serious or fatal COVID-19. Gaps in population immunity from gaps in vaccination coverage expose people to risk — vaccines only work when given (*18*).

Sustaining optimized protection for a safe, long-term exit of the pandemic will almost certainly require well-timed second booster doses. The design of second booster dose strategy will be based on emerging evidence of duration of protection afforded by the vaccines.

The pathway forward is clear. Vaccinate with confidence and finish strong! Every person vaccinated and every person boosted receives clinically meaningful direct protection from serious/critical/fatal COVID-19. Medical practitioners need to ensure that their patients are vaccinated, especially their patients with comorbidities — it is safe and effective to do so. Families need to ensure that parents, grandparents, and great-grandparents are vaccinated in addition to their children. Immunization programs need to work to reach everyone not yet vaccinated, not yet boosted and confidently protect them with the vaccines we have. Regulatory authorities and manufacturers should work to remove the contraindication to vaccinating during pregnancy so pregnant women can join the vaccination campaign and be protected from COVID-19. There is no evidence to support a pregnancy contraindication, and over two-thirds of countries recommend vaccinating pregnant women, including with China-produced inactivated vaccines (*19–20*).

Everyone wants to return to normal life. Vaccination is the key, and time will run out for the vaccination campaign. Although the campaign has been marvelously successful to date, protecting the vast majority of people, the campaign is not completed yet. China-produced vaccines are up to the task of protection, and although the last 10% will be the most difficult to reach, the results of success will be well worth the effort and are essential for a smooth exit from the pandemic.

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Perspectives

Promote COVID-19 Vaccination for Older Adults in China

Shujie Zang[1]; Xu Zhang[1]; Zhiqiang Qu[1]; Xi Chen[2,3]; Zhiyuan Hou[1,#]

The coronavirus disease 2019 (COVID-19) vaccine effectively reduces the possibility of severe illness and mortality in older adults and is essential for controlling the epidemic. Compared with developed countries, the coverage of full vaccination and booster vaccination for older adults aged 60 or above in China is poor, making it urgent to accelerate their vaccination in China. We discussed potential reasons for low vaccination coverage for older adults aged 60 or above and presented strategies to promote their COVID-19 vaccination in China.

As of July 2022, COVID-19 has caused more than 560 million cases and 6 million deaths worldwide (*1*). Compared with other age groups, older adults aged 60 or above are at a higher risk of severe illness and death after COVID-19 infection due to weak immune function and comorbidities (*2*). China began opening COVID-19 vaccination for older adults in April 2021, following the first phase of emergency vaccination for people in high-risk and critical positions and the second phase of mass vaccination for adults aged 18–59. The COVID-19 vaccine is available for free regardless of residency. Although the government emphasized promoting vaccination for older adults at the end of 2021, COVID-19 vaccination coverage continued inching upward but at a slowing rate from January to June 2022, especially for a booster vaccination (Figure 1). As of August 10, 2022, the full vaccination rate was 85.6% and the booster vaccination coverage was only 67.8% for older adults in China, that were lower than those in countries like the United States (92.1%, 70.7%), Germany (91.2%, 85.9%), and Japan (92.4%, 90.3%). The Omicron wave in Shanghai and nationwide further highlights the urgency of vaccination for older adults.

In China, the poor vaccination coverage among older adults is found for COVID-19 vaccine as well as general routine vaccines. There is usually insufficient awareness of general vaccines among older adults. Prior to the COVID-19 pandemic, there was a lack of publicity about vaccination and vaccines were generally self-paid for older adults, leading to low awareness and coverage of general vaccines. The coverage of influenza and pneumonia vaccines is only 6.6% and 1.2% among older adults, respectively (*3*–*4*). Additionally, institution-based nursing care would improve the efficiency of vaccination services; while in China, most older adults live at home and only about 3% live in nursing homes (*5*). The relatively scattered home-dwelling elderly present inconveniences and barriers to vaccination services. More importantly, there is a separation of clinical services and preventive services such as vaccination, and general practitioners (GPs) are not involved in vaccination services in China. Although GPs provide vaccination services in most countries, it is only delivered by dedicated vaccinators at community vaccination clinics in China (*6*). The GPs have close contact with older adults and are familiar with their health status, but in China they have no responsibility for vaccination advocacy and services including COVID-19 vaccination. Ambiguous statements in guidelines regarding COVID-19 vaccination contraindications for older adults further make it difficult for vaccinators to assess the vaccination eligibility of the older adults with underlying diseases (*7*). Many vaccinators are even reluctant to recommend or provide vaccination services for older adults due to insufficient disclosure of adverse events following immunization (AEFI) and a lack of effective protection for themselves.

COVID-19 vaccine hesitancy has spread worldwide including in China (*8*–*9*). Chinese older adults have more concerns on the effectiveness and safety of COVID-19 vaccines than other age groups. Due to under-enrollment of Chinese older adults in clinical trials of inactivated COVID-19 vaccines, there is insufficient evidence of its efficacy and safety for Chinese older adults at the early stage of COVID-19 vaccine campaign. However, real-world data from the Omicron wave in Hong Kong Special Administrative Region (SAR) in early 2022 show that both the BNT162b2 mRNA and CoronaVac vaccines are over 95% effective against the most severe/lethal COVID-19 in all older age groups when used as recommended in three doses and are not distinguishable from each

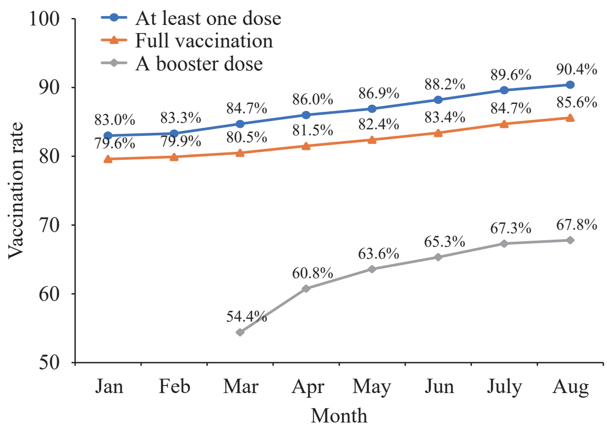

FIGURE 1. Percentages of Chinese older adults completing COVID-19 vaccination from January to August 2022.
Note: Data were extracted from the State Council Information Office of the People's Republic of China.
Abbreviation: COVID-19=coronavirus disease 2019.

other (*10*). In addition, the AEFI surveillance system from China CDC shows that there are even fewer adverse effects following CoronaVac vaccination in older adults than in other age groups (*11*). Therefore, older adults in China should get fully vaccinated and boosted as soon as possible, with no reason to wait for a different vaccine.

Omicron waves in Shanghai, Hong Kong SAR, and other regions have largely increased the perceived risk of COVID-19 infection and the public awareness of COVID-19 vaccination. To promote the COVID-19 vaccination among older adults, it is critical to shift the vaccination sequence to prioritize older adults as the vaccination population. Since the presence of chronic conditions does not lead to additional side effects of COVID-19 vaccination and no evidence shows that COVID-19 vaccination would affect chronic disease control, older adults with chronic conditions should be given the priority of vaccination (*12*). As for other specific vaccine contraindications, timely clarification in the guidelines is essential for assessing vaccination eligibility. Additionally, allowing the GPs to engage in vaccination campaigns for older adults might be another helpful strategy. GPs should be allowed the responsibility for and participation in COVID-19 vaccination eligibility assessment, vaccine recommendation and appointments. Targeted health education and door-to-door vaccination services should also be promoted for the home-dwelling elderly.

The AEFI surveillance system should also be improved to timely inform older adults. In China, the AEFI surveillance system is limited to reports from vaccination clinics, healthcare facilities, CDCs, and vaccine manufacturers, but is not accessible to the public (*13*). In contrast, the Vaccine Adverse Event Reporting System (VAERS) in the US accepts the AEFI reports from healthcare professionals, vaccine manufacturers, as well as the public (*14*). The additional layer of safety monitoring, V-safe, captures registrants' feelings after COVID-19 vaccination through text messages and web-based surveys (*15*). China should receive reports from the public on AEFIs and release AEFIs data regularly to effectively reduce public concerns.

Finally, an additional vaccination accident insurance besides basic insurance for AEFIs may be a policy option for addressing older adults' concerns on the safety of COVID-19 vaccines. There are two forms of compensation for serious adverse events associated with COVID-19 vaccine internationally: one is for commercial insurance companies to act as insurers, such as the no-fault compensation program for COVID-19 vaccines in 92 low and middle-income countries, and the other is for the government to pay compensation as insurers, like severe side effect insurance of COVID-19 vaccine in Thailand (*16–17*). In China, commercial insurance companies have designed additional insurance for AEFIs, but the public needs to pay premiums themselves, and some of them exclude older adults. Our survey from older adults and their family members found that among the vaccine-hesitant groups, 51% would increase the willingness of COVID-19 vaccination following the provision of additional insurance with government subsidies, with 43% no changes and 6% reductions in vaccination willingness. This result suggests that the government's assistance in paying premiums for older adults could help remove barriers to insurance and reduce vaccine hesitancy.

CONCLUSION

In the context of the global Omicron pandemic and the low coverage of full and booster vaccination of older adults in China, there is an urgent need to accelerate the process of COVID-19 vaccination of older adults. Strategies such as making older adults a priority vaccination population, paying attention to home-dwelling older adults, allowing GPs to participate in vaccination campaigns, developing domestic mRNA vaccines, improving the AEFI surveillance system in China, and providing additional COVID-19 vaccination accident insurance could serve as effective measures to promote COVID-19 vaccination for older adults in China.

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Recollections

Recollections of the COVID-19 Epidemiological Intelligence Task Force in China CDC, July 2021 to March 2022

Lei Zhou[1]; Guoqing Shi[1]; Hao Li[1]; Yanping Zhang[1]; Qun Li[1,#]

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has been going on for nearly three years since the coronavirus outbreak were first reported (*1–3*). China managed to control the unexpected first wave in Wuhan city, Hubei Province by using strict suppression measures (*4–5*). Later, to prevent imported infections and control subsequent local transmission, China adjusted and implemented a proactive strategy widely known as the Dynamic COVID-Zero Strategy (*6–7*).

Chinese Center for Disease Control and Prevention (China CDC) has continuously played an important role in China's fight against COVID-19 since 31 December 2019, when National Health Commission of the People's Republic of China (NHC) sent a team of experts to Wuhan, Hubei Province to provide technical support for epidemic prevention and control decision making (*8*). To effectively support China's proactive COVID-19 response strategies, including the general policy of preventing the coronavirus from re-entering the country and causing new epidemics, and the principles of early detection, early reporting, quarantine, and treatment (*4*), China CDC established an emergency response intelligence management framework for risk awareness and assessment. Since the April 2021, identification of the Delta variant of interest and its rapid emergence as the dominant severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant in the global pandemic, the number and magnitude of imported cases and subsequent domestic outbreaks in China have increased. When the Delta variant caused a large outbreak in July 2021 that originated in the international airport in Nanjing, Jiangsu Province and ultimately infected 1,162 people in 14 provincial-level administrative divisions (PLADs) across the country, there was an urgent need for China CDC to provide more efficient and accurate situational awareness, risk assessment, and timely technical recommendations (*5*). To improve the capacity, efficiency, and effectiveness of response to the Delta variant epidemic wave, a specific COVID-19 Epidemiological Intelligence Task Force (EITF) was established in China CDC in late July 2021. EITF was maintained, improved, and continuously upgraded through April 2022, and was expanded in response to a series of Omicron outbreaks from February to April 2022.

EITF is a successful, concrete model of an Emergency Operations Center (EOC) working during outbreak response and providing essential technical support for decision making — from integration of data collection and analysis, to situational awareness and assessment, and to making suggestions for resource deployment and strategy improvement. In this recollection, we describe and share the EITF framework and mechanisms with national and sub-national technical institutions with the aim of improving future preparedness and response.

EXPERIENCE AND FINDINGS

Mission and Responsibilities

The EITF mission is to provide effective and efficient technical support for national response to COVID-19 outbreaks. For this mission, the EITF must provide timely data collection & analysis and risk awareness & assessment, and propose timely emergency response actions to control outbreaks — for example, whether and where to deploy resources or whether an airplane or train should be monitored and passengers traced.

Essential Framework

The EITF essential framework ensures regular operations and includes a commander, an info-group, an epi-group, an integration-group, and a logistics-group (Figure 1). The four EITF groups collaborate closely, in parallel, and under a unified lead by the commander. Each group has specific tasks according to their responsibilities and works toward the EITF

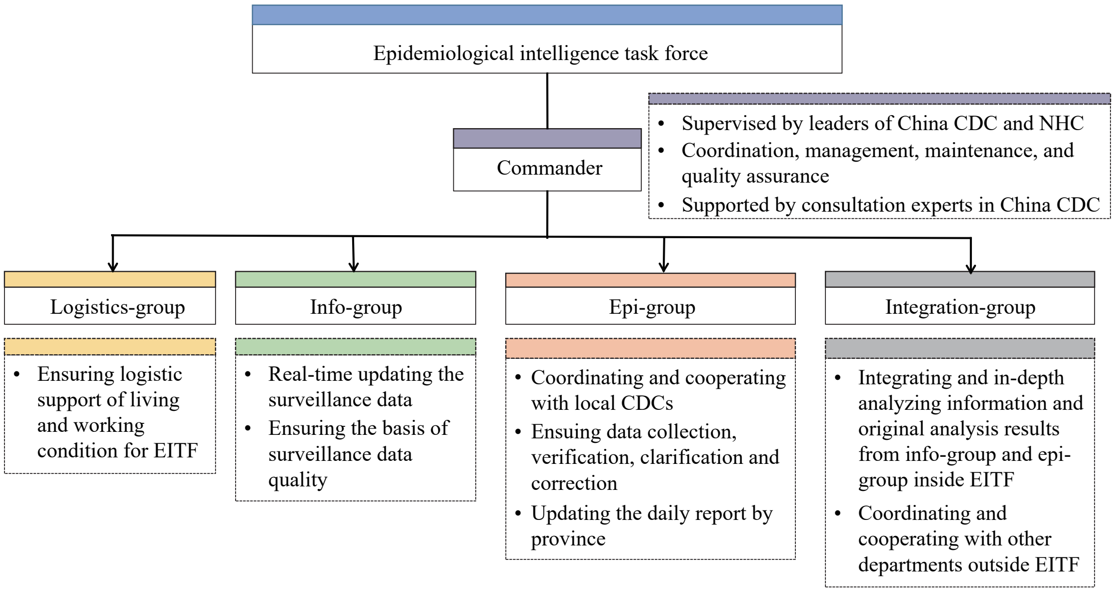

FIGURE 1. Framework and structure of EITF.
Note: Info denotes information. Epi denotes epidemiology.
Abbreviation: EITF=epidemiological intelligence task force; NHC=National Health Commission.

mission. The commander is supervised by China CDC and NHC leadership and supported by expert consultants in China CDC. He or she is responsible for coordination, management, maintenance, and quality of all outputs, including reports, recommendations, and suggestions.

The info-group has a fundamental responsibility for surveillance data quality and is responsible for monitoring, collecting, cleaning, and managing surveillance data in the online national surveillance systems of China CDC (*9–10*), including the Notifiable Infectious Disease Reporting System (NIDRS) (*10–11*) and the COVID Screening Positive Reporting System (COVID SPRS).

The epi-group is fundamental to risk assessment, and is responsible for epidemiological field investigation findings and information collection, verification, clarification, and correction through coordination and cooperation with local CDC liaisons (Table 1). The epi-group is responsible for real-time analysis of case-patient descriptions, outbreak descriptions, original source of infection reports, and transmission chain descriptions, and is responsible for completing the daily analysis report of each PLAD.

The integration-group is the core analytic group, and is responsible for integration and in-depth analysis of information, and original analyses from the EITF info-group and epi-group, occasionally combining with other COVID-19-relevant data and information outside of EITF, to complete risk assessment and recommendation reports for decision makers in China CDC and NHC.

The logistics-group is responsible for supporting living and working conditions to ensure normal operation of EITF and provides a strong foundation for the work of the other three groups and the entire EITF. Logistics-group duties include supporting working locations and environments, equipping computers and ensuring internet connectivity, providing safe dining conditions, and providing infection control and prevention measures as needed.

The size of the four groups was scaled according to epidemic situation and EITF needs — for example, EITF was expanded in March 2022 in response to Omicron outbreaks and Omicron's more rapid transmission. To closely track changes in COVID-19 epidemic situations in one or more PLADs or areas, the epi-group usually required several small epi-teams. When EITF was established in July 2021, it included one commander, a 5-person info-group, a 10-person epi-group, a 5-person integration-group, and a 3-person logistics-group. The original 24-person EITF was able to deal with sporadic and small scale COVID-19 outbreaks occurring in no more than 10 PLADs simultaneously. However, to manage the COVID-19 resurgence and the more contagious Omicron importations into the mainland of China, in March 2022, EITF was expanded to 74 persons — the largest thus far — consisting of one commander, a 15-person info-group, a 57-person epi-group divided into 6 epi-

TABLE 1. Information requirements of EITF.

Type of information	Source of information	Liaison group	Time requirement	Specific contents requirement
Demographic and basic information of each PCR positive individual	NIDRS, COVID SPRS	Info-group	Update in real-time	Demographic information, illness onset information, sampling and testing information, date of admission and discharge, severity of illness, etc
Field core information of each PCR positive individual	Liaisons in local CDCs	Epi-group	Within 4 hours after report	Case detection methods, exposure history by travelling or living in area with outbreaks, contact history of any positive individuals, etc
Field investigation report of each PCR positive individual	NIDRS, liaisons in local CDCs	Epi-group	Within 24 hours after report	Detailed exposure history, potential sources of infection, risk assessment, control measures
Gene sequencing analysis results	National Institute of Viral Disease control and prevention (NIVD), China CDC	Info-group	Update in real-time	Whole gene sequences, in comparison with the prior sequences in NIVD, GeneBank and GISAID
Environmental test results	Liaisons in local CDCs	Epi-group	Update in real-time	Nucleic acid test results of environmental samples collected from the living, working and visiting location and contacted items
Nucleic acid screening results	Liaisons in local CDCs	Epi-group	Update in real-time	Date, location and number of sampling and testing when implementing nucleic acid screening each time
Movement track tracing	Liaisons in relative departments of joint multisectoral mechanism, such as MIIT, MoPS, MoT, CAA, etc	Epi-group	Update in real-time	Mobile phone signal movement, electronic payment records, monitoring video records, etc. within the past 14 days before illness onset or testing positive, and spatiotemporal relationship of different cases by analyzing the movement tracks

Note: Info denotes information. Epi denotes epidemiology.

Abbreviation: EITF=epidemiological intelligence task force; NIDRS=notifiable infectious disease reporting system; COVID SPRS=coronavirus disease screening positive reporting system; PCR=polymerase chain reaction; GISAID=global initiative of sharing all influenza data; MIIT=the Ministry of Industry and Information Technology; MoPS=the Ministry of Public Security; MoT=the Ministry of Transportation; CAA=the Civil Aviation Administration.

teams, a 7-person integration-group, and a 4-person logistics-group.

Workflow and Mechanisms

The essence of EITF workflow is data and information streaming, which was developed into a cycle in EITF for highly efficient data sharing (Figure 2). For example, when an individual tested positive for SARS-CoV-2, he or she was firstly reported to COVID SPRS and subsequently to NIDRS. Info-group staff extracted data on all reported cases from COVID SPRS and NIDRS several times per day and shared the data extracts with the epi-group. When receiving data from the info-group, responsible epi-group staff contacted their provincial CDC liaisons to obtain core information and the field investigation case reports in a timely manner, completed or updated the daily report of the PLADs, and shared the up-to-date data with the integration-group the following morning. Normally, the integration-group summarized information from the info-group and the epi-group, updating the national situation report and providing summarized information to the commander every morning. In some emergencies, the integration-group or the commander would work directly with the info-group and the epi-group to complete an urgent analysis.

EITF received seven types of data and information as essential input (Table 1) and produced three major types of regular outputs, including several types of reports, meetings with local CDCs, and recommendations to decision makers (Figure 3). Inputs and outputs were coordinated among the three major working groups in EITF — the info-group, the epi-group, and the integration-group.

There were 5 mechanisms to ensure normal operation of EITF: 1) EITF could directly report to decision makers in China CDC and NHC; 2) an EITF liaison could directly coordinate and cooperate with liaisons of other departments, such as Ministry of Industry and Information Technology, Ministry of Public Security, Ministry of Transportation, Civil Aviation Administration, and State Administration of Railways under the National Joint Multisectoral Mechanism; 3) EITF could directly coordinate and cooperate with departments in NHC; 4) EITF liaisons could directly contact designated provincial liaisons in local CDCs for any needs on behalf of NHC; and 5) EITF could directly coordinate and cooperate with national working groups in the field that was deployed by NHC to affected PLADs.

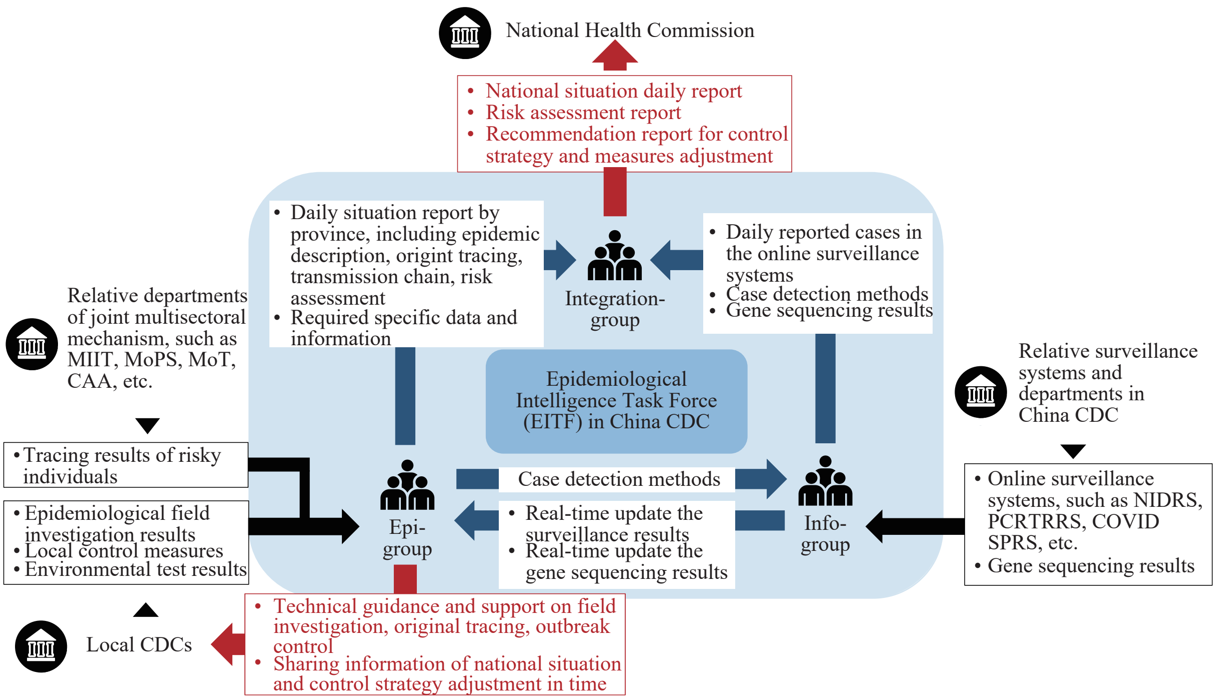

FIGURE 2. Workflow of EITF.

Note: Info denotes information. Epi denotes epidemiology.

Abbreviation: EITF=epidemiological intelligence task force; NIDRS=notifiable infectious disease reporting system; COVID SPRS=coronavirus disease screening positive reporting system; MIIT=the Ministry of Industry and Information Technology; MoPS=the Ministry of Public Security; MoT=the Ministry of Transportation; CAA=the Civil Aviation Administration.

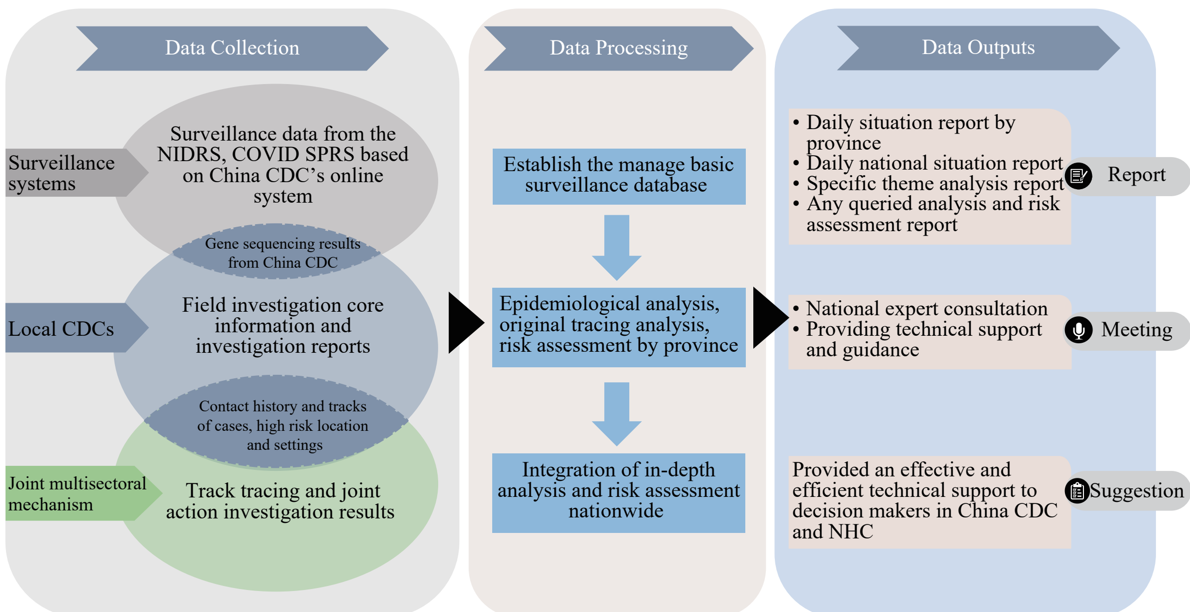

FIGURE 3. Dataflow in EITF.

Abbreviation: EITF=epidemiological intelligence task force; NHC=National Health Commission; NIDRS=notifiable infectious disease reporting system; COVID SPRS=coronavirus disease screening positive reporting system.

Effectiveness and Efficiency

In the past year, EITF has dealt with approximately 70 domestic outbreaks, collected and processed the information on more than 30,000 individuals who screened positive for COVID-19, raised approximately 4,000 alarms, coordinated over 180 joint multisectoral tracings, completed more than 1,500 technical reports, and held over 100 meetings with local CDCs and national working groups. For example, in Shandong Province, the local CDC and government urgently terminated unnecessary control measures against a train upon a decision based on an EITF risk assessment that indicated there was no risk of virus transmission or spread on the train because the individual was not infectious while on the train (*12*).

EITF outputs provided effective and efficient technical support to NHC and China's COVID-19 response. For example, control measures — especially the at-risk population tracing measures — were strengthened and accelerated as needed, while the overly strict and ineffective tracing and management measures were stopped in a timely manner (*13*). Risk periods for virus spread and transmission were able to be pinpointed, especially when transmission was associated with crowded indoor places like restaurants, pubs, bars, cinemas, or public transportation.

CONCLUSIONS

Improving health emergency response capacity at all levels in a country, especially the essential epidemic intelligence capacity of receiving, verifying, analyzing, assessing, and investigating public health events, is crucial to ensure a timely and effective response to public health emergencies. The EOC has proved to be an important model for not only emergency response, but also health emergency coordination, management, and operation capacity building (*14–15*). Institutionalization and standardization are the fundamental bases of efficient and effective EOC operation.

Based on experience and lessons learned from previous responses, the World Health Organization (WHO) formulated a simple and unified emergency operation management framework — the Incident Management System (IMS) — for agencies at all levels, and developed an emergency response framework (ERF) to provide employees with basic guidelines for evaluation, classification, and response of public health emergencies (*16*). To further support and guide international health emergency responses, the WHO established the global public health emergency operation center network (EOC-net) in 2012 and released the public health EOC framework in 2015 to guide construction of EOCs globally (*12*,*14–15*).

Today, China CDC, with our EOC officially established in 2016, plays a role in command and coordination, resource integration, risk communication, and technical support for event response (*15*). China CDC has launched a first-level emergency response since January 2020, and as a part of the emergency response framework at that time, the predecessor of EITF was a surveillance and investigation team that had only 20 professional staff. Later, EITF was established to fulfill emergency response needs and exercised its core functions collocated with EOC.

Based on the EOC model, EITF has gradually standardized and institutionalized the position setting, manpower mobilization, personnel training, and working mechanisms by developing standard operating procedures (SOPs). During the past eight months, EITF achieved its mission effectively and efficiently by organically combining structure and function, including establishing dynamic groups of multi-disciplinary experts and professionals, a fully equipped venue, and a virtual platform for communication and coordination. EITF provided essential practices in China CDC's EOC and serves as a replicable model EOC during COVID-19 and other health emergency response at all levels of China. A national EITF network with China CDC's and provincial EITFs can be established, which will build epidemiological capacity and improve emergency response efficiency in China.

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