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Cover Photo: Italian officials greeted the third group of Chinese medical experts (Fan Lyu, front, China CDC) by "bumping elbows", March 25, 2020 (provided by Xin Hua News Agency).

Preplanned Studies

Recent Trends and Challenges with COVID-19 — Africa, April 4, 2020

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Summary

What is already known about this topic?

Since the first COVID-19 confirmed case was reported, the current epidemic in Africa has rapidly increased.

What is added by this report?

As of April 4, 2020, a total of 7,405 confirmed cases and 305 deaths had been reported from 51 countries across Africa. The cumulative number of reported COVID-19 cases varied among the five regions of Africa, of which northern Africa reported the largest number of confirmed cases. The five countries with the highest number of cases are South Africa, Algeria, Egypt, Morocco, and Tunisia.

What are the implications for public health practice?

Early detection, early isolation, early reporting, and early treatment of the COVID-19 are important and critical measures for the successful control of further transmission of COVID-19. Now more stringent prevention and control measures have been implemented in Africa, but due to often insufficient basic medical facilities and medical services, Africa is still facing challenges to the pandemic and needs to strengthen national health systems and develop immediate and future health plans.

The first confirmed case of coronavirus disease 2019 (COVID-19) in Africa was reported in Egypt on February 15, 2020 (*1*). As of April 4, 2020, 50 days after the first confirmed case was reported, a total of 7,405 confirmed cases and 305 deaths had been reported from 51 countries across Africa (*2*). In the 50 days since the first case was reported in Africa, COVID-19 spread relatively slow, especially in the first 20 days with 22 confirmed cases reported in 6 countries. However, by Day 23, the number of confirmed cases reported started increasing every day. By Day 30, 24 countries had reported a total of 251 confirmed cases; by Day 40, a total of 2,245 confirmed cases had been reported in 44 countries; by Day 50, the cumulative number of confirmed cases reported in 51 countries had grown rapidly to 7,405 (*3*) (Figure 1).

The cumulative number of reported COVID-19 cases varied among the 5 regions of Africa with the number of cases growing most rapidly in Northern Africa, which, as of April 4, 2020, reported 3,382 confirmed cases and accounted for 45.31% of the total reported cases in Africa. The number of cases reported in Central Africa and Eastern Africa increased more slowly, with 473 and 669 reported cases and 6.34% and 8.96% of the total reported cases in Africa, respectively (*2*). The 5 countries with the highest total numbers of confirmed cases are South Africa (1,505 cases), Algeria (986 cases), Egypt (985 cases), Morocco (844 cases), and Tunisia (495 cases), and they cumulatively reported a total of 4,815 confirmed cases, which accounts for 65.02% of the total reported cases in Africa. (*2*)

With an increase in the number of reported cases of the COVID-19 in Africa, there is extreme concern for whether Africa will reach a level of emergency that Europe reached, which as of April 4, 2020, the cumulative number of reported cases of the COVID-19 in Europe has reached 541,171 (*2*). The first confirmed case in Europe was reported by France on January 25, 2020 (*4*), and by Day 36 after the first case was reported, more than 1,000 cases were reported (*5*) and more than 5,000 cases were reported by Day 42 in Europe (*6*). Comparing the epidemic development in Europe, Africa reported more than 1,000 cases on Day 37 after the first case was reported (*7*) and more than 5,000 cases by Day 46 (*8*).

From the first case report to Day 35, the number of reported cases and the growth rate were almost identical in Europe and Africa. However, after Day 35, the growth of the number of reported cases in Europe began to accelerate when compared with Africa, and by Day 50, Europe reported 36,264 cases while Africa reported 7,405 cases. By Day 60 (*9*), the cumulative number of the reported cases in Europe had reached nearly 200,000 (195,262 cases) and by Day 70, it had reached well over 500,000 (541,171 cases) (*10*) (Figure 2). Epidemic trends in Europe remind us that the next three to four weeks will be a crucial time for

the development of the COVID-19 epidemic in Africa. Will Africa experience a sudden and rapid increase in the number of reported cases as Europe did?

The World Health Organization (WHO) classified the transmission modes of the COVID-19 as imported cases only, local transmission, and community

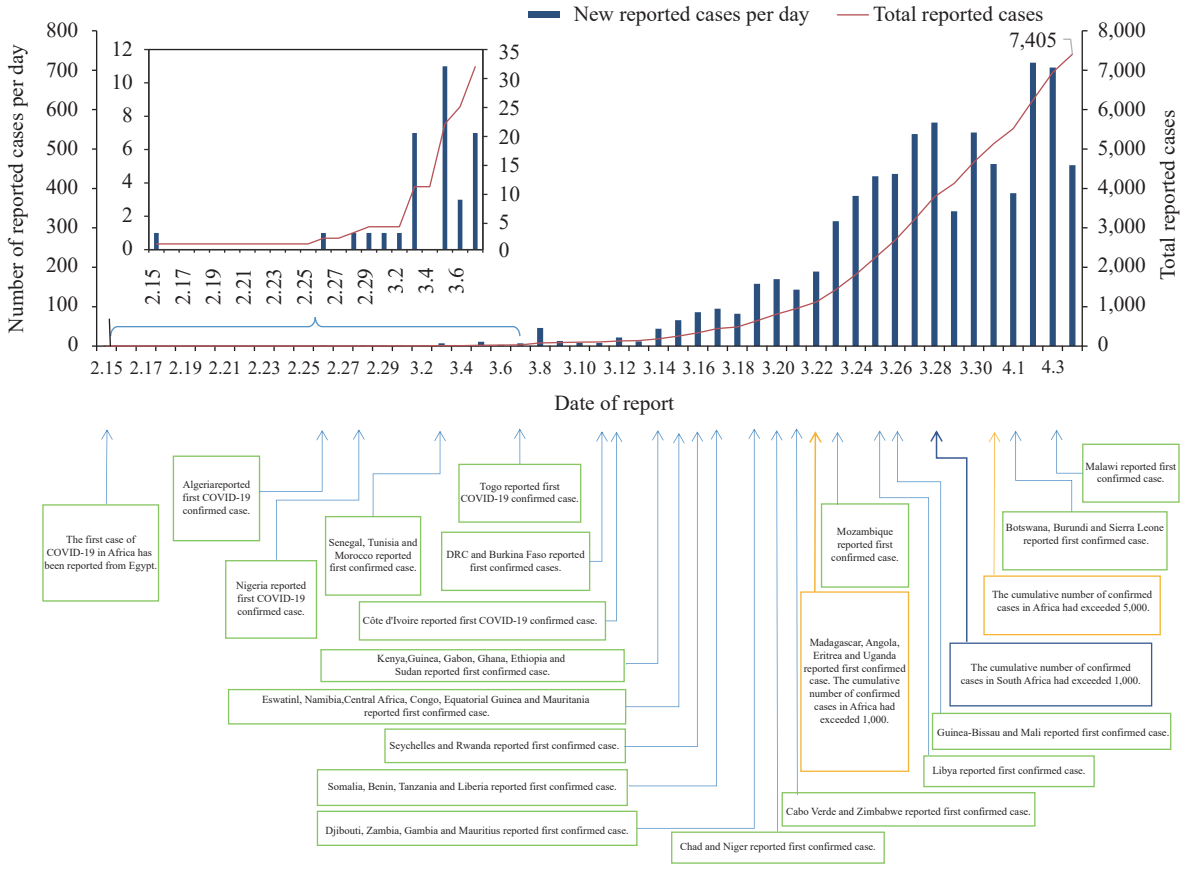

FIGURE 1. COVID-19 cases reported by day in Africa.

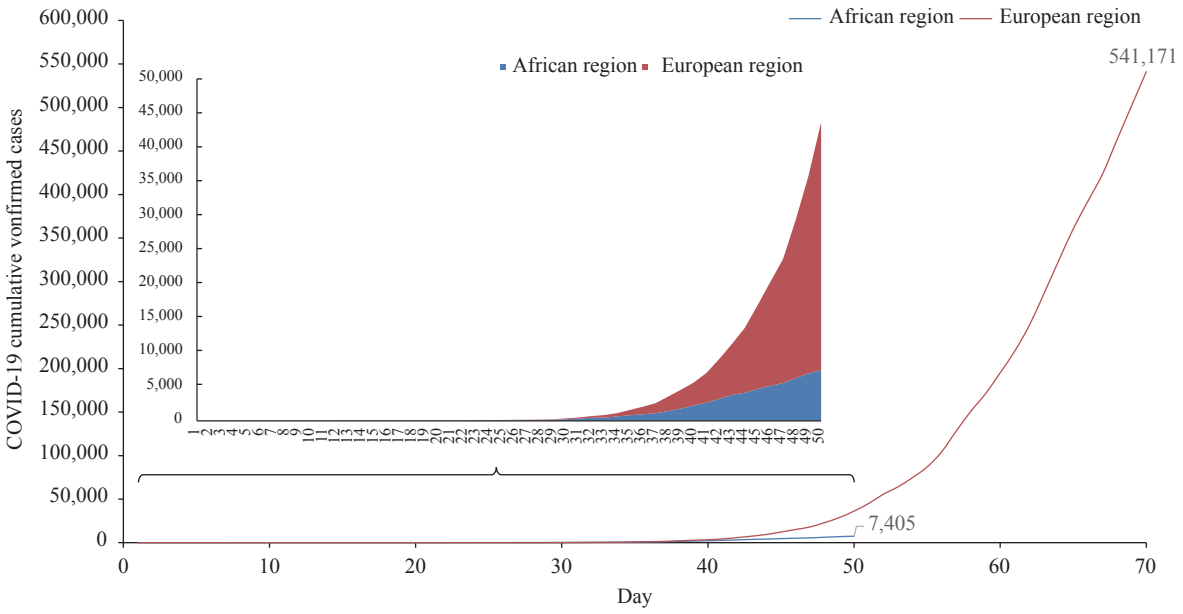

FIGURE 2. COVID-19 cases reported by day after the first case was reported in Africa and Europe.

transmission. The imported cases only classification indicates locations where all cases have infections acquired from outside of the reporting location. Local transmission indicates locations where the source of infection is within the reporting location (*2*). The changes in transmission modes of COVID-19 in 54 countries in Africa and 53 countries in Europe are almost identical. As the number of countries reporting COVID-19 cases increases, so does the number of countries that are changing from imported cases only to local transmission. As of April 4, 2020, 66.67% (36/54) of countries in Africa were classified as having local transmission and 25.93% (14/54) were imported cases only (*2*,*11*) (Figure 3A); but by this time, 96.23% (51/53) of countries in Europe were classified as having local transmission and only 3.77% (2/53) were imported cases only (*2*). In Europe, 60 days after the first case was reported, more than 90% of countries with COVID-19 were classified as having local transmission, and the cumulative number of reported cases also increased rapidly to nearly 200,000 (195,262 cases) (*9*–*10*) (Figure 3B).

DISCUSSION

The number of confirmed COVID-19 cases detected and reported in each country are influenced by many factors including effective interventions, expanding test strategies, and strict infectious source management. With regard to the number of confirmed cases currently reported, there may be a problem in Africa that the number of reported confirmed cases may be lower than the actual number of infections due to restraints in testing capacity and number of tests available in African countries.

"The Four Early Measures" (Early Detection, Early Isolation, Early Reporting, and Early Treatment) of COVID-19 are important and critical to the successful control of further transmission of the coronavirus (*12*–*13*). Expanded testing is a much-needed strategy that countries in Africa urgently need to strengthen, especially for the screening of key populations (*14*). The development of the COVID-19 epidemic from Europe suggests that the epidemic in Africa will become more severe if comprehensive control measures are not firmly implemented as increasing numbers of African countries transition into having local transmission and community transmission.

From the response strategy to COVID-19 adopted by most African countries, more strict prevention and control measures for COVID-19 have been implemented in Africa. To prevent imported

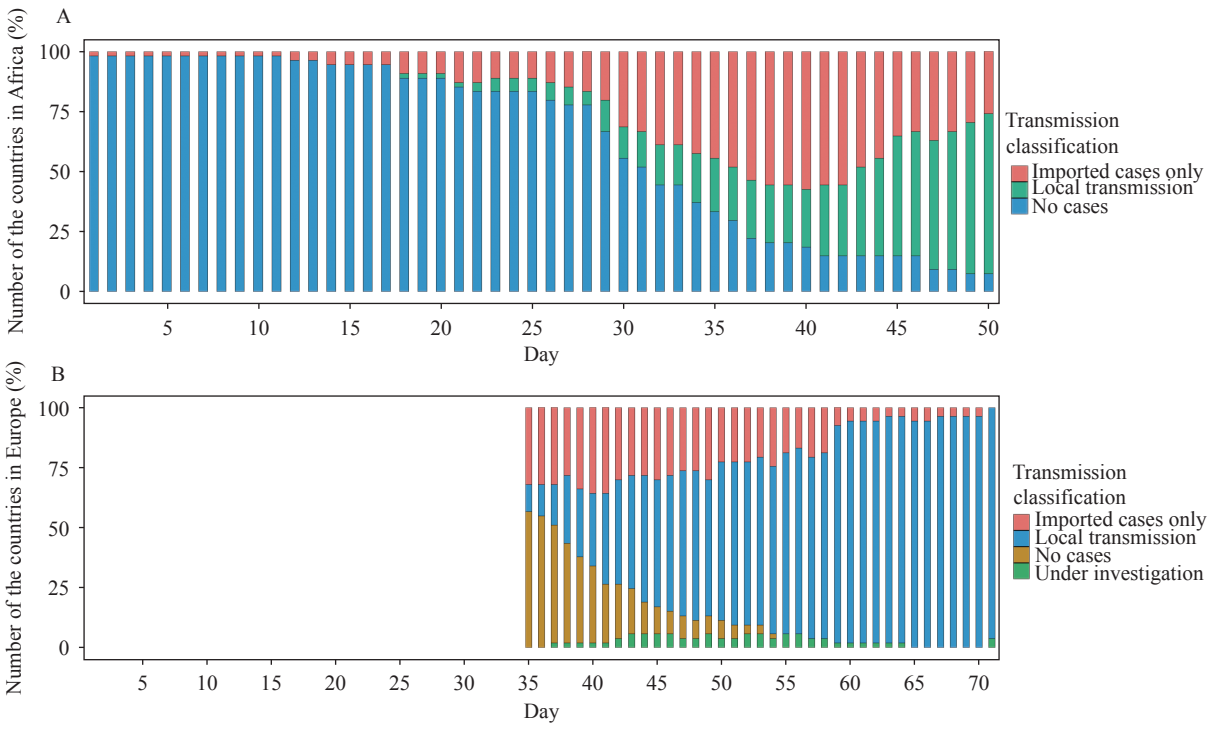

FIGURE 3. Changes in transmission modes of COVID-19 in African (A) and European (B) countries after the first case was reported. In the first 35 days after the first case report, there was no data on COVID-19 transmission in European countries.

transmission of COVID-19, most African countries have closed their borders, and a few have closed international air traffic or imposed travel restrictions to and from specific countries. Virtually almost all African countries have imposed mandatory quarantine measures for all travelers or travelers arriving from high-risk areas of COVID-19. In order to control local transmission and community transmission of the COVID-19, most African countries have implemented special measures for social distancing and movement restriction including closure of educational institutions, banning public gatherings, and closing public spaces. Some African countries are imposing national and partial lockdown or curfews at night with the aim of severely restricting non-essential movement. These measures may be directly responsible for the slowed growth of the COVID-19 epidemic in Africa since the first confirmed case was reported (*15*).

On April 4, 2020, 50 days after the first case was reported in Africa, the cumulative number of confirmed cases worldwide exceeded 1 million (1,051,697) with nearly 57,000 deaths. On that day, 79,394 new confirmed cases and 6,665 deaths were reported globally, with the majority of the new confirmed cases and deaths concentrated in the United States and Europe (*2*). Africa, the world's second largest continent, is facing challenges in the face of the global COVID-19 pandemic. First, the number of confirmed cases and the number of affected countries are increasing rapidly; second, the number of countries switching from imported transmission to local and community transmission is increasing rapidly; third, although many necessary prevention and control measures have been taken, many African countries are not yet ready for specific measures on how to respond to the impending community transmission of COVID-19; fourth, the capacity of basic medical facilities and medical services in many African countries are insufficient, making it difficult to respond to a sudden increase in COVID-19 cases.

The COVID-19 adds an additional disease burden to already existing priority diseases in Africa, such as AIDS, tuberculosis, malaria, and viral hepatitis, and emerging and re-emerging infectious diseases, such as Ebola, dengue, yellow fever, Lassa fever, cholera, and measles, which are still affecting African countries (*16–17*). Frequent outbreaks of these infectious diseases have repeatedly struck and undermined Africa's already strained public health systems. The COVID-19 pandemic has again sounded the alarm in Africa, which urgently needs to strengthen national health systems and develop and implement plans for health development. Only by truly improving the capacity of infectious disease prevention and control and the comprehensive capacity of public health can Africa ensure economic and social development and global health security (*18*).

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Preplanned Studies

Surveillance on the Immune Effectiveness of Quadrivalent and Trivalent Split Influenza Vaccines — Shenzhen City and Changzhou City, China, 2018–2019

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Summary

What is already known about this topic?

Vaccinations are the most effective way to prevent influenza virus infections and severe outcomes. Influenza vaccine effectiveness can vary by seasons.

What is added by this report?

This report monitors the antibody level among the population over time after administration of the quadrivalent or trivalent split influenza vaccine.

What are the implications for public health practice?

Real-time monitoring of serum antibody changes after vaccination provides important data for the development of reasonable and effective strategies for influenza prevention and control.

The influenza virus causes contagious acute respiratory disease with considerable morbidity and mortality in general population worldwide. The World Health Organization (WHO) estimates that 5%–10% of the world population each year becomes infected with the seasonal influenza virus, mainly influenza A and B viruses, resulting in approximately one billion influenza cases (*1*), 3–5 million cases of severe illness, and 290,000–650,000 fatal cases (*2*). So far, there have been four influenza pandemics in history caused by the influenza A virus including the 1918 Spanish flu [A(H1N1)], the 1957 Asian flu [A(H2N2)], the 1968 Hong Kong flu [A(H3N2)], and the 2009 swine-origin flu [A(H1N1) pdm09] (*3*). Meanwhile, influenza B has caused many local outbreaks with high morbidity and mortality (*4*), and in some epidemic seasons, the influenza B virus disease burden actually exceeds that of the influenza A virus.

Because influenza viruses are prone to immunogenic changes, the WHO annually recommends specific vaccine strains in preparation for the next epidemic. In addition to the influenza A viruses H1N1 and H3N2, two different genetic lineages of influenza B virus B/Victoria and B/Yamagata have been co-transmitted worldwide since the 1980s (*5*–*6*). At the end of the 2017–2018 influenza season, the Chinese National Influenza Center (CNIC) reported that the influenza B epidemic in China was mainly B/Yamagata lineage strains, so an inactivated, quadrivalent split-virion influenza vaccine (IIV4s) has been developed containing one A/H1N1 strain, one A/H3N2 strain, and two B strains from B/Victoria and B/Yamagata lineages. The first domestically produced quadrivalent split influenza vaccine was launched in China in June 2018. Both the trivalent and quadrivalent influenza vaccines were used in the following 2018–2019 season. The comparison of the immune effects of the two vaccines among the population needs further investigation (*7*). Important indicators of the vaccines, such as the post-vaccination seroconversion rate, protective antibody titer, and immunity duration, deserve timely surveillance.

Subjects were enrolled using random cluster sampling. In a community of Shenzhen, 75 subjects were vaccinated with domestically-produced quadrivalent split influenza vaccine, and 30 participants were recruited as controls (not vaccinated with any component). In a community of Changzhou, 74 volunteers were vaccinated the trivalent split influenza vaccine, and 38 participants were selected as controls (Figure 1A). The volunteers enrolled in the study were healthy with no contraindications to influenza vaccinations, and the children's guardian gave informed consent. To reflect the natural effects of the vaccines, the vaccines used for the study subjects were local vaccines available in different cities. The information of the vaccines was available under request. The study was approved by the Ethics Review Committee of National Institute for Viral Disease

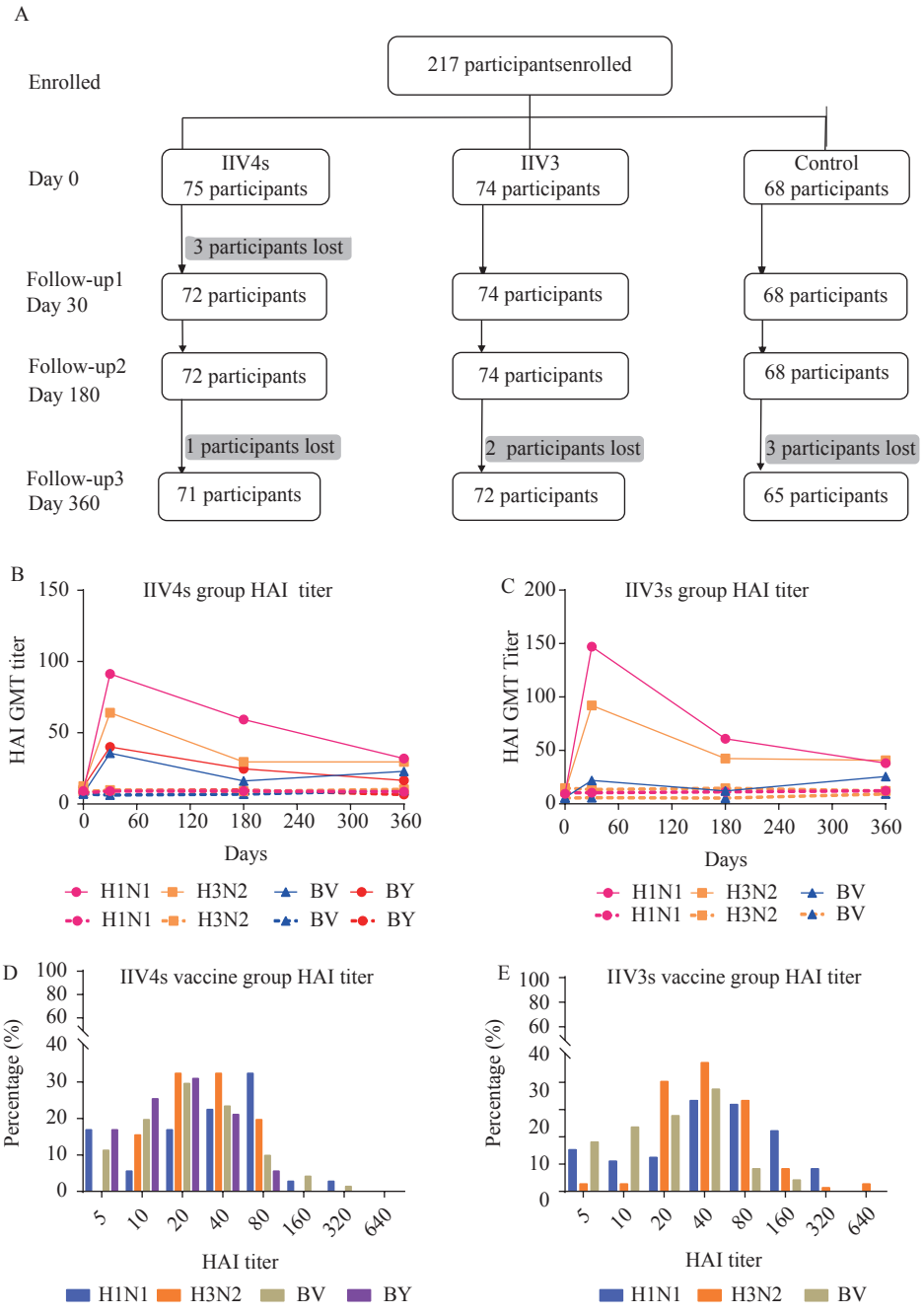

FIGURE 1. Monitoring flow chart and antibody levels in the monitored subjects in Shenzhen and Changzhou, 2018–2019. (A) Flowchart of initial participant enrollment and follow-up distribution among different group in the study of surveillance on the immune effectiveness of quadrivalent and trivalent split influenza vaccines in southern China, 2018–2019 season. (B) Quadrivalent (IIV4s) vaccines group and control group antibody change trends. (The solid line represents the vaccine group and the dotted line represents the control group). (C) Trivalent (IIV3s) vaccines group and control group antibody change trends. (D) Quadrivalent (IIV4s) vaccines group serum antibody levels percentage in 360-day. (E) Trivalent (IIV3s) vaccines group serum antibody levels percentage in 360-day. HAI=hemagglutination inhibition; BV=B/Victoria; BY=B/Yamagata.

Control and Prevention, China CDC. The study was conducted in accordance with the principles of the Declaration of Helsinki and the standards of good clinical practice as defined by the International Conference on Harmonization. After obtaining written informed consent, the subjects were interviewed and given questionnaires, then followed up regularly.

Venous blood was collected from subjects a total of four times: on Day 0 before vaccination, at Day 30, Day 180, and Day 360 post-vaccination. Sera were

isolated from these samples, and serum preparation steps were performed with reference to the "National Influenza Surveillance Technology Guide (2017 Edition)" of CNIC as previously reported (*8*). The hemagglutination inhibition titer (HAI) was used to evaluate the immunogenicity of seasonal influenza vaccine components. Four agglutination unit antigens were prepared from chicken embryo-adapted strains: A/Michigan/45/2015 (H1N1), A/Singapore/INFIMH-16-0019/2016 (H3N2), B/Colorado/06/2017 (B/Victoria), and B/Phuket/3073/2013 (B/Yamagata). Positive control serum was prepared as described previously (*9*). The HAI titer was calculated as the reciprocal of the serum dilution at which erythrocyte agglutination is inhibited in turkey red blood cells. Seroconversion was defined in accordance with the European Medicines Agency (EMA) criteria (*10*): HAI titers of <10 at baseline and ≥40 at Day 30 post-vaccination, of >10 at baseline with at least a four-fold increase from baseline at Day 30 post-vaccination, or when HAI titer <1:10 then calculate geometric mean titer (GMT) according to 1:5.

A database of the subject and sample information was established using EpiData (version 3.1, EpiData Software, Epi Info V6, Denmark), and the questionnaire data were entered in parallel. Statistical analyses were performed using SAS® (version 9.4, SAS Institute, Cary, NC, USA). A one-way analysis using a chi-square test and a multi-factor analysis using non-conditional logistic regression were performed to analyze the factors affecting the seroconversion rates among subjects. Test level significance was set at α=0.05. Graphs were generated using GraphPad Prism (version 7.0, GraphPad Software Inc., San Diego, CA, USA) and Excel 2016 (version 2016, Microsoft Corporation, Redmond, WA, USA).

Subject enrollment began on November 20, 2018, and a total of 217 subjects were monitored through December 8, 2019. A total of 75 subjects were inoculated with IIV4s with 36% (27/75) male and 64% (48/75) female. The basic information of the study subject was shown in the Supplementary Table S1, available in http://weekly.chinacdc.cn/. The age distribution of the IIV4s and IIV3s vaccination groups in different gender was balanced (Supplementary Table S2, available in http://weekly.chinacdc.cn/). The seroconversion rates against H1N1, H3N2, B/Victoria, and B/Yamagata in the IIV4s-vaccinated subjects were 69.4% (50/72), 59.7% (43/72), 54.2% (39/72), and 51.4% (37/72), respectively. A total of 74 subjects were inoculated with IIV3s (40 male [54.1% (40/74)] and 34 females [45.9% (34/74)]. The seroconversion rates against H1N1, H3N2, and B/Victoria in the IIV3s vaccine recipients were 79.7% (59/74), 70.3% (52/74), and 36.5% (27/74), respectively. There was no statistical difference in the seroconversion rates against H1N1 and H3N2 between the IIV4s and IIV3s vaccine groups. However, the seroconversion rate against B/Victoria in the IIV4s vaccine group was higher than that in the IIV3s vaccine group (Table 1).

Among IIV4s-vaccinated subjects, 87.5% (63/72) had seroconversion against at least one of the influenza A strains, H1N1 and H3N2, among the IIV4s population at 30 days. Meanwhile, 68.1% (49/72) had seroconversion against at least one of the influenza B strains, B/Victoria and B/Yamagata, among the IIV4s population at 30 days. The highest seroconversion rates of all the four components were against H1N1 for both male [61.5% (16/26)] and female [73.9% (34/46)] subjects.

Different factors may impact the vaccine effects of the target components. There was a statistical difference between male and female subjects in the seroconversion rates against B/Victoria. The seroconversion rates against H1N1, H3N2, B/Victoria, and B/Yamagata were lower in the elderly group (≥60 years old; 24 [33.3%(24/72)] subjects) than in the adult group {18–59 years old; 48 [66.7%(48/72)] subjects}, and the rate ratios were statistically different (p<0.05). Health-care workers [29 (39.73%) subjects] had a significantly higher seroconversion rate against H3N2 compared with non-medical staff subjects (75.9% *vs.* 47.7%, respectively) (Table 2).

Among IIV3s-vaccinated subjects, 90.5% (67/74)

TABLE 1. The overall positive rate of the IIV4s in Shenzhen and IIV3s in Changzhou, 2018–2019.

Item	H1N1	H3N2	B/Victoria	B/Yamagata
IIV4s	69.4% (50/72)	59.7% (43/72)	54.2% (39/72)	51.4% (37/72)
IIV3s	79.7% (59/74)	70.3% (52/74)	36.5% (27/74)	–*
χ^2	2.04	1.786	4.605	–*
p value	0.153	0.181	0.032	–*

* Trivalent spilt vaccine do not contain B/Yamagata strain.

had seroconversion against at least one of the influenza A strains, H1N1 or H3N2. In the IIV3s-vaccinated group, the highest seroconversion rates in male was against H3N2 (82.5%, 33/40) and H1N1 had the highest seroconversion rates among female subjects (85.3%, 29/34). In the adult group, the seroconversion rate against H1N1 was 83.3% (40/48), which is higher than that in the elderly group with the rate of 73.1% (19/26) (Table 2).

A multivariate analysis was performed on the 30-day seroconversion rates in the IIV4s- and IIV3s-vaccinated populations. An unconditional multi-factor logistic regression analysis revealed that, for the IIV4s-vaccinated group, the factors significantly influencing high seroconversion rates were age for H1N1, healthcare workers for H3N2, sex and age for B/Victoria, and age for B/Yamagata. In contrast, a similar analysis of the seroconversion rates at 30 days post-administration of the IIV3s vaccine group did not find any statistically significant factors (Table 3).

The changes in antibodies against seasonal influenza strains H1N1, H3N2, B/Victoria, or B/Yamagata in the surveillance subjects at different time points are followed up. For both the IIV4s and IIV3s influenza vaccination groups, the antibody level measured by geometric mean titer [GMT] at baseline (Day 0) was low (<20) in all subjects (Supplementary Table S3, available in http://weekly.chinacdc.cn/). In both the vaccine groups, the serum antibody GMT reached a peak at 30 days post-vaccination for all the components, after which the antibody titer gradually decreased with time. At 30 days post-vaccination, the GMT in IIV4s-vaccinated subjects against H1N1, H3N2, B/Victoria, and B/Yamagata were 91.37, 64.11, 35.64, and 40.00, respectively (Figure 1B). The antibody titers against H1N1 and B/Yamagata showed a downward trend from 30 days to 360-day post-vaccination, and the 360-day post-vaccination antibody titers decreased by 1.86 times and 1.4 times, respectively, compared with the 30-day HAI GMT titers. The control group showed a similar trend with low levels of the antibodies for all four time points. The serum GMTs against H1N1, H3N2, and B/Victoria from the IIV3s-vaccination subjects at 30 days post-vaccination were 147.06, 92.07, and 21.99, respectively (Figure 1C). The antibodies against H1N1 and H3N2 decreased significantly from 30 to 360 days post-vaccination.

Studies have demonstrated that a serum HAI GMT titer of ≥40 can prevent 50% of influenza infections (*11*). At 360 days post-vaccination, the percentages of IIV4s-vaccinated subjects with serum HAI titers

TABLE 2. Comparison of serum levels of seasonal influenza antibodies in Shenzhen and Changzhou between different groups, 2018–2019.

Characteristic		IIV4s									IIV3s					
		H1N1		H3N2		B/Victoria		B/Yamagata			H1N1		H3N2		B/Victoria	
		SR	*p*	SR	*p*	SR	*p*	SR	*p*		SR	*p*	SR	*p*	SR	*p*
Sex	Male (N=26)	61.5% (16/26)	0.274	57.7% (15/26)	0.792	38.5% (10/26)	0.044	42.3% (11/26)	0.246	Male (N=40)	75.0% (30/40)	0.222	82.5% (33/40)	0.013	32.5% (13/40)	0.440
	Female (N=46)	73.9% (34/46)		60.9% (28/46)		63.0% (29/46)		56.5% (26/46)		Female (N=34)	85.3% (29/34)		55.9% (19/34)		41.2% (14/34)	
Age	18–59 years (N=48)	81.3% (39/48)	0.002	68.8% (33/48)	0.027	64.6% (31/48)	0.012	64.6% (31/48)	0.002	18–59 years (N=48)	83.3% (40/48)	0.295	66.7% (32/48)	0.357	43.8% (21/48)	0.078
	≥60 years (N=24)	45.8% (11/24)		41.2% (10/24)		33.3% (8/24)		25.0% (6/24)		≥60 years (N=26)	73.1% (19/26)		76.9% (20/26)		20.7% (6/26)	
Healthcare workers	Yes (N=29)	86.2% (25/29)	0.011	75.9% (22/29)	0.022	58.6% (17/29)	0.533	55.2% (16/29)	0.598	Yes (N=21)	76.2% (16/21)	0.634	61.9% (13/21)	0.592	33.3% (7/21)	0.723
	No (N=44)	52.3% (23/44)		47.7% (21/44)		50.0% (22/44)		47.7% (21/44)		No (N=53)	81.1% (43/53)		73.6% (39/53)		37.3% (20/53)	

Abreviation: SR=seroconversion rate.

TABLE 3. Binary logistic regression analysis of the IIV4s in Shenzhen, 2018–2019.

Item	IIV4s	H1N1	H3N2	B/Victoria	B/Yamagata
Affecting factors	Age	Healthcare workers	Sex	Age	Age
OR (95% CI)	5.515 (1.888, 16.109)	3.293 (1.164, 9.312)	0.358 (0.128, 1.004)	3.755 (1.305, 10.800)	5.775 (1.938, 17.208)
p Value	0.002	0.025	0.037	0.014	0.002

Abreviation: OR=odds ratio; CI=confidence interval.

against H1N1, H3N2, B/Victoria, and B/Yamagata of ≥40 were 60.6%(43/71), 52.1%(37/71), 39.4% (28/71), and 26.8%(19/71), respectively (Figure 1D); these percentages in the IIV3s-vaccinated subjects against H1N1, H3N2, and B/Victoria were 38.9%, 45.8%, and 69.4%, respectively (Figure 1E). In contrast, the percentages of IIV4s control group subjects with an HAI titer of ≥40 against H1N1, H3N2, B/Victoria, and B/Yamagata were 13.2%, 7.9%, 10.5%, and 5.3%, respectively; similarly, these percentages in the IIV3s control group subjects were 10.7%,7.1%, and 3.6% for H1N1, H3N2, and B/Victoria, respectively. Thus, the current influenza vaccine should be given not only before the current flu season, but also before the next flu season.

DISCUSSION

Different regions all over the world are annually affected by influenza. Thus, monitoring the serum antibody levels against the influenza vaccine can provide more scientific evidence for screening the effectiveness of influenza vaccine strains.

This study showed that the immunogenicity of IIV4s and IIV3s met the requirements for influenza vaccines, but IIV4s was immunologically superior versus IIV3s for the lineage B strain. The seroconversion rates of quadrivalent and trivalent split influenza vaccine are similar to those previously reported. Several studies have found that the individuals' gender, age, health status, and immunization history may affect immune responses against seasonal influenza vaccine (*12*–*13*). In this study we found that age, gender, healthcare workers may affect seroconversion rates after vaccination. The observed seroconversion rates against H1N1 and H3N2 at 30 days post-vaccination in this study indicated that the immune effects of IIV4s vaccination is similar to that of IIV3s vaccination. However, we can notice that the positive seroconversion rate against B/Victoria among IIV4s-vaccinated group was higher than that in the IIV3s group. This better immune effect of the quadrivalent influenza (*14*) vaccine in the population may be due to the cross reactivity of the additional component B/Yamagata to B/Victoria. Meanwhile, this may be because of the geographic differences in the two cities we enrolled. Compared with the trivalent vaccine, the quadrivalent influenza vaccine has a wider scope of protection for the population, and the quadrivalent vaccine is especially beneficial when the B/Yamagata influenza virus is widespread.

The antibody levels peak at 30 days post-vaccination (*15*), and then decline so that considerable rates of the surveillance population will have insufficient HAI titers before the arrival of the next influenza season. Therefore, it will be necessary to receive another influenza vaccine before the next flu season arrives.

Based on the current influenza vaccine utilization, the vaccination effect varies between seasons. The timely surveillance of the vaccination effects will benefit strategic use of vaccines.

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Perspectives

COVID-19 Control in Italy: Personal Experience from March 25–April 8, 2020

Fan Lyu[1,#]

To combat the rapidly escalating COVID-19 epidemic in Italy, China's third expert team against the COVID-19 pandemic in Italy departed on March 25, 2020. I joined the expert team on March 25–April 8, 2020. As the chairman of Italian Red Cross, Francesco Rocca, said he appreciated the Chinese experts who, after their arduous work on the front lines of China for over a month, chose to move ahead by flying to Italy to offer help (*1*). Medical experts of Italian National Institute of infectious diseases said that Chinese experts have gained a great deal of experience that Italy urgently needs, and that due to the considerable success China has had in fighting the epidemic, they wanted to work with Chinese experts on an international level in Italy (*2*).

However, there have been some concerns on whether China's experience in fighting COVID-19 could also be practical for European countries. In fact, making the best practices and lessons learned in China to be applicable in other regions to solve joint public health issues has been a major challenge for me. The goal of this paper is to introduce my personal experiences working in Italy, which is organized into the following several points: identifying problems through rapid assessment, forming recommendations based on evidence, and communicating for action. In addition, effective preparation is essential to ensure effective and efficient work of international aid.

Key Questions to be Answered

Italy is a developed country with a high proportion of aging people. Before departure, I had two conceptions about the epidemic situation in Italy: one was the high case-fatality rate of COVID-19 due to its high elderly population structure; the other was the unwillingness to obey preventive measures such as wearing face mask, staying at home, or maintaining social distancing while Italian people pursued democratic values and freedom and making a consensus that only sick people should follow these measures. Public perception and opinions might be major barriers to COVID-19 control in Italy. To provide more effective measures and strategies according to the local situation of the COVID-19 epidemic, the following questions should be answered: what is the actual picture of the COVID-19 epidemic in Italy and what recommended approach is realistic for COVID-19 control in Italy? Detailed information was clearly needed.

Results of Rapid Assessment

Shortly after arriving in Italy on March 26, a rapid assessment was conducted through literature review, field observation, and communication with local medical staff and residents to obtain more information on their local epidemic status as well as the existing prevention and control strategies. It was observed that most people could wear masks in public and that the government had already taken some strict measures aiming for COVID-19 containment including punishment with detention, fines, or imprisonment to prevent people from gathering or moving unnecessarily, and local medical institutions were found to be capable of providing proper professional treatment for inpatients. In addition, two urgent issues were concluded through the assessment.

First, the risk of family transmission was high because many mild patients were treated at home. In Tuscany, there were 3,786 ongoing cases of confirmed COVID-19 on March 26 including 275 cases in intensive-care units (ICUs), 1,111 cases in hospitals, and 2,400 (about 58.5% of total cases) cases receiving home care. According to national data which was officially released on March 27, 36,653 cases (42% of the total) were found to be infected during home isolation. In light of this, we advised the local government to strengthen the standard management of home care for mild patients and consider centralized treatment for such patients, and the proposal was also strongly endorsed by Italian experts. According to Reuters on March 30, Andrea Crisanti, a microbiology professor at the University of Padua, said that measures in Italy to prevent the spread of COVID-19 appeared to be ineffective and should be changed. Crisanti said that instead of telling people with mild symptoms to self-isolate at home with the rest of their family, the

authorities should set up centers to separate them from their families as was done in China (*3*).

Second, viral nucleic acid testing was insufficient locally. According to medical staff and health authorities we interviewed shortly after arriving in Tuscany, nucleic acid testing had been mainly carried out for some hospitalized patients and some patients with high fevers who sought medical treatment in Tuscany. The percentage of positive tests in Italy was as high as about 15%, and the proportion of severe cases accounted for 28% of total confirmed cases. It seemed likely that a number of infections might have been neglected and have become the potential sources of infections. Delays in testing result in not only late diagnoses but also a higher case-fatality rate. Based on this, scaling-up testing was strongly recommended.

Following the recommendations, the local authorities in Tuscany have begun to rent hotels for centralized treatment of some mild patients since March 31, and the number of tests gradually increased since late March.

Key Lessons from Working in Italy

I have three key points for effective work in aiding the fight against COVID-19 based on my personal experiences in Italy.

Effective preparation: The important task of assisting Italy involved sharing Chinese experience. Members of China's expert teams should be familiar with China's experiences of COVID-19 prevention and control including integrated prevention and control systems, specific technical guidelines and programs, and cutting-edge research findings including knowledge about the pathogens, transmission dynamics, and strategic concerns of the disease (*4*–*6*). In addition, it is also essential to consult experts of former teams about their experiences in aiding Italy. Finally, a supportive network of talent needs to be established and could be composed of experts from diverse fields including disinfection, laboratory testing, and the global health center experts, etc.

Rapid risk assessment to understand local contexts: We interviewed local medical staff, prevention and control personnel, overseas Chinese people, etc., in order to gain a comprehensive understanding of the current status of local epidemics and control and prevention work. It is important to accurately identify the strong links and weak links of the prevention and control strategy through an integrated analysis of the information gathered from this rapid assessment. The results from analysis should provide strong evidence to make recommendations for a local strategy for COVID-19 control and prevention. This is key for making practical recommendations based on China's experiences and the local conditions in Italy.

Communicating for action: Three recommendations were formed based on the results of our rapid risk assessment, two of which were accepted by local authorities (centralizing treatment of mild patients and scaling-up of testing). The third recommendation was to strengthen epidemiological investigations as epidemiological investigations of confirmed cases were insufficient. We further recommended that the local team strengthen epidemiological investigations in order to find close contacts and to promptly test and quarantine these contacts. However, after discussion with local professionals, the recommendation could not be adopted due to limited human resources. Therefore, interviewing local people with local knowledge is one of the determinants to making recommendations more appropriate and feasible in local contexts.

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Perspectives

Early Hearing Detection and Intervention in the United States: Achievements and Challenges in the 21st Century

Xidong Deng[1,#]; Marcus Gaffney[1]; Scott D. Grosse[1]

INTRODUCTION

Congenital hearing loss affects approximately two infants per 1,000 live births in the United States (USA), making it one of the nation's most common developmental disabilities (*1*). When left undetected, permanent congenital hearing loss can negatively impact children through delays in their speech, language, social, and emotional development (*2*). Children who are identified as deaf or hard of hearing (D/HH) should begin receiving intervention services as early as possible to help mitigate the potential adverse effects (*3*).

Although the importance of identifying hearing loss during the first few months of life was recognized almost 80 years ago (*4*), nationwide efforts to reduce late identification of congenital hearing loss did not begin until the 1990s. This was a result of advances in newborn hearing screening technologies, increased epidemiologic evidence that many D/HH children were not identified early (*5*), and resources from the federal government (*6*). By 2000, all USA states had started implementing programs to support universal newborn hearing screening (UNHS) in hospitals, early diagnosis, and enrollment in intervention for children diagnosed as D/HH. These state programs are commonly referred to as the Early Hearing Detection and Intervention (EHDI) programs (*7*).

In this paper, we outline the initial implementation of EHDI in the USA, followed by a review of the key factors that influenced the evolution of EHDI programs over the past 20 years. We discuss national and state efforts in establishing and promoting UNHS-related legislation, best practices, and developing public health infrastructure to help ensure the provision of hearing screening, diagnostic, and intervention services. We also highlight challenges that EHDI programs have experienced and discuss potential directions for continued improvements in the future.

ACHIEVEMENTS

State and Federal Laws in the USA

State and federal laws have served as an important component in many public health achievements (*8*) including EHDI. Analyses have shown that states that implemented UNHS related legislation had significantly higher newborn hearing screening rates than states with no legislation (*9*). In the early 1990s, Hawaii and Rhode Island became the first states to pass UNHS related legislation. While the legislative requirements varied, by 2003, 37 of the 50 states in the USA had enacted some type of UNHS legislation. In 2016, only 4 states (Idaho, North Dakota, South Dakota, Washington) did not have laws related to hospital newborn hearing screening (*10*).

Legislative support of UNHS/EHDI by the federal government began with the Children's Health Act of 2000 (*11*). This Act authorized two federal agencies — the Health Resources and Services Administration (HRSA) and Centers for Disease Control and Prevention (CDC) — to support EHDI activities at the state level. The 2017 EHDI Act (S. 652, PL 115-71) authorizes HRSA to continue awarding funds to states, territories, and healthcare providers for continuous improvement of EHDI programs. These projects help to identify effective strategies to address screening, loss to follow-up, diagnosis and services, enrollment into early intervention services, family engagement and support systems, and professional education. The Act authorizes CDC to provide both funding and technical assistance to support the development and implementation of data management and tracking systems within state EHDI/UNHS programs and to develop national data standards and track progress towards achievement of EHDI goals.

Best Practices

Awareness of infant hearing loss and the need for early identification has been endorsed by a number of

professional organizations, including the Joint Committee on Infant Hearing (JCIH) beginning with their 1994 position statement. JCIH is comprised of representatives of member organizations from the fields of audiology, otolaryngology, pediatrics, and nursing and was established in 1969. Its primary activities have been the "publication of position statements summarizing the state of the science and art in infant hearing and recommending the preferred practice in early identification and appropriate intervention of newborns and infants at risk for or with hearing loss" (*12*).

Building on the 1994 statement, the JCIH 2000 position statement (*13*) identified Principles and Guidelines for state EHDI programs, which continue to be relevant twenty years later. The 2000 position statement highlighted public health tracking and surveillance systems as essential for the early detection and intervention of congenital hearing loss and established benchmarks to monitor compliance and outcomes at each step in the EHDI process. These benchmarks, often referred to as the EHDI 1-3-6 plan, call for hearing screening no later than 1 month of age, diagnosis no later than 3 months of age for infants not passing the screening, and enrollment into intervention no later than 6 months of age for those identified as D/HH.

Over the past 20 years there has been a growing body of evidence linking UNHS, early identification of hearing loss, and timely entry into intervention with improved language outcomes, lasting benefits for the child's development, and cost savings (*14*–*18*). Based on these findings and expert consensus opinion, JCIH updated its best practice guidelines in 2007 and 2019. The JCIH 2007 position statement reaffirmed the 1-3-6 plan and emphasized the importance of implementing state-based information infrastructure to monitor the quality of EHDI services (*19*). In its latest position statement (*3*), JCIH recommended that states who already meet the 1-3-6 benchmarks strive to meet a 1-2-3 month timeline (screening completed by 1 month, audiology diagnosis by 2 months, enrollment in early intervention by 3 months). It also recommended enhanced information infrastructure that interfaces with clinical electronic health records and population-based information systems, to support improved performance and quality measurement and reporting.

Public Health Surveillance

With enactment of the Children's Health Act of 2000, federal funding became available through the CDC and HRSA for EHDI activities. The funding and assistance provided by CDC to state programs supported the development and implementation of data management and tracking systems, called EHDI Information System (EHDI-IS). These confidential, computerized, population-based systems serve as tools for states to collect and consolidate data at different stages of the EHDI process to support effective tracking and follow-up of hearing services for all infants. Over the past 20 years, these systems have evolved from basic data repositories with limited case management and reporting capabilities to complete, integrated information systems. Today most EHDI-IS provide near real-time and direct data access, as well as decision support for public health officials to track and monitor care and service provision for infants and children at risk of congenital hearing loss. (Figure 1).

Since 2007, states annually submit data from their EHDI-IS to CDC through the Hearing Screening and Follow-up Survey (HSFS) (*20*), which is used to assess the nation's progress towards the EHDI 1-3-6 benchmarks. Over the years there has been a steady increase in the documented percentages of infants meeting these benchmarks (Figure 2). The percentage of infants screened by one month of age increased from an average of 91.6% during 2005–2006 to 95.5% during 2016–2017. During the same timeframe, the infants meeting the intervention benchmarks increased by more than ten percentage points (from 32.2% to 44.3%). The biggest improvement was in diagnosis. During 2005–2006, only approximately 15.0% of infants who did not pass their hearing screening were diagnosed before three months of age. The percentage of infants meeting this diagnosis benchmark increased to 40.0% during 2010–2011, and then to nearly 50.0% during 2016–2017.

CHALLENGES

Although timely completion of hearing screening has been consistently achieved for most newborns in the past decade, challenges remain in ensuring the timely receipt of follow-up diagnostic and intervention services for all children at risk. During 2016–2017, among all reported cases nationwide, less than 50% of infants not passing hearing screening were confirmed to have received diagnosis before the recommended benchmark of 3 months of age, and less than half of children identified as D/HH were enrolled in intervention before 6 months of age. Wide variations

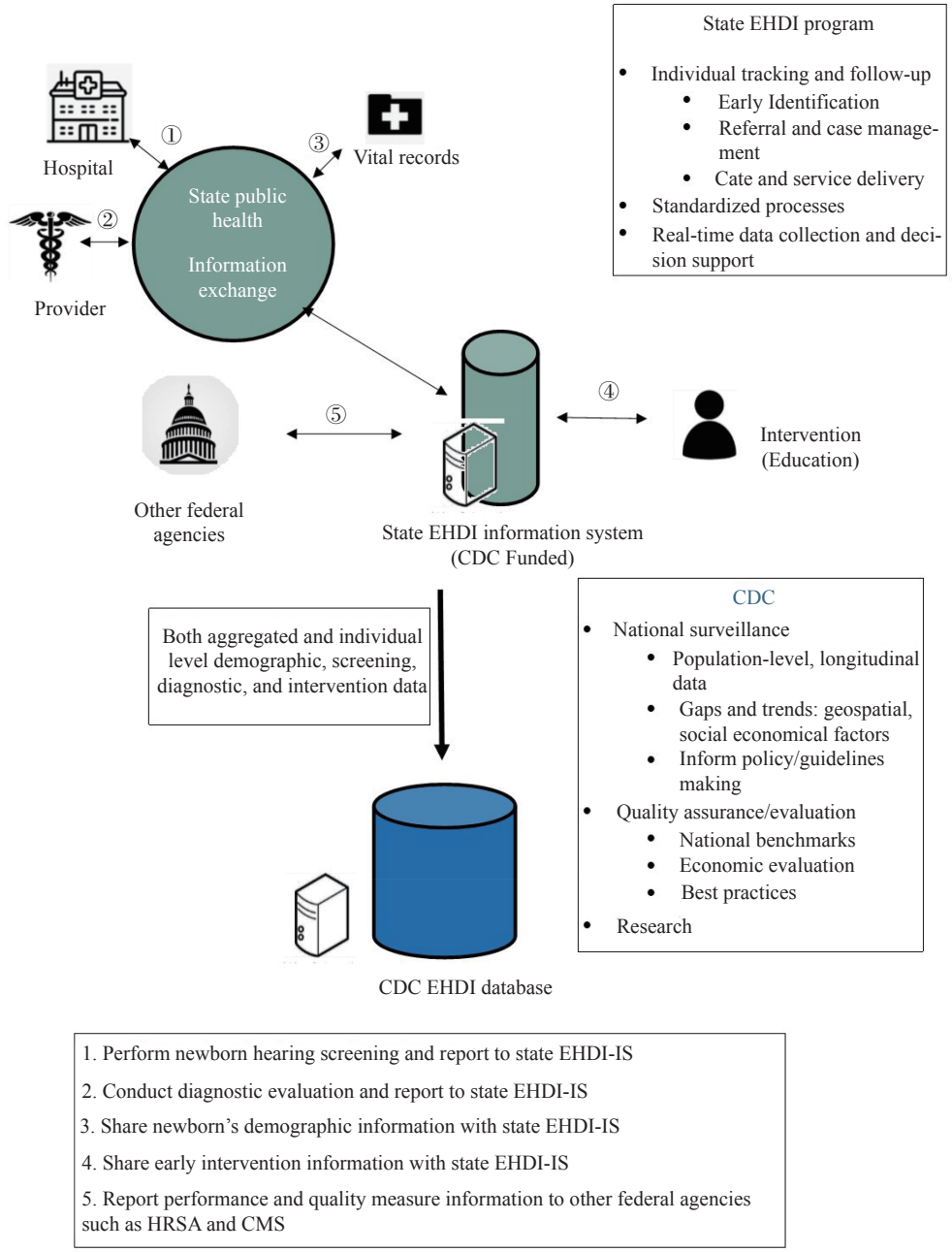

FIGURE 1. Federal and state Early Hearing Detection and Intervention (EHDI) tracking and surveillance information infrastructure. Abbreviation: CDC=Centers for Disease Control and Prevention; EHDI-IS=EHDI Information System; HRSA=Health Resources and Services Administration; CMS=Centers for Medicare and Medicaid Services.

in meeting these benchmarks exist at the state level, with some programs performing well above the national average, and others having not been as successful. First, such variations could be attributed to lack of effective follow-up strategies; reductions in resources available to some programs, and differences in state statutes, regulations, or policies. Second, differences in the infrastructure and capabilities of the state-based EHDI-IS limit the ability of some programs to accurately identify, match, collect, report, and analyze data on all births. Some states still largely rely on old technologies, such as mail and fax to collect and report EHDI data. Variation in data definitions among state programs can also contribute to differences in the reported results, making it difficult for CDC to monitor performance (*21–22*). Closely related to the implementation of modern information systems is the implementation of systematic evaluation and quality assurance programs. Some state EHDI programs have not had time or resources yet to

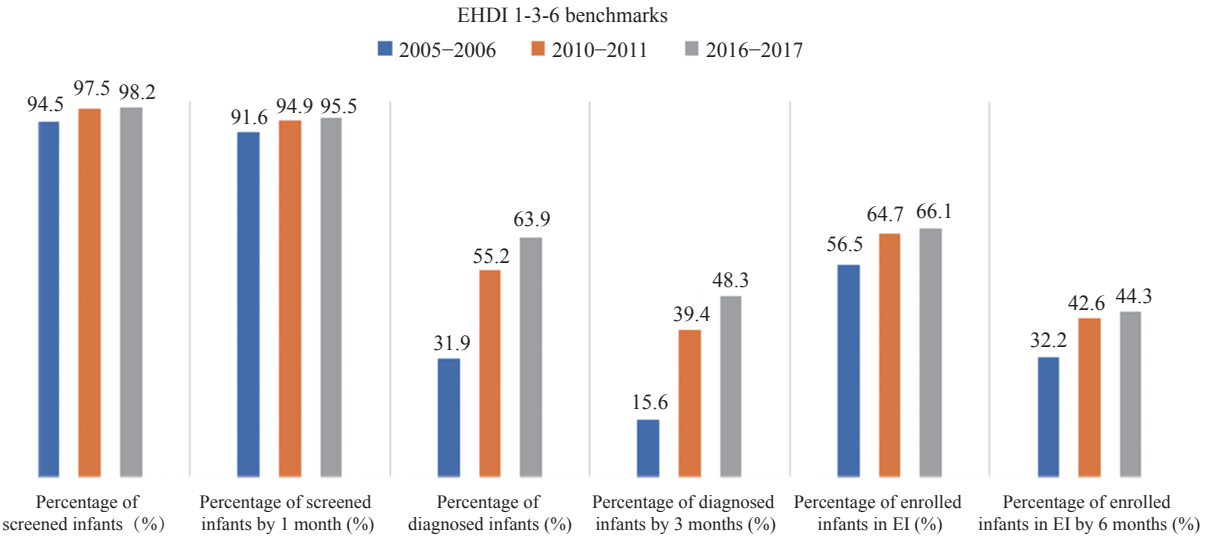

FIGURE 2. Percentage of infants screened, diagnosed, and enrolled in early intervention — Hearing Screening and Follow-up Survey, United States, 2005–2006, 2010–2011, and 2016–2017. Abbreviation: EHDI=Early Hearing Detection and Intervention；EI=Early Intervention.

implement such systematic evaluation and quality assurance programs. Finally, geographic, racial, and socio-economic disparities in the provision of diagnostic and intervention services persist within many states (*23*–*25*). Given the clinical resources that are needed to adequately diagnose congenital hearing loss early, and the economic resources associated with it, it is not surprising that people living in rural, remote areas and/or with lower socio-economic status may be more likely to experience delays in receiving recommended services.

PATH FORWARD

Over 95% of babies in the USA now receive a hearing screening before one month of age, up from only 20% in 1999. Each year in the USA, over 6,000 infants who are D/HH are being identified early. With this progress, more children, along with their families, have the opportunity to experience improved outcomes in language development and overall well-being (*1*,*26*).

Sustaining these achievements and advancements in EHDI programs will likely require concerted efforts from all stakeholders, including government agencies, research institutions, hospitals, audiologists and pediatricians, rehabilitation and intervention service providers, and others.

First, it is important for public health agencies to continue highlighting the value of identifying children who are D/HH as early as possible among healthcare providers and administrators and, contingent on their funding appropriations, to assist (e.g., technical and financial) with implementation of best practices. This includes ongoing training at the community level, which can help ensure families with children at risk to be full participants in the EHDI process. Second, it is important to enhance population-based public health surveillance systems that can provide timely and accurate data on all newborns. To enhance tracking, follow-up, case management, and reporting, such systems may wish to adopt nationally recognized functional standards, data definitions, and quality measures. They may also leverage evolving health information technologies for information exchange and analysis. In addition, increased efforts might be considered to improve the availability of specialized services to under-served populations (e.g., using telemedicine). With all stakeholders continuing to collaborate and coordinate their efforts, infants and young children with permanent hearing loss will be more likely to acquire the "fundamental language, social, and cognitive skills that provide the foundation for later schooling and success in society" as foreseen 30 years ago in *Healthy People 2000* (*27*).

Disclaimer: The opinions expressed in this article are the authors' own and do not reflect the view of the Centers for Disease Control and Prevention, the Department of Health and Human Services, or the United States government.

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Announcements

Establishment of the NIAC Technical Working Group on COVID-19 Vaccines

COVID-19 Vaccines Technical Working Group

Vaccines against the COVID-19 virus are being developed in China and other countries at an accelerated pace to prevent and control COVID-19. Strategies and policy for the use of the vaccines are based on scientific evidence including epidemiology, vaccinology, health economics, ethics, and production factors. The National Immunization Advisory Committee (NIAC) makes evidence-based recommendations for the use of vaccines and is supported by working groups of technical experts. We report the establishment of a technical working group for COVID-19 vaccines, its terms of references, anticipated products, and membership.

The NIAC was established in 2017 by China's National Health Commission (NHC) at the request of the State Council to make evidence-based recommendations to the NHC on the inclusion of vaccines in the Expanded Program on Immunization (EPI) and recommendations for use of vaccines (*1*). NIAC was included in the vaccine law enacted by the People's Congress in 2019. Chinese Center for Disease Control and Prevention (China CDC) scientists, with NIAC members and external experts, lead and staff technical working groups (TWGs) to support the NIAC vaccine recommendations using an evidence-to-recommendation framework to formulate draft vaccine recommendations for consideration by the NIAC (*2*). We report the establishment of a NIAC TWG for COVID-19 vaccines, describe its terms of reference and anticipated products, and provide contact information for the TWG.

PURPOSE

The purpose of the technical working group on COVID-19 vaccines is to support the NIAC in making and keeping up-to-date evidence-based recommendations to the NHC on use of COVID-19 vaccines in China based on 1) evidence about the epidemiology of COVID-19, 2) awareness of COVID-19 vaccines and their characteristics, development, evaluations, and projections of production, 3) awareness of clinical trials and regulatory pathways, 4) evidence from public engagement with likely vaccine target populations on acceptability of vaccines and potential recommendations, and 5) evidence that will emerge from safety, effectiveness, and implementation monitoring.

COVID-19 vaccines will almost certainly be necessary for the COVID-19 pandemic response, including for protection of health care workers and responders, maintenance of essential services, and for immunizing the population to stop risk of COVID-19 infection and transmission.

There are currently no approved vaccines against the COVID-19 virus infection, but COVID-19 vaccines are being developed rapidly in China and other countries and vaccine candidates are entering Phase I human clinical trials. Several strategies are being used for vaccine development including subunit vaccines, inactivated virus vaccines, adenovirus vectored vaccine, live attenuated influenza virus vectored vaccine, and nucleic acid vaccine (mRNA, DNA) (*3*). The characteristics and safety profiles of vaccines that will become available are largely unknown, and since no coronavirus vaccines have ever been licensed in any country, including human-tested SARS and MERS vaccines, there is no direct experience regarding coronavirus vaccine immunization programs to draw from.

Pragmatic planning for science-based recommendations on the use of COVID-19 vaccines can contribute to the public health response to the COVID-19 epidemic. Planning and communications encompass the entire lifecycle of COVID-19 vaccines from development and testing through its use, monitoring, and injury-related compensation. Vaccine clinical trials can be planned and conducted with the uses of the vaccines in mind, including inclusion of study populations that resemble likely vaccine target populations and therefore minimizing the need for off-label use of licensed vaccines. Without adequate planning and communication to the public and

stakeholders, there is potential for suboptimal and inequitable use of vaccines and for social disruptions due to a mismatch between actual and expected vaccine implementation from the public, government, and other key stakeholders. Because the NIAC has a responsibility to make recommendations for inclusion of vaccines into the EPI system, the committee has an important role in supporting the availability, affordability, and strategic use of COVID-19 vaccines in China.

TERMS OF REFERENCE

Monitor COVID-19 vaccines development. Be aware of and monitor COVID-19 vaccine research and development, technical strategies for clinical evaluation, and market authorization policies; provide suggestions for clinical trials, vaccine evaluations, and preparation for production capacity during public health emergencies.

Support NIAC immunization policy development. Provide technical support to the NIAC with considerations for prioritization and sequencing of potential target populations, immunization schedules, and other COVID-19 vaccine policy recommendations.

Prepare for and monitor COVID-19 vaccines use. Develop and recommend strategies for post-marketing safety surveillance and assessment of effectiveness and implementation of COVID-19 vaccines.

Develop vaccination education and communication materials. Prepare materials for professional education and public communications for COVID-19 vaccines and immunization strategies and policies.

TWG COMPOSITION AND PRODUCTS

The TWG and its consultants include NIAC members, China CDC staff, academics, industry leaders, and members of civil society organizations that collectively have expertise in COVID-19 epidemiology, medicine, public health, laboratory, infectious disease, vaccine regulation, manufacturing, vaccine safety and pharmacovigilance, clinical trials, ethics, law, and communications.

The primary product of the technical working group will be technical guidelines on the use of COVID-19 vaccines in China. The TWG will publish periodic reports in *China CDC Weekly* (*CCDCW*) and the *Chinese Journal of Vaccines and Immunization* (*CJVI*) on the TWG products and activities, the status of vaccines being considered for use in China, results of policy-relevant research and evaluations, meeting reports, availability of material for training and education, and communications messages.

TWG point of contact is Dr. Fuzhen Wang, TWG Secretary (wangfz@chinacdc.cn).

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