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To Share Healthy Lives

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Cover Image: Designed by Yonghu Sun from Shandong Provincial Institute of Dermatology and Venereology.

Announcements

The 67th World Leprosy Day — January 26, 2020

World Leprosy Day was proposed by French humanitarian Raoul Follereau in 1954 (*1*) and has been annually observed around the world on the last Sunday of each January with the aim of raising global awareness and knowledge about this ancient disease and calling attention to the fact that leprosy can be prevented, treated, and cured. Since 1988, the China Leprosy Association initiated China Leprosy Day on the same day.

Although leprosy has been declared "eliminated" as a public health problem at a global level by the World Health Organization (WHO) in 2005, around 200,000 new cases are reported globally each year (*2*). In 2011, the Chinese Ministry of Health, together with 11 other ministries, implemented the "National Strategic Plan for Eliminating Harm of Leprosy, 2011–2020 in China", aiming to reduce both the rate of grade 2 disability (G2D) and severe adverse drug reactions (ADR) caused by multidrug therapy (*3*). Since then, tremendous progress has been achieved including reducing the rate of G2D to 19% and the rate of ADR to 0% (*4*). There were only 521 new cases registered in 2018. This progress accelerates the achievement of a leprosy-free world.

World Leprosy Day will be taking place on January 26, 2020. China's Leprosy Day theme is "To relieve leprosy poverty & to share healthy lives".

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Preplanned Studies

Towards a Leprosy-Free Country — China, 2011–2018

Meiwen Yu[1,#]; Peiwen Sun[1]; Le Wang[1]; Hongsheng Wang[1]; Heng Gu[1]; Xiangsheng Chen[1]

Summary

What is already known about this topic?

Leprosy is a chronic infectious disease that is endemic in several countries. Control of leprosy has had targets set by World Health Organization's (WHO) Global Strategy 2016–2020 and by China through a national leprosy-control plan (2011–2020).

What is added by this report?

Data from the Leprosy Management Information System in China was analyzed and showed a national prevalence of 0.178 per 100,000 and detection rate of 0.037 per 100,000 residents in 2018. In addition, all the main targets for 2020 have been met by 2018 except for the proportion of counties or cities to reach a prevalence of less than 1/100,000 and the proportion of children cases with grade 2 disability (G2D).

What are the implications for public health practice?

There are still challenges remaining to close the gaps between current progress and the targets set forth by the WHO and China. However, lessons learned in China in developing and implementing the national program may be invaluable for future plans to achieve and sustain elimination of leprosy at global and country level.

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*, which essentially affects the peripheral nervous system but also involves the skin, eyes and sometimes certain other tissues. This disease is usually endemic in tropical countries, especially in developing countries. Historically in China, the endemicity of leprosy was much higher along the coast and in the Yangtze Valley. In 1950, the leprosy control program was initiated and organized by the Chinese Ministry of Health (MOH, now the National Health Commission), which implemented vertical programs from national to county levels. Repeated mass or general surveys were conducted in the 1950s, 1960s,

and 1970s in most areas of the country to detect most of new and historical cases in the country for treatment with monotherapy of dapsone (*1*). The introduction of multidrug therapy (MDT) to leprosy programs in China in the mid-1980s resulted in a significant reduction in the prevalence of the disease.

Based on the definition of WHO for elimination of leprosy as a public health problem (a prevalence of less than 1 case per 10,000 residents), China had eliminated this disease at the national level in 1981 and at the provincial level in 1992 (*1*). Nonetheless, this disease continued to be disproportionally detected in some areas with 1.2% of counties or cities not having reached this WHO criteria as of 2010 and resulting in a significant proportion of their patients to be disabled. To address these issues, the MOH published a national leprosy-control plan (2011–2020) to specially aim at controlling leprosy and its harms through public health investment directly allocated for leprosy control (*2*). The program aims to improve along three axes: the total number of leprosy patients; the percentage of counties or cities with a prevalence lower than 1/100,000; and the proportion of newly detected cases with grade 2 disabilities (G2D).

The Leprosy Management Information System in China (LEPMIS) is an updated version of the original National Leprosy Recording and Reporting System (*3*) that was initiated in 1990 to collect individual data on all leprosy patients reported from all counties or cities in Mainland China for establishing a national computerized database. Data from the database are analyzed regularly by the National Center for Leprosy Control and reported at annual national leprosy meetings in China and shared with the WHO. Diagnosis of leprosy was based on clinical, bacteriological, and sometimes histopathological profiles. When calculating for prevalence, patients who were not clinically cured were considered clinically active, while case detection rate was defined as the number of newly detected cases divided by population. The newly detected patients with WHO grade 2 (visible) deformities or damages were defined as "disabled" for the calculation of the disability proportion and rate of new cases.

Data from LEPMIS indicated that both the prevalence or the case detection rate of leprosy significant declined between 2010 and 2018 to reach a national prevalence of 0.178 per 100,000 and detection rate of 0.037 per 100,000 residents in 2018 (Figure 1). The number of registered cases and new cases in 2018 decreased by 58.6% and 60.6%, respectively, from that in 2010 (*4*–*5*).

The registered cases declined from 5,479 in 2011 to 2,479 in 2018 and most cases were found in Yunnan, Sichuan, Guizhou, and Guangdong. A total number of 6,602 new cases were detected from 2011 to 2018, with an average annual decline of 11.0% compared with 1,324 in 2010 (Table 1). During 2011–2018, 4,254 (64.4%) cases occurred in priority provinces of Yunnan, Guizhou, Sichuan, and Guangdong.

Among the newly detected cases in 2011–2018, male cases totaled 4,479 with a proportion of 67.8% and children under 15 years old cases totaled 141 with a proportion of 2.1%. Additionally, during this period, 11.5% of new cases were detected among people migrating from traditionally leprosy endemic areas to major cities such as Beijing, Shanghai, Guangzhou, and Shenzhen.

The number of newly detected cases with G2D was

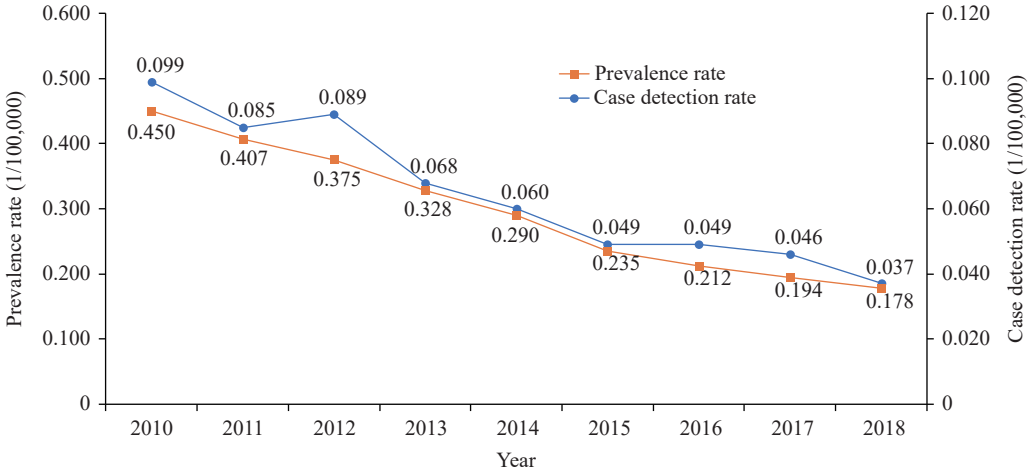

FIGURE 1. The prevalence rate and case detection rate of leprosy in China, 2010−2018.

1,508 cases during 2011–2018 and the proportion of new G2D cases had remained mostly at the level around 20.0%. The proportion of G2D slowly declined to 19.0% in 2018. The rate of new leprosy cases with G2D decrease from 0.222 per 1,000,000 residents in 2010 to 0.071 per 1,000,000 residents in 2018 at the population level. Eight cases with G2D were found among children during 2011–2018, giving a proportion of G2D of 5.7% (8/141). In 2018, one case with G2D was found among children giving a proportion of G2D among children cases of 14.3% (1/7).

There were 237 counties or cities with a prevalence rate above 1/100,000 by the end of 2010. After 8 years of implementing the leprosy program in China, by the end of 2018, there were still up to 75 counties or cities where the prevalence target of more than 1/100,000 was not achieved, accounting for 2.6% of the total number of counties or cities in the country (Table 2).

DISCUSSION

A total of 208,619 new cases of leprosy were reported globally in 2018, and 23 countries were identified by the WHO as "global priority countries" as accounting for 95.6% of the global load. China was not among these 23 priority countries, and the new case detection rate in China, approximately 0.037/100,000, was comparable to that of the United States (*6*) and was much lower than the global average of 2.74/100,000.

By the end of 2018, 184,212 cases were registered globally as receiving MDT, with a leprosy prevalence of 0.24/10,000. This global prevalence was over 10 times higher than the rate 0.178/100,000 reported in China in 2018. In addition, the prevalence calculated in China includes patients who were not clinically cured regardless of receiving or completing MDT, so the prevalence in China would be lower if the WHO

TABLE 1. Epidemiological profiles of leprosy in China, 2011−2018*.

Year	Registered cases	Prevalence rate (1/100,000)	Newly detected cases						
			Total	Case detection rate (1/100,000)	Male	Children under 15 years old	Mobile cases	Cases with G2D	Grade 2 disability rate (1/1,000,000)
2011	5,479	0.407	1,144	0.085	779	29	114	309	0.229
2012	5,071	0.375	1,206	0.089	847	29	103	346	0.256
2013	4,465	0.328	924	0.068	616	14	103	188	0.138
2014	3,961	0.290	823	0.060	560	14	109	165	0.121
2015	3,230	0.235	678	0.049	474	20	89	126	0.092
2016	2,925	0.212	672	0.049	457	19	93	148	0.107
2017	2,697	0.194	634	0.046	417	9	74	127	0.091
2018	2,479	0.178	521	0.037	329	7	71	99	0.071
Total	3,788†	0.276†	6,602	0.060†	4,479	141	756	1,508	0.137†

Abbreviation: G2D=grade 2 disablity.
*The data from 2011 to 2015 were published in Chinese Journal of Dermatology in 2017, and in this study, the data were extended to 2011−2018.
† Average data.

TABLE 2. Main targets proposed by China's National Program and the WHO's Global Strategy and status of these targets by 2018 in China.

Indicator	Target of National Program by 2020*	Target of Global Strategy by 2020†	Status by the end of 2018 at national level
Reduction in the number of registered cases from that in 2010	>50%	NA	58.6%
Proportion of newly diagnosed cases with grade-2 disability	<20%	NA	19.0%
Grade 2 disability rate at population	NA	<1/1,000,000	0.071/1,000,000
Grade 2 disability rate among newly detected pediatric cases	NA	0%	14.3%
Proportion of counties or cities reaching the prevalence of less than 1/100,000 (N)	>98% (2,856)	NA	97.4% (2,851)

Abbreviation: NA=Not applicable.
* China National Program for Eliminating Harms Due to Leprosy (2010−2020).
† WHO Global Leprosy Strategy 2016−2020: Accelerating towards a leprosy-free world.

method of calculating of prevalence, i.e. cases under MDT were calculated as registered cases, was applied.

For China to take the last steps towards becoming a leprosy-free country, innovative strategies were introduced such as symptom-driven case-detection methods combined with pay-for-performance schemes to maximize early case-finding and start earlier treatments to better prevent the development of disabilities. The symptom-driven case-detection method refers to encouraging health providers to refer any patients with symptoms suspected as leprosy for further clinical evaluation and diagnosis (*7*–*8*). The pay-for-performance scheme refers to a purchase mechanism by which subsidies were provided to compensate health providers for successful referrals for patients who were ultimately diagnosed with leprosy.

By 2018, all the main targets for 2020 have been met except for the proportion of counties or cities to reach a prevalence of less than 1/100,000 and the proportion of children cases with G2D. Globally, China might be one of the first countries to propose a leprosy elimination goal defined as a prevalence of less than 1/100,000 at the county or city level, but this goal may be difficult to achieve due to uneven disease burdens, access to and distribution of health resources, and socioeconomic status across the country.

In conclusion, China has made significant progress in the fight against leprosy, but several challenges remain. Public health systems specifically established and budgets specifically allocated for leprosy control at different levels ensured the successes of effectively controlling the disease. However, sustainability of the systems and investments is a challenge. Population migration makes case detection, treatment, and follow-up more challenging, and approximately one-tenth of newly detected cases occur annually among domestic migrants with new cases also being detected in international migrants. To address this challenge, the International Forum for Leprosy Precision Prevention and Treatment was held in China in 2018 and 2019 to congregate international representatives from Belt and Road Initiative countries.

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Review

Prevention and Treatment of Leprosy — China, 2009–2019

Qing Zhao[1]; Yonghu Sun[1]; Hong Liu[1]; Furen Zhang[1,#]

Since 1981, worldwide leprosy prevalence has declined sharply due to the implementation of multidrug therapy (MDT) conducted by the World Health Organization (WHO). The national prevalence of leprosy finally decreased to 0.05 per 10,000 population in 1998, which meant the WHO threshold of leprosy elimination (below 1 per 10,000 population) was reached in China through a well-organized control network and through the implementation of MDT (*1*). However, the number of newly registered leprosy cases each year, the grade 2 disability (G2D) rate, as well as the rate of fatal adverse drug reactions (ADR) had not significantly changed since 1998 (*2–3*), so leprosy is still seen as a public health problem in China. In addition, dermatological clinics rather than leprosy control stations became the main source for leprosy case finding at every level. Delayed diagnosis was common due to a general lack of awareness and adequately precise techniques among dermatologists to detect *Mycobacterium leprae* (*M. leprae*) that results in leprosy.

In order to eliminate the harm of leprosy, Ministry of Health of the People's Republic of China published a national leprosy-control plan (2011–2020) in 2011. Since then, both the number of newly detected leprosy patients and newly diagnosed cases with G2D each year have been reduced compared to 2009. The rate of life-threatening condition – dapsone hypersensitivity syndrome (DHS) was reduced to 0.0% in all pre-screened populations in 2018. According to the WHO, the number of new cases and reported new cases with G2D globally only slightly decreased from 2009 to 2018 (*4*). China's progress in leprosy control is due largely to the efforts of the government, leprosy control institutions, doctors, and scientists. These stakeholders have made tremendous contributions in setting up effective strategies to monitor leprosy patients, developing accurate techniques to measure infections, and finding useful ways to prevent adverse events from occurring during treatment. This report summarizes progress towards leprosy harm elimination in China.

Activities by China Towards the National Strategy

Efficient Surveillance

In 1990, the Ministry of Health initiated the National Leprosy Recording and Reporting System and gave management responsibility to the National Center for STD and Leprosy Control (*5*). The system is used for documenting demographic and medical records of all leprosy cases by trained doctors and staff at a national level. The system allows for easier tracking of patients, summaries of annual national and provincial-level leprosy control programs, and analysis of epidemiological trends and clinical aspects of leprosy. These products of the surveillance system enables the government to design more effective control programs. The computerized leprosy records continue to play an important role in leprosy surveillance.

In recent years, the main methods of detecting leprosy in patients has changed from active case-finding surveys to skin clinic case-finding as the number of leprosy patients significantly declined, which has made early case detection a new challenge in the leprosy control program. In addition to the system mentioned above, every level of government has begun implementation of several measures to improve early case detection. First, the government provided adequate financial and policy support for leprosy control institutions to carry out a variety of leprosy case-finding campaigns. Second, public health education was performed to strengthen the awareness of leprosy among the public. Meanwhile, symptom surveillance and referral of suspected leprosy cases to regional medical centers from local institutions for confirmation of diagnosis was a crucial strategy for early diagnosis, especially in the provincial and district levels.

Precise Prophylactic Measures

Chemoprophylaxis such as using a single dose of

rifampicin or conducting long-term follow-ups have been given to contacts of newly diagnosed leprosy patients to at least partially interrupt transmission of leprosy. However, epidemiological studies suggest that 95% of individuals exposed to *M. leprae* will not be infected. Among those 5% infected individuals, only 20% would develop leprosy, indicating that chemoprophylaxis or long-term follow-ups might protect only a small proportion of leprosy contacts and that a host's genetic factors played a major role in the pathogenesis of the disease.

Since 2009, thirty-one independent susceptibility loci of leprosy have been discovered through genome-wide association studies (GWASs) and candidate-gene studies conducted by the research group of the Shandong Provincial Institute of Dermatology and Venereology (SPIDV) (*6*–*12*). Based on the genetic variants associated with leprosy in the Chinese population, SPIDV made a risk prediction model through a weighted genetic risk score (GRS) with an area under the curve (AUC) of 0.743 (*13*). When using 22.38 as GRS cut-off value, the sensitivity and specificity were 67.1% and 69.7%, respectively. In order to prevent 64.9% people affected by leprosy, 39.31% of contact subject should receive post-exposure prophylaxis or be followed up with according to the model. The risk prediction model might be a more effective and economical tool to detect higher-risk groups among all leprosy contacts.

Early Diagnosis

Early diagnosis of leprosy is a crucial step for preventing disability. Traditional laboratory techniques such as acid-fast bacilli staining showed low sensitivity and specificity. In the past few years, efforts have been made to establish more efficient and accurate diagnostic methods. Paucibacillary (PB) patients were more prone to be misdiagnosed compared to multibacillary (MB) leprosy patients, so early diagnostic methods, especially for early diagnosis of PB patients, were needed. There were mainly two strategies for the development of new early diagnostic methods.

Serological analysis could be a convenient and useful tool for diagnosis of MB leprosy. The Beijing Tropical Medicine Research Institute (BTMRI) evaluated the ability of *M. leprae* antigen specific immune responses to support the leprosy diagnosis (*14*–*17*). In addition, BTMRI tested a panel of *M. leprae*-stimulated host markers in an overnight whole-blood assay and found that *M. leprae*-induced CXCL8/IL-8 showed potential diagnostic and discriminatory value for PB patients (*18*). These simple tools could be set up in endemic areas without clinical molecular laboratories.

Furthermore, detection of *M. leprae*-specific DNA could be more sensitive. New primer sets for the *M. leprae*-specific repetitive element (*RLEP*) gene were designed by BTMRI and single tube nested PCR (STNPCR) and SYBR Green PCR assays were performed to test *M. leprae* for PB patients (*19*). SPIDV developed the droplet digital polymerase chain reaction (ddPCR) assay using primers for *M. leprae*–specific *RLEP* and *groEL* genes to detect *M. leprae* in PB patients with a high sensitivity of 79.5% (*20*). All diagnostic approaches assisted with earlier diagnosis of leprosy and reduced the rate of disability in new leprosy patients.

Precision Treatment

Since MDT was introduced for leprosy in 1981 by the WHO, the number of leprosy patients has been reduced dramatically. Even though leprosy transmission could be quickly stopped by administration of MDT, the occurrence of DHS among some leprosy patients raised another problem. In China, the incidence of DHS was 1.0% and the mortality was 11.1% among all patients with DHS between 2006 and 2009 (*3*), so preventing the occurrence of DHS was prioritized. In 2013, *HLA-B*13:01* (odds ratio, 20.53; $p=6.84\times10^{-25}$) was discovered as a strong risk factor for DHS by both the SPIDV and the National Center for STD and Leprosy Control independently in the Chinese population (*21*–*22*), which has been validated in Indonesia, India (*23*), Thailand (*24*), Malaysia, and Republic of Korea. SPIDV developed an *HLA-B*13:01* kit with both a sensitivity and a specificity of 100%. Since 2015, SPIDV has carried out a nationwide clinical trial to evaluate the efficacy of *HLA-B*13:01* screening to prevent DHS. A total of 1,512 patients were genotyped for *HLA-B*13:01*, and 1,251 patients were *HLA-B*13:01*-negative. These leprosy patients were treated with dapsone, and none of the 1,251 patients developed DHS. Therefore, screening for *HLA-B*13:01* prior to dapsone administration could decrease the incidence of DHS in Chinese population (*25*).

Discussion

Based on the national strategy, there has been significant progress towards the harm of leprosy in China. Prevalence, incidence, rate of grade 2 disability,

and the incidence of DHS reached historically low levels. The strategy depends on several pillars including all levels of government, the China Leprosy Association, and leprosy-related research institutes. Full government support and well-organized surveillance were crucial for the detection and treatment of leprosy patients. Also, instead of applying chemoprophylaxis or long-term follow-ups to all contacts of leprosy patients, precision prophylactic measures based on genetic factors would be a more cost-efficient way to prevent infection transmission to high-risk contacts. In addition, laboratory-supported diagnostic methods can significantly reduce the number of misdiagnosis or delayed diagnosis patients. Finally, DHS has been eliminated by pre-screening for *HLA-B*13:01* in China.

In 2016, the WHO carried out "The Global Leprosy Strategy 2016–2020: accelerating towards a leprosy-free world", and significant strides have been made in China for controlling leprosy. However, more than 20 countries are still considered high-burden countries for leprosy. In order to share new clinical and research progress with other countries that are facing challenges for leprosy control, the First International Training Program on Leprosy For Developing Countries was held in China from June 23 to July 7, 2019. The training program was funded by the Ministry of Science and Technology (MOST) of China and organized by SPIDV. In this two-week program, 22 trainees from 10 countries with high-leprosy burdens were trained and received certification from the MOST of China. The aim of the training course was to improve the capacities of leprosy control institutions and for individuals to recognize early symptoms and provide technical assistance for leprosy prevention, diagnosis, and treatment. The collaborative platform has been established and further efforts can be collected to continue progress towards a leprosy-free world.

The findings above are subject to some limitations. First, samples involved in the genetic studies were all from Chinese participants. The efficacy of the risk model based on genetic variants should be tested via clinic and the model's ability to be extended to other countries needs to be investigated because of population heterogeneity. Second, more studies should be done to evaluate the diagnostic approaches mentioned before using these methods in routine clinical practice. Third, the allele frequency of *HLA-B*13:01* differs between populations. Moreover, for some *HLA-B*13:01* carriers, dapsone has been removed from the MDT regimen to prevent DHS. The modified MDT regimen with only two drugs, rifampicin and clofazimine, needs to be investigated for possible increased relapse risk of the disease and risk of failed treatment. Therefore, many barriers still exist in achieving global elimination of leprosy.

In conclusion, China has made significant progress in controlling leprosy, and more international cooperation between China and other countries would accelerate leprosy elimination. Efforts to achieve zero disability, zero death, and zero discrimination in leprosy nationwide need to be sustained.

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Vital Surveillances

Different Starting Dominant Strain of Seasonal Influenza in China and Other Neighboring Asian Countries in 2019–2020 Winter Season

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Abstract

Introduction: Seasonal influenza is a prevalent and highly contagious acute respiratory disease that causes a major global disease burden. New strains of influenza viruses also have the potential to cause an influenza pandemic. Due to the high variability and the consequent uncertainty about virus strains, the prevention and control of influenza are faced with many challenges. Surveillance is considered a key strategy to lead to the prevention and control of influenza, and influenza is one of first infectious diseases to be monitored globally.

Methods: The Chinese National Influenza Surveillance Network conducts routine influenza surveillance and includes 410 network laboratories and 554 sentinel hospitals based on the requirements of National Influenza Surveillance Guidelines. China and other countries submit epidemiological and virological data to the WHO FluMart database, which can be viewed online.

Results: Seasonal influenza H3N2 virus was the dominant subtype in China when entering the 2019–2020 winter influenza season, while neighboring countries such as Japan and Republic of Korea reported the dominance of H1N1pdm09 and Mongolia and Russia reported a higher proportion of type B virus than type A virus.

Conclusions and Implications for Public Health Practice: Asian countries entered the 2019–2020 winter influenza season with different type/subtypes of influenza virus dominant in different areas. Influenza surveillance needs to be strengthened to closely monitor changes in the antigenicity and genetic characteristics of emerging viruses.

Introduction

The high variability and the consequent uncertainty about influenza virus lead to the establishment of influenza surveillance network globally. The Chinese National Influenza Surveillance Network is an early detection system for influenza and for a few other emerging global infectious diseases. The construction of the influenza surveillance network has prepared technical and expert teams at the provincial and city level to respond to emerging infectious diseases, especially those resulting from respiratory viruses. Countries submit epidemiological and virological data to the World Health Organization (WHO) FluMart database, which can be viewed through FluNet of the WHO. In this study, the influenza activity in China and Asian countries in the 2019–2020 winter season was analyzed, and the results showed that seasonal influenza H3N2 virus was the dominant subtype in China, H1N1pdm09 dominated in Japan and Republic of Korea, and more type B virus were detected than type A virus in Mongolia and Russia. This suggests that different countries and areas may face very different disease burdens. Surveillance as well as information exchange among countries and regions are essential to closely monitor changes of the emerging viruses.

Methods

All 554 sentinel hospitals in the Chinese National Influenza Surveillance Network report information on influenza-like illness (ILI) cases to Chinese National Influenza Surveillance Information System (CNISIS) and collect respiratory samples within three days of onset, including throat swabs, nasal swabs, etc. of ILI cases (those whose body temperature is ≥38 ℃ with sore throat or cough). These samples are then transported to the 410 National Influenza Surveillance Network Laboratories. Network laboratories determine whether the sample is influenza virus positive as well as its type and subtype using real-time reverse transcription polymerase chain reaction (RT-PCR) test. Laboratory test results were summitted to CNISIS

and WHO FluMart. Virological surveillance data of neighboring countries were downloaded from WHO FluNet (https://www.who.int/influenza/gisrs_laboratory/flunet/en/).

Results

The positive rate of influenza virus in samples collected from ILI cases in China increased in the southern provinces since Week 40 and increased in northern provinces beginning around Week 42. As of Week 52 (from December 23 to 29, 2019), influenza activity is still increasing. During Week 52, influenza network laboratories tested 10,493 specimens, of which 4,707 (44.9%) were positive for influenza, and the total identified influenza A and influenza B viruses were 3,628 (77.1%) and 1,079 (22.9%), respectively. During Week 52, the percentage of specimens that tested positive for influenza in Southern China was 46.3% (2,299/4,965), which was higher than that of the previous week 40.2% (2,025/5,034), and the percentage of specimens that tested positive for influenza in Northern China was 43.6% (2,408/5,528), which was also higher than that of the previous week 38.5% (2,030/5,266) (Figure 1A and B).

Since Week 40 of 2019, H3N2 has been the dominant virus in China (Figure 2) with the proportion of H3N2 virus among all influenza viruses tested increasing from 48.5% to as high as 75.0% in Week 50. The H3N2 virus accounted for 94.5% of all type A influenza viruses in Week 52, the highest proportion since Week 40. H3N2 has not been the dominant subtype in China since mid-2017 (Figure 1A and B). However, in countries neighboring China, influenza types and subtypes have been highly variable since the beginning of the winter influenza season in late 2019 in the northern hemisphere. Among the neighboring countries that have detected more than 150 influenza viruses and reported to WHO FluNet from Week 40 to Week 52, H1N1pdm09 virus was dominant in Japan and Republic of Korea, H3N2 was dominant in India and Laos, and influenza B in

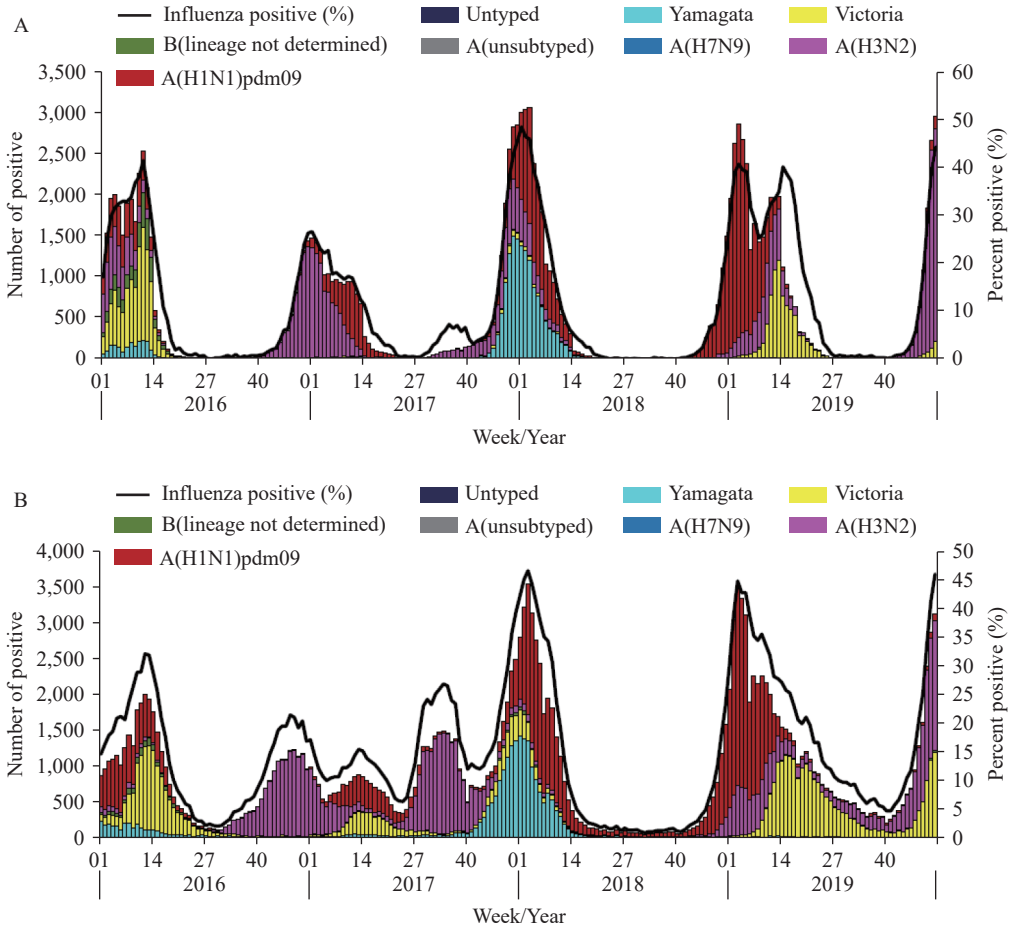

FIGURE 1. Influenza positive tests reported by network laboratories in north (A) and south (B) China.

Mongolia and Russia was more frequently detected than influenza A with the proportion of type B influenza estimated at 80.7% (71/88) in Mongolia and 77.2% in Russia in Week 52. Figure 3 illustrates the variable proportion of different types and subtypes of influenza virus since October 2019.

The Chinese National Influenza Center further tested the antigenicity of circulating influenza viruses in China. Twenty-four A(H1N1)pdm09 viruses collected since September 1, 2019 were antigenically analyzed with haemagglutinin inhibition (HI) tests, and 87.5% (21/24) viruses (21/24) were well inhibited by ferret antisera raised against the vaccine virus egg-propagated A/Brisbane/02/2018(H1N1), which was the vaccine virus. All tested viruses (24/24) were well inhibited by ferret antisera raised against MDCK-propagated A/Brisbane/02/2018(H1N1). A total of 111 A(H3N2) viruses collected since September 1, 2019 were antigenically analyzed with HI tests using guinea pig red blood cells (RBCs) in the presence of oseltamivir, 9% of the viruses (10/111) were well inhibited by ferret antisera raised against egg-propagated vaccine virus A/Kansas/14/2017(H3N2), and 18.0% viruses (20/111) were well inhibited by ferret antisera raised against MDCK-SIAT1 cell propagated A/Kansas/14/2017(H3N2). Fifty-seven B-Victoria lineage viruses collected since September 1, 2019 were antigenically analyzed, 19.3% viruses (11/57) were well inhibited by ferret antisera raised against egg-propagated B/Colorado/06/2017, the vaccine strain virus, and all tested viruses (57/57) were well inhibited by ferret antisera raised against MDCK

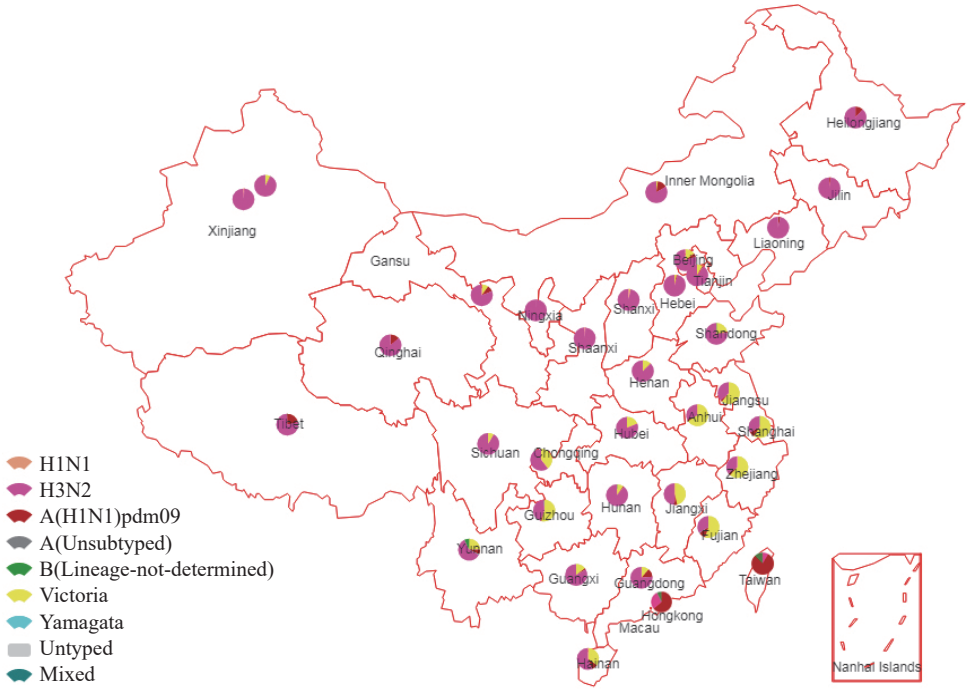

FIGURE 2. The proportion of different types and subtypes of influenza virus in China.

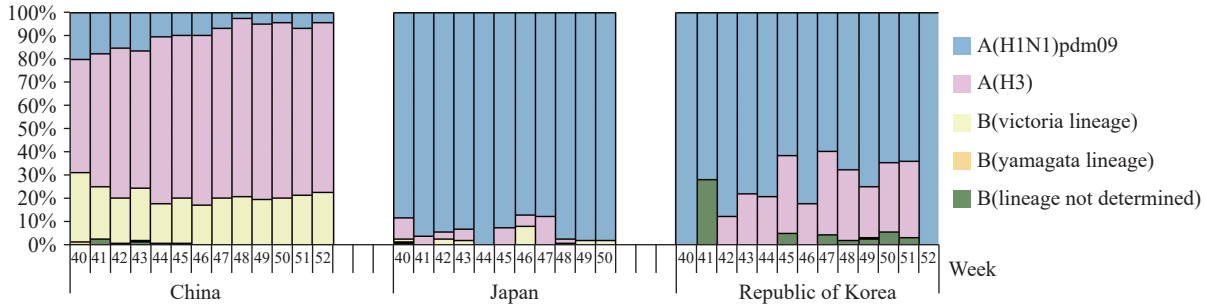

FIGURE 3. The proportion of different types and subtypes of influenza virus in China, Japan and Republic of Korea since October 2019.

grown B/Colorado/06/2017. No B-Yamagata lineage viruses have been isolated since September 2019.

Conclusions and Commentary

Although great progress has been made since the discover of influenza virus in 1933, technical bottlenecks in the prevention and control of influenza in the world remain, as influenza viruses are highly variable (*1*). Influenza still causes regular epidemics involving 290,000 to 650,000 deaths each year (*2*), and has great repercussions for human health. When a new influenza virus appears, the general lack of immunity in the population can lead to an influenza pandemic (*3*–*4*). Both preventing the occurrence of an influenza pandemic and predicting which virus will cause the pandemic are still not possible (*5*). Therefore, an effective strategy that can be adopted is to establish a powerful influenza surveillance network to track variations observed in influenza viruses in real time, which can lead to an earlier warnings for influenza epidemics or pandemics.

The Chinese National Influenza Surveillance Network is one of the earliest detection systems for emerging infectious diseases worldwide. It helps improve the capacity of public health systems for the prevention, control, and early warning of emerging influenza-associated infectious diseases. Currently, the influenza surveillance network includes 410 network laboratories and 554 sentinel hospitals, which follow the requirements of National Influenza Surveillance Guideline. As of 2019, 99.6% of the sentinel hospitals are able to report surveillance data every week, and 96.6% of the network laboratories have the capacity to perform real-time PCR testing and virus isolation. With this surveillance network, data can be obtained promptly for risk assessment and earlier warnings of coming influenza epidemics.

With the increasing movement of people around the world, the influenza virus will rapidly spread to various countries and regions. WHO FluNet is a global web-based tool for influenza virological surveillance first launched in 1997 by the WHO, and the virological data entered into WHO FluNet are critical for tracking the movement of viruses globally and interpreting epidemiological data (https://www.who.int/influenza/gisrs_laboratory/flunet/en/). Country-level data are publicly available and updated weekly.

In this study, we compared the surveillance data of China with data of neighboring countries available on WHO FluNet. Countries and regions were shown not to have the same dominant influenza strains, even for countries at the same latitude or in close proximity. Because vaccines show different levels of effectiveness against different influenza strains (*6*–*8*), the results of this study suggest that different countries and areas may face widely varying disease burdens. Many factors may explain the differing predominant epidemic strains in the countries such as varying immunity levels for different influenza type/subtype in each population, previous dominant epidemic strains, and even climate and environmental factors. The limitation of this study is that it is not yet clear which one is the determining factor. The proportions of different types and subtypes of influenza viruses as well as its genetic and antigenic characterization are constantly changing and continuing to improve the timeliness of surveillance is essential for detecting unusual epidemics promptly.

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Notes from the Field

A Novel Coronavirus Genome Identified in a Cluster of Pneumonia Cases — Wuhan, China 2019–2020

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Emerging and re-emerging pathogens are great challenges to the public health (*1*). A cluster of pneumonia cases with an unknown cause occurred in Wuhan starting on December 21, 2019. As of January 20, 2020, a total of 201 cases of pneumonia in China have been confirmed. A team of professionals from the National Health Commission and China CDC conducted epidemiological and etiological investigations. On January 3, 2020, the first complete genome of the novel β genus coronaviruses (2019-nCoVs) was identified in samples of bronchoalveolar lavage fluid (BALF) from a patient from Wuhan by scientists of the National Institute of Viral Disease Control and Prevention (IVDC) through a combination of Sanger sequencing, Illumina sequencing, and nanopore sequencing. Three distinct strains have been identified, the virus has been designated as 2019-nCoV, and the disease has been subsequently named novel coronavirus-infected pneumonia (NCIP).

Phylogenetic analysis was conducted to determine the relationship between 2019-nCoVs and other

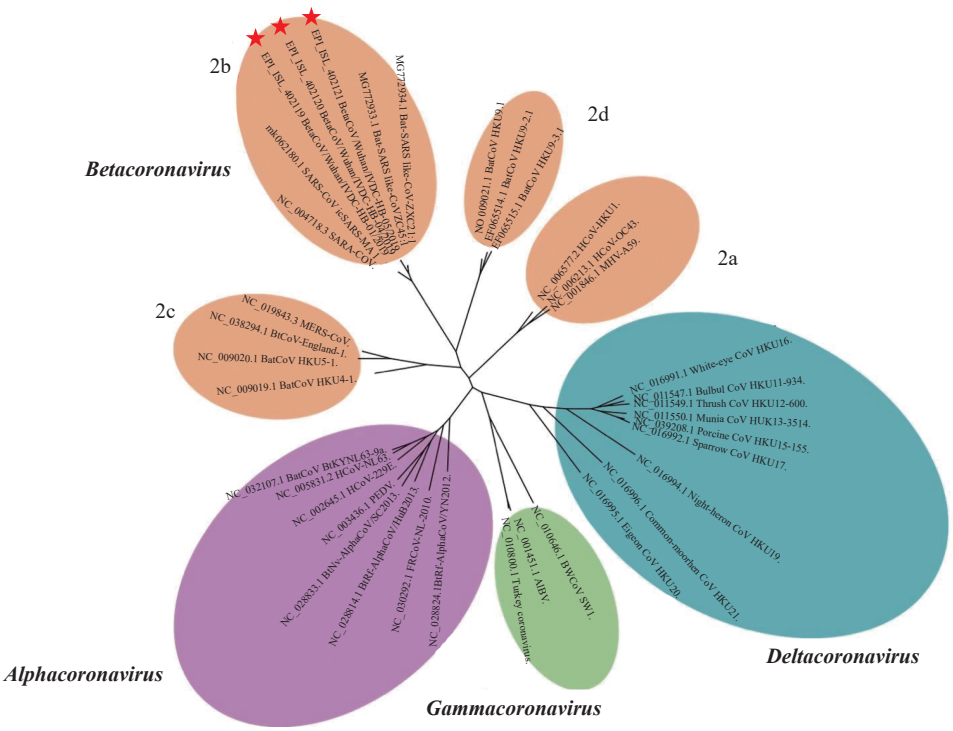

FIGURE 1. Phylogenetic relationships between the genomes of the new types of *Betacoronavirus* and other *Orthocoronavirinae* genomes. The viruses in the subfamily *Orthocoronavirinae* were classified into four genera (prototype or Refseq strains shown): *Alphacoronavirus* (purple), *Betacoronavirus* (orange), *Gammacoronavirus* (green), and *Deltacoronavirus* (blue). Classic subgroup clusters for the *Betacoronavirus* were labelled 2a–2d. The tree was based on complete genomes shown above using the maximum likelihood method under the GTR + I + Γ model of nucleotide substitution as implemented in PhyML. The new types of *Betacoronavirus*, labelled with red stars, were placed into the lineage of *Betacoronavirus* 2b, which contain the following: avian infectious bronchitis virus (AIBV), Middle East respiratory syndrome coronavirus (MERS-CoV), mouse hepatitis virus (MHV), porcine enteric diarrhea virus (PEDV), severe acute respiratory syndrome coronavirus (SARS-CoV), SARS-related coronavirus (SARSr-CoV), and Human coronavirus (HCoV).

sequences under the *Orthocoronavirinae* subfamily using MAFFT v7.455 (Figure 1) (*2*), and maximum likelihood inference was calculated using PhyML v3.3 (*3*), employing the GTR + I + Γ model of nucleotide substitution, and 1,000 bootstrap replicates. The 2019-nCoVs have features typical of the coronavirus family and were placed in the *Betacoronavirus* 2b lineage. Alignment of these strains' full genomes and other available genomes of *Betacoronavirus* showed the closest relationship with Bat SARS-like coronavirus isolate bat-SL-CoVZC45 (Accession Number: MG772933.1) (Identity 87.99%). The typical crown-like particles of the 2019-nCoVs can be observed under transmission electron microscope (TEM) with negative staining (www.gisaid.org). The origin of the 2019-nCoVs is still being investigated. However, all current evidence points to wild animals sold illegally in the Huanan Seafood Wholesale Market.

Several complete genome sequences of 2019-nCoVs were successfully obtained and released recently via www.gisaid.org to provide a first look at the molecular characteristics of this emerging pathogen, and all related information has also been reported to the World Health Organization (WHO). Several rapid and sensitive detection tests have been developed by China CDC and will be applied to the prevention and control of this 2019-nCoV outbreak.

Data availability. The new *Betacoronavirus* genome sequence has been deposited in GISAID (www.gisaid.org) under the accession number EPI_ISL_402119, EPI_ISL_ 402020 and EPI_ISL_402121.

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