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Outbreak Reports

Five Independent Cases of Human Infection with Avian Influenza H5N6 — Sichuan Province, China, 2021

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Summary

What is known about this topic?

The emerging H5Ny lineages of the avian influenza virus (AIV) with genomic reassortments have posed a continuous threat to animals and human beings. Since the first case of avian influenza A (H5N6) virus infection in 2014, the World Health Organization has reported a total of 38 cases by August 6, 2021.

What is added by this report?

A total of 5 new cases of H5N6 that occurred from May 2021 to July 2021 in Sichuan Province, China were reported in this study. Epidemiological and laboratory information of the five cases were investigated. The genomic analysis of the H5N6 genomes showed the features of AIV genomic reassortments and key residue substitutions.

What are the implications for public health practice?

The emergence of human cases infected by AIV H5Ny lineages through time demonstrates a risk of the persistence and evolution of the virus to trigger sporadic outbreaks and even pandemics, which need continuous surveillance.

As a highly contagious virus, the avian influenza virus (AIV) circulates among birds as its reservoir host (1). The spillover to human beings and other animal species occurs frequently, leading to cross-species infection that may trigger mild outbreaks and even pandemics (2). In recent years, AIV H5Ny lineages (i.e., H5N1, H5N2, H5N6, and H5N8) have proved the capacity for zoonotic spread and genomic reassortments amongst this viral group and thus pose a severe threat to animals and human beings (3–4). Among these AIVs, H5N6 was first detected in 1975 (5), and the first reported case of human infection with a novel H5N6 was dated in 2014 (6–7). By August 2021, the World Health Organization (WHO) reported a total of 38 laboratory-confirmed cases of human infection with influenza A(H5N6) virus,

including 21 deaths. This year, 10 sporadic human infections have been recorded in Sichuan Province, Anhui Province, Guangxi Zhuang Autonomous Region, and Chongqing Municipality (8).

INVESTIGATION AND RESULTS

Herein, we report the 5 cases infected by AIV H5N6 in Sichuan Province, China in 2021. These 5 independent cases occurred in 5 different districts or counties from 4 cities (Figure 1A, i.e., Jinjiang District of Chengdu City, Kaijiang County and Xuanhan County of Dazhou City, Bazhou District of Bazhong City, and Nanxi District of Yibin City). All four cities are located in the east of Sichuan Province, China (Figure 1A). A case was sampled by nasopharyngeal swabs and sent to the laboratory for quantitative polymerase chain reaction (qPCR) testing. The positive results will be sequenced and sent to China CDC for virus isolation. When a case was found, the local CDC and the municipal and/or provincial CDCs form two or three levels of investigation groups to carry out the epidemiological investigation of avian influenza cases. The timeline and investigation group for each case were shown in Table 1.

Patient 1 in Jinjiang District of Chengdu City was a 49-year-old (y) female who developed headache and nasal stuffiness on May 13. On May 26, the respiratory tract sample was tested for influenza viruses in Huaxi Hospital and was found to be H5N6 influenza virus positive, and on the next day, Chengdu Municipal CDC and Sichuan Provincial CDC confirmed the laboratory test as positive for H5N6 (Figure 1B and Table 1). The patient (Patient 2) from Kaijiang County of Dazhou City, who was a 57y male, had symptom onset on June 22 with cough and asthma. The patient was laboratory confirmed as H5N6 infection by Sichuan CDC on July 8. Patient 3 was a 51y female, from Xuanhan County of Dazhou City, that had a headache on June 25. Through qPCR testing of alveolar lavage fluid specimens, the case was laboratory diagnosed as H5N6 infection by Sichuan

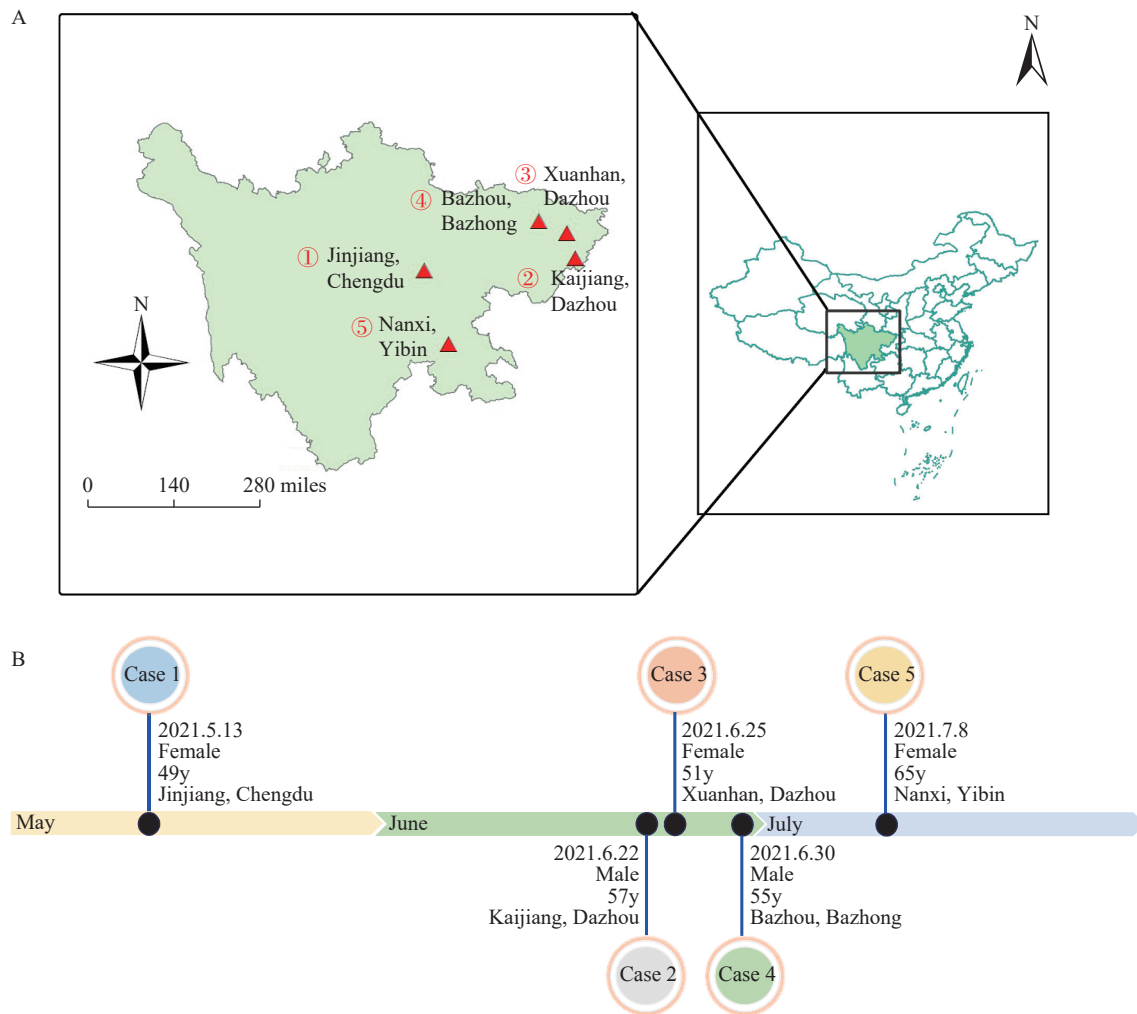


FIGURE 1. Temporal and spatial distribution of human infections with avian influenza A(H5N6) viruses in Sichuan Province, China, May to July 2021. (A) Geographical distribution of H5N6 virus infection among humans*; (B) The timeline and the basic demographic information of the H5N6 human cases.

Abbreviation: y=years old.

* The sequence number of case-patients in place is based on the disease onset date.

CDC on July 7. Patient 4 was a 55y male in Bazhou District of Bazhong City. He developed initial symptoms of fever on June 30 and was laboratory confirmed as H5N6 infection on July 6. Patient 5, female, 65y, from Nanxi District of Yibin City had symptom onset on July 8. The pharyngeal swab from Patient 5 was laboratory tested as H5N6 positive on July 20.

The epidemiological investigation found that all 5 patients had been exposed to live poultry before their disease onset (Table 1). Patient 1 bought duck from a poultry market on May 5, i.e., 8 days before the symptom onset. Patients 2, 3, 4, and 5 lived in rural areas and raised chickens, ducks, and geese in their backyard for self-consumption. Patients 2 and 3 had visited the live poultry markets (LPMs) and purchased

baby poult before symptom onset. Patients 4 and 5 had no history of visiting LPMs 4 weeks before their illness onset. The poultry farmed by Patient 5 were usually sent to the adjacent pond for breeding where wild birds (predominantly, white cranes) were frequently observed. There were dead poultry that were farmed by Patients 2, 3, 4, and 5, and they had contact with or ate these dead poultry before their symptom onset (Table 1).

In light of laboratory testing of samples collected from the poultry market contacted by Patient 1, H5N6 were qPCR detected positive. The poultry feeding settings of Patient 2–5 were tested, with positive results in the environment samples related to all four patients (Supplementary Table S1, available in <http://weekly.chinacdc.cn/>).

All five patients had a history of contact with birds, so the following measures were taken. 1) Ten days of health monitoring was implemented of close contacts and possible exposed personnel of all patients. 2) Poultry and environmental disposal were carried out in affected areas. The patients' families and the patients' neighbors' families carried out poultry culling and disposal, and thoroughly disinfected bird-related environments. 3) Strengthened management of poultry breeding sites and live poultry trading markets. This involved comprehensive rectification, cleaning, and disinfection of the live poultry trading market in the district and county. 4) Influenza-like illness (ILI) surveillance was strengthened in affected districts and counties. For outpatient and emergency patients who met the definition of ILI and patients with severe acute respiratory tract infection, the history of poultry exposure was inquired for and respiratory tract samples were collected for testing. During the strengthened surveillance period, the positive rate of ILI had a mild upward trend, but these ILI were all influenza B viruses. Influenza A viruses had not been isolated (except for one case of H9N2) in all of Sichuan Province, and there was no A (subtype not determined). 5) Strengthened health education by carrying out publicity and education on avian influenza prevention and control knowledge throughout the province, improving the disease prevention awareness of professional people, and reducing the risk of human infection with avian influenza virus.

The full genome of the virus from Patient 3 (A/Sichuan/06681/2021(H5N6), Dazhou/2021) and 6 gene segments except for PB2 and PA of the virus from Patient 4 (A/SiChuan-Bazhong/1/2021(H5N6), Bazhong/2021) were successfully sequenced. The nucleotide sequences similarity of 8 segments of Dazhou/2021 were analyzed with the online Basic Local Alignment Search Tool (BLAST) (Table 2), and the PB2 segment was found to have similarity with chicken H3N2 strain from Guangxi, China (96%) in 2014; PB1 and PA genes were 97%–98% similarity to that of H5N6 strains from poultry environment samples in Guangdong in 2017–2018 season. NA and NP segments were highly similarity to human infecting H5N6 strains from Anhui Province in 2020 (99%). The MP segment has a high similarity with chicken H5N8 strain from Kostroma, Russia in 2020 and the NS segment was highly similar to chicken H3N2 strain from Ganzhou, China in 2016. Interestingly, for strain Bazhong/2021 in our study, only the NS segment has a different closest strain i.e., H4N2 and H3N2 from

Jiangxi, China in 2016, compared to the NS of Dazhou/2021 (Table 2). The maximum likelihood (ML) phylogenies tree [root at A/Goose/Guangdong/1/96(H5N1)] was generated by RAxML (version 8.2) program (9). The genomes of Dazhou/2021 and Bazhong/2021 have a similarity >99% for all the 6 available segments. The molecular phylogenetic analysis showed that the HA genes of both Dazhou/2021 and Bazhong/2021 belong to the 2.3.4.4b and have the highest homology with A/chicken/Omsk/0112/2020 (A/H5N8) from Omsk Russia (Figure 2). The genomes of Dazhou/2021 and Bazhong/2021 have a similarity >99% for all the 6 available segments. The molecular phylogenetic analysis showed that the HA genes of both Dazhou/2021 and Bazhong/2021 belong to the 2.3.4.4b and have the highest homology with A/chicken/Omsk/0112/2020 (A/H5N8) from Omsk Russia (Figure 2).

The molecular characterization of the Dazhou/2021 and Bazhong/2021 strains were analyzed and related key sites in all H5N6 were analyzed at the same time (Supplementary Table S2, available in <http://weekly.chinacdc.cn/>). The cleavage site of HA protein possessed a multiple basic amino acids motif (LREKRRKR↓G), which indicated high pathogenicity to chickens. The amino acid of the NS1 protein of these 2 strains at position 92 was aspartic acid. However, most H5N6 strains (n=1,329) have the 92E mutation; this D92E mutation has been correlated with increased virulence and/or cytokine resistance (10). NA protein was deleted at the stalk region (position 59–69), and no oseltamivir-associated resistance mutations in amino acid residues were found. Host-specific related sites, such as receptor binding Q226L of HA fragment and E627K of PB2 fragment were not found, which indicated that both Dazhou/2021 and Bazhong/2021 strains still possess features of avian origin.

DISCUSSION

The AIV H5N6 was first reported as a low-pathogenic AIV (LPAIV) decades ago (5). Since the strain a/gs/gd/1/96 (H5N1) appeared in the 1990s, outbreaks of highly pathogenic AIV (HPAI) have occurred frequently. Before 2010 there was no evidence of reassortment of the H5N1 viruses with NA subtypes other than N1 (11). However, H5 reassorted with different specific NA subtypes, termed H5N2, H5N3, H5N5, H5N6, H5N8 after 2010 (12). These

TABLE 1. Demography and epidemiological profiles of the 5 cases in Sichuan.

Case No.	Region	Age of case/years old	Date of onset	Date of hospitalization	Date of laboratory confirmation	Date of visited LPM	Contact with dead poultry	Consumption of dead poultry	Date of used Tamiflu	Outcome	Date of Investigation	Investigation group
1	Jinjiang, Chengdu	49	2021-05-13	2021-05-16	2021-05-26	2021-05-05	Unknown	No	2021-05-27	Death	2021-05-26	Sichuan, Chengdu and Jinjiang CDC
2	Kaijiang, Dazhou	57	2021-06-22	2021-07-05	2021-07-08	2021-06-13	Yes	Yes	2021-07-08	Death	2021-07-08	Sichuan, Dazhou and Kaijiang CDC
3	Xuanhan, Dazhou	51	2021-06-25	2021-07-02	2021-07-07	2021-06-04	Yes	Unknown	Not used	Death	2021-07-06	Sichuan, Dazhou and Xuanhan CDC
4	Bazhou, Bazhong	55	2021-06-30	2021-07-04	2021-07-06	Unknown	Yes	No	2021-07-05	Recovered	2021-07-05	Sichuan, Bazhong and Bazhou CDC
5	Nanxi, Yibin	65	2021-07-08	2021-07-13	2021-07-20	Unknown	Yes	Yes	2021-07-19	Recovered	2021-07-18	Yibin and Nanxi CDC

Abbreviation: LPM=live poultry market.

TABLE 2. Similarity of 8 segments of the viruses analyzed by online basic local alignment search tool.

Segments	Bazhong/2021 Identity/Length (%)	Dazhou/2021 Identity/Length (%)	Collection location
PB2	No sequence detected	A/chicken/Guangxi/165C7/2014 (A/H3N2) 2,263/2,342 (96%)	Guangxi, China
PB1	A/Env/Guangdong/zhanjiang/C18277136/2018-04-02 (A/H5N6) 2,304/2,344 (98%)	A/Env/Guangdong/zhanjiang/C18277136/2018-04-02 (A/H5N6) 2,310/2,345 (98%)	Guangdong, China
PA	No sequence detected	A/Env/Guangdong/zhanjiang/C17277346/2017-12-05 (A/H5N6) 2,184/2,233 (97%)	Guangdong, China
HA	A/chicken/Omsk/0112/2020 (A/H5N8) 1,766/1,776 (99%)	A/chicken/Omsk/0112/2020 (A/H5N8) 1,760/1,772 (99%)	Omsk, Russia
NP	A/Anhui/2021-00011/2020 (A/H5N6) 1,552/1,565 (99%)	A/Anhui/2021-00011/2020 (A/H5N6) 1,555/1,564 (99%)	Anhui, China
NA	A/Anhui/2021-00011/2020 (A/H5N6) 1,422/1,432 (99%)	A/Anhui/2021-00011/2020 (A/H5N6) 1,423/1,431 (99%)	Anhui, China
MP	A/chicken/Kostroma/304-10/2020 (A/H5N8) 1,025/1,027 (99%)	A/chicken/Kostroma/304-10/2020 (A/H5N8) 1,026/1,027 (99%)	Kostroma, Russia
NS	A/Environment/Jiangxi/47054/2016 (A/H4N2) 870/891 (97%)	A/chicken/Ganzhou/GZ43/2016 (A/H3N2) 873/890 (98%)	Jiangxi, China

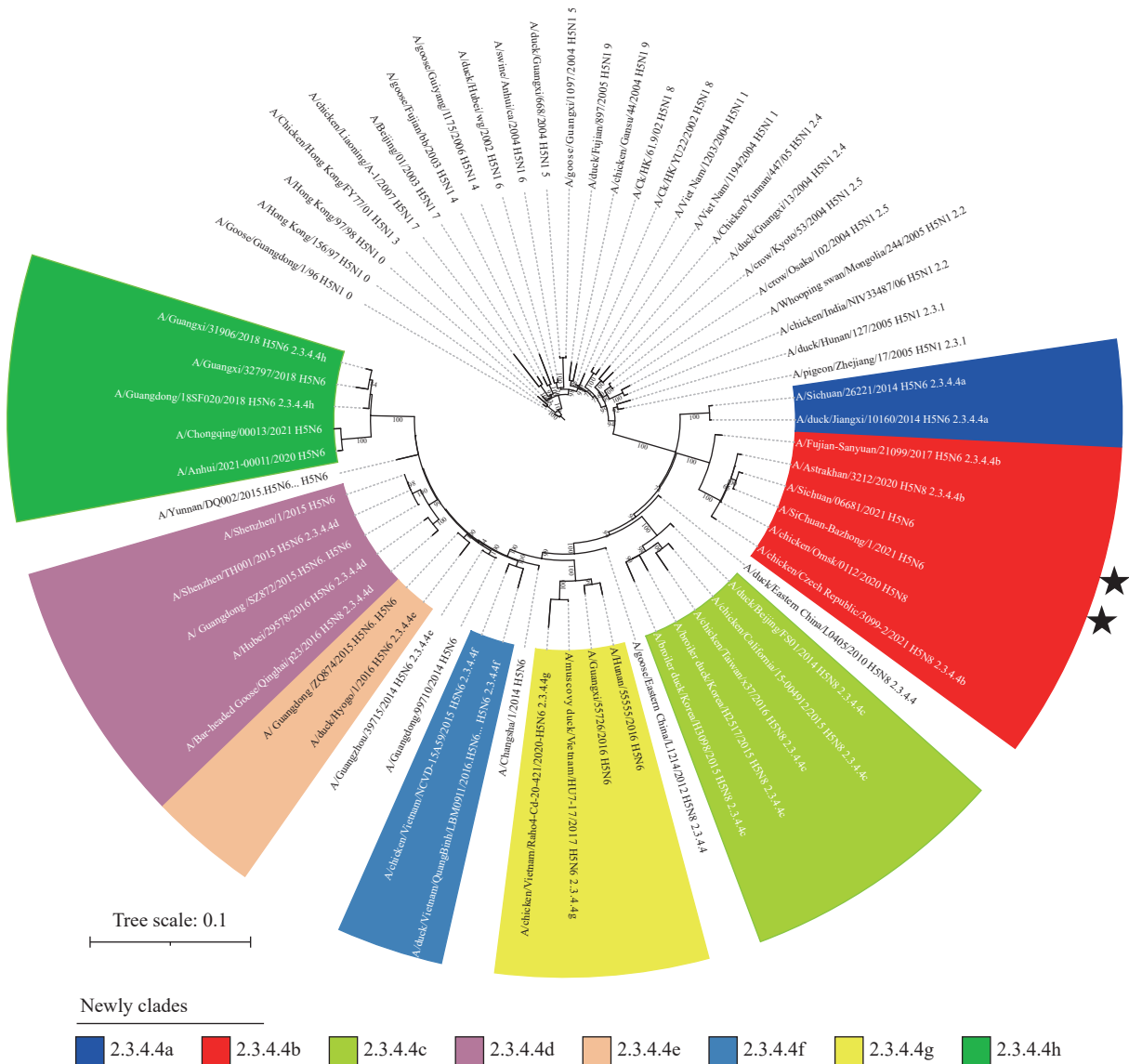


FIGURE 2. Maximum likelihood phylogenetic relationships of H5 viruses' hemagglutinin (HA) genes.

Note: Phylogenetic included most of H5 clades (names were showed at leaves tip) and rooted to A/Goose/Guangdong/1/96(H5N1), constructed with 1,000 bootstrap replicates (above branches). The two stars indicate the strains of this study.

new virus subtypes emerged through multiple genetic reassortments of different subtype viruses within resident domestic and wild bird populations and continued to circulate in domestic poultry populations, leading to wider geographical spread and raising great concern based on their pandemic potential (13). With the cross-infection of wild birds and poultry, the epidemic of viruses in poultry has accelerated. To date, a total of 38 laboratory-confirmed cases of human infection with influenza A (H5N6) virus, including 21 deaths. Our study found that all the 5 patients had been exposed to live poultry before their disease onset. Given this, more research, enhanced surveillance,

including genomic epidemiology, is necessary on wild birds, poultry, and the environment.

The novel clade 2.3.4.4 H5N6 that was first reported in 2013, then reported in Laos and Vietnam in 2014/2015, with evidence of sustained transmission and further geographical spread in both countries. Later on, a series of poultry outbreaks in Japan, Myanmar, and the Republic of Korea have been found to be related by H5N6. By 2017, it began spreading to some European countries such as Greece, Germany, the Netherlands, and Switzerland (14). Due to the genetic diversity of the virus, the World Health Organization (WHO) subdivided 2.3.4.4 into a–h

clades, a total of 8 new clades. Even if it is so finely divided, recent serological studies have found that the vaccine strains recommended by WHO cannot fully cover the emerging strains in these clades (15). Thus, the balance between viral evolution and the capacity of the candidate vaccine protection needs to be timely updated which will reduce infection events and mortality in humans and animals.

Fortunately, there is no evidence of sustainable human-to-human transmission of H5N6, considering that all cases in this study were independent and have no epidemiological correlation. A one-health approach needs to be strengthened to trace the source of infection in time, block the cross-species spread of the virus, reduce risks, and protect people's health.

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SUPPLEMENTARY TABLE S1. Poultry environment investigation and testing.

Case No.	Region	Source of poultry	Poultry species	Specify the upstream supplier	Poultry species of upstream supplier	qPCR of poultry environment	qPCR of upstream supplier environment	qPCR of living environment
1	Jinjiang, Chengdu	Market	Chicken, duck	Chenghua district market	Chicken, duck	+	+	+
2	Kaijiang, Dazhou	Domestic	Chicken, duck	Luo's chicken and duck farm	Chicken, duck	+	+	+
3	Xuanhan, Dazhou	Domestic	Chicken, duck	Yunchengzhai chicken farm	Chicken, duck	+	+	+
4	Bazhou, Bazhong	Domestic	Chicken, duck, goose	Not purchased in 2021	Not purchased in 2021	+	ND*	+
5	Nanxi, Yibin	Domestic	Chicken	Private vendors in Wangjia town	Chicken	+	ND	-

* ND: Not done.

SUPPLEMENTARY TABLE S2. The molecular characteristics of the H5N6 influenza viruses isolated from Sichuan Province.

Genes	AA position	Bazhong/2021	Dazhou/2021	All H5N6*	Phenotypic effect
HA	N158D	N	N	N 1803 S 5 D 4	The substitution at residue 158 leads to a loss of glycan chain modification in the 150-loop, which avoids the potential steric hindrance for binding human receptors.
				Q 1813	
				LRERRRKG 1388 LREKRRRKG 305 SRERRRKG 47 LKERRRKG 29 QRETRG 10 H 1744 Y 2 T 1648 V 37 M 4 I 1	
NA	H274Y	H	H		Reduces the susceptibility of neuraminidase inhibitors
PB2	T271A	T	T		Enhances viral replication in mammalian cells in vitro
NS1	Q591K	Q	Q	Q 1693 H 1 E 1673 K 18 V 2	Increases pathogenicity in mice Associates with increased virulence of AIVs in mammals
				D 1689 N 3	
				P 1681 L 367 E 1329 D 355 G 1	
M2	L26F, V27A, A30T, S31N, G34E	D	D	L-V-A-S-G 1455 L-V-A-N-G 165 L-A-A-S-G 16 L-I-A-S-G 10 L-G-A-N-G 6	Correlated with increased virulence and/or cytokine resistance Antiviral amantadine resistance
				L-V-A-S-G	
				L-V-A-S-G	

Note: Bold is consistent with the results of this study.
* Only show top 5, if the candidates are more than 5.

Preplanned Studies

Gender Differences in Familial Status, Socioeconomics, Functional Capacities and Wellbeing Among Oldest-Old Aged 80 Years and Above — China, 1998–2018

Yi Zeng^{1,2,#}

Summary

What is already known on this topic?

Little is known about gender differences in health, family, and socioeconomics among oldest-old in China,

What is added by this report?

This study aims to fill this knowledge gap through analyzing gender differences in familial status, socioeconomics, functional capacities, and self-reported wellbeing using the 1998, 2008–2009, and 2017–2018 waves of the Chinese Longitudinal Healthy Longevity Survey. We found that compared with the male oldest-old, the female oldest-old are seriously disadvantaged in familial status, socioeconomics, and capacities of activities of daily living, physical performances, cognitive function, and self-reported wellbeing.

What are the implications for public health practice?

We discussed possible contributing reasons for our findings and strongly suggest that the female oldest-old should be prioritized higher.

The numbers of oldest-old aged 80 years and above who will most likely need care in daily life and health services will climb from nearly 20 million in 2010 to about 120 million in 2050 in China (1). However, little is known about the oldest-old in most developing countries including China (Supplementary Materials, available in <http://weekly.chinacdc.cn/>). To fill in this knowledge gap for scientific studies and policymaking, this paper presents easily understandable analyses of gender differentials in familial status, socioeconomics, activities of daily living (ADL), physical performance, cognitive functions, self-reported health, and life satisfaction among the oldest-old aged 80 years and above in China. The definitions of the measurements of the activities of daily living, physical performance, self-reported health, and life satisfaction are described in “measurements of the health statuses” of Supplementary Materials.

The Chinese Longitudinal Healthy Longevity Study

(CLHLS) was conducted in 1998–2018 and purposefully over-sampled the oldest-old aged 80 years and above, plus a compatible sub-sample of younger-old aged 60–79. We use the datasets of oldest-old aged 80 years and above collected in 1998, 2008–2009, and 2017–2018 waves of CLHLS in the present study to perform meaningful comparative analyses on gender differences in the 3 periods (each roughly 10 years apart) from 1998 to 2018. The included sample sizes were 8,805 oldest-old in the 1998 wave, 12,281 oldest-old in the 2008–2009 wave, and 10,437 oldest-old in the 2017–2018 wave. *P* values vary among different 5-year-old age groups and periods. In total, there are 210 *P* values in Figures 1–4 that are available upon request to the author.

As shown in Figure 1A, the proportion of female oldest-old who were married was lower than their male counterparts. However, the overwhelming majority were widowed, especially the oldest-old women: 66%–98% of female oldest-old were widows, which was much higher than male oldest-old. The proportions of never-married and divorced male and female oldest-old were extremely low.

Figure 1B presented sex-age-specific percentage distributions of living with spouse and/or children (including children, grandchildren, and other family members), and those living alone. The overwhelming majority of Chinese oldest-old lived with spouses and/or children: 68%–90% for females, 80%–89% for males. Female oldest-old were less likely live with spouse/children up to ages 90–94, and the proportion of oldest-old women who lived alone were higher than the oldest-old men up to ages 90–94.

Figure 2A indicated that about 66%–93% of female oldest-old were illiterate with no schooling, in contrast to 29%–58% of their male counterparts. Many Chinese oldest-old women were found to be illiterate, and females were significantly disadvantaged.

Figure 2B indicated that percent of pension receivers among Chinese female oldest-old were much lower than their male counterparts. The majority of the

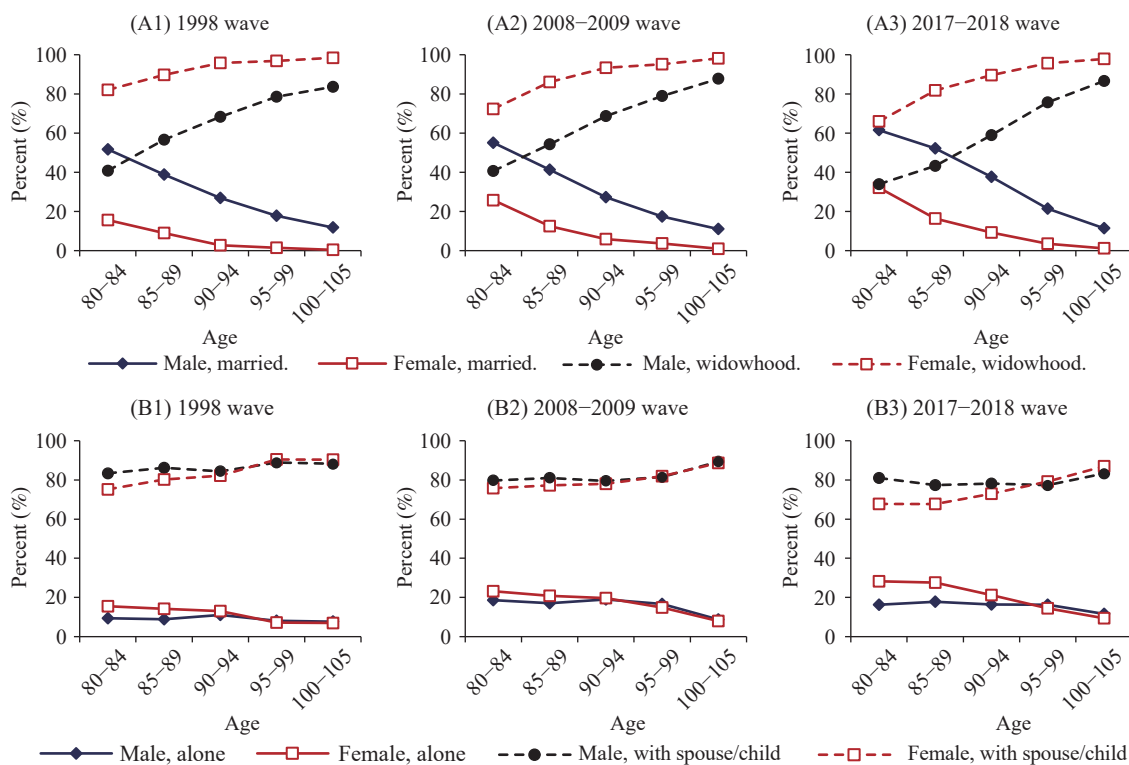


FIGURE 1. Gender differences in familial status among the oldest-old in China, 1998–2018. (A) Percentage of marital statuses among the oldest-old; (B) Percentage of living arrangements among the oldest-old.

Chinese oldest-old rely mainly on their children for financial support, and the gender differentials in primary source of financial supports were enormous: oldest-old women rely on their children much more than oldest-old men (Figure 2C).

About 48%–89% of oldest-old men's primary caregivers were their children, in contrast to 75%–92% of their female counterparts (Figure 2D). The female oldest-old in China relied more on their children as caregivers, as compared to male oldest-old whose primary caregivers were more likely their spouse. This was consistent with a much higher proportion of widowhood existing in female oldest-old than in male oldest-old. Children were often the primary resource of financial support of the oldest-old and also the primary resource of caregiving when the oldest-old were sick.

As shown in Figure 3A, percent of activities of ADL active status declined quickly after age 80, especially after age 85–89. The curve of females who were ADL active was substantially lower than the male curve after age 80–84. The oldest-old women were substantially less active than the oldest-old men in daily living.

Figure 3B indicated that about 80%–88% and 77%–85% of male and female oldest-old aged 80–85, respectively, could stand-up from a chair without using

their hands; but the percent decreased quickly after age 85–89. About 38%–53% male centenarians could stand-up from a chair without using their hands, compared to 27%–37% female centenarians. Female oldest-old persons' capacities to perform picking-up a book on the floor from standing position were significantly worse than their male counterparts (Figure 3C). Male oldest-old physically performed better than female oldest-old did, and the gender gap became larger after age 90–94.

Figure 3D demonstrates that percent of good cognitive function among the Chinese oldest-old declined quickly with increase of age. The Chinese female oldest-old persons' cognitive capacity was much worse than their male counterparts, and the gender gaps were remarkably large.

As shown in Figure 4A, about 40%–62% of the male oldest-old reported "good health" in contrast to the corresponding percentages of 34%–59% of the female oldest-old. The percentages of self-reported good health among Chinese oldest-old declined slightly from age 80–84 to age 100–105, and even slightly increased from ages 95–99 to ages 100–105 in 2008–2009 and 2017–2018, respectively among females at these very advanced ages. Such pattern of age variations differed from the age patterns of ADL,

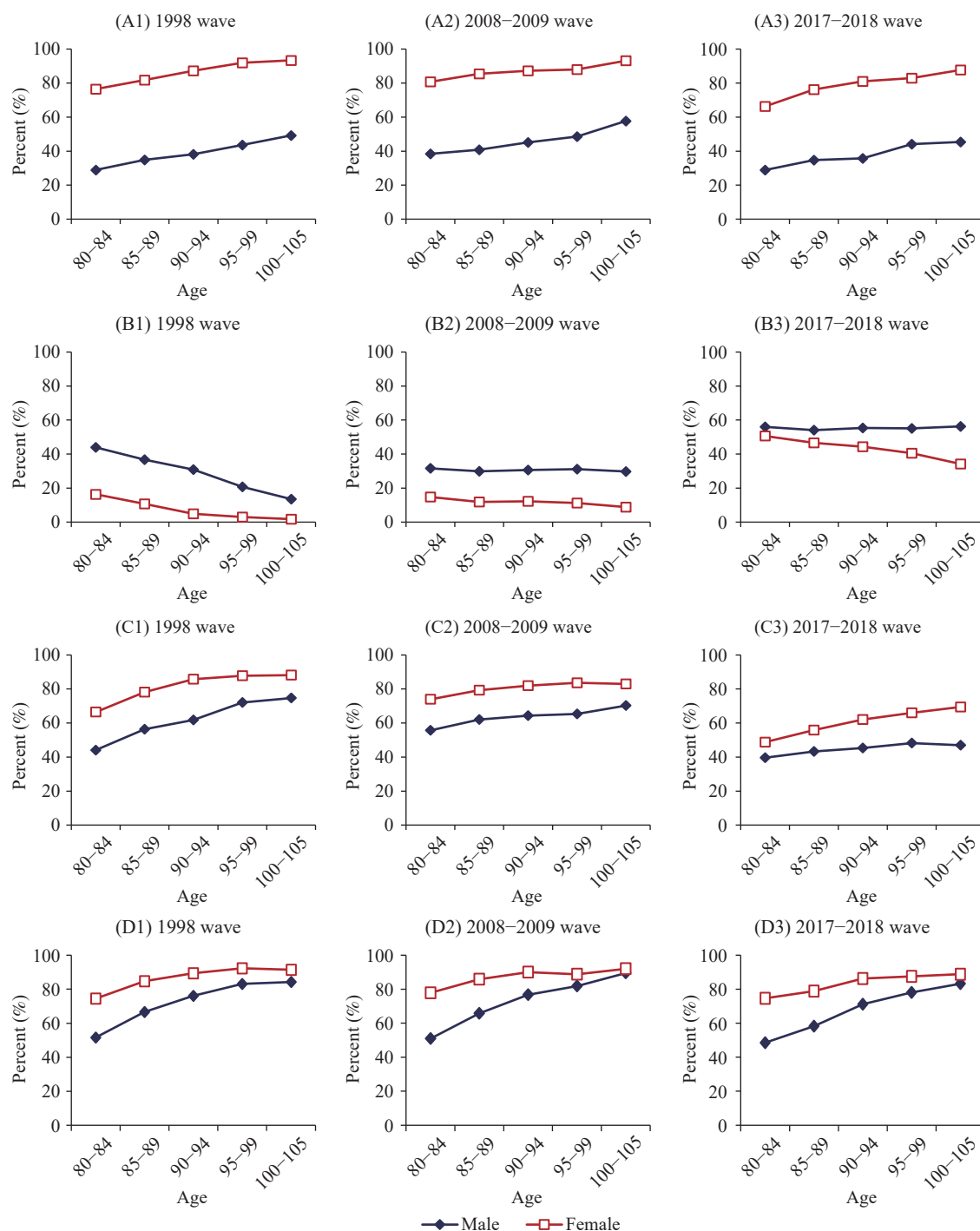


FIGURE 2. Gender differences in socioeconomic statuses among the oldest-old in China, 1998–2018. (A) Percent of illiterate among the oldest-old. (B) Percent of pension receivers among the oldest-old. (C) Percent of the oldest-old who mainly rely on children for financial support. (D) Percent of the oldest-old whose primary caregivers were children.

physical performance, and mini-mental state examination (MMSE). Figure 4D presented the results of self-reported good life satisfaction, which showed that gender differences in self-reporting good life satisfaction among Chinese oldest-old were mostly negligible in 1998, 2008–2009, and 2017–2018.

DISCUSSION

Populations of the oldest-old aged 80 years and over are growing extremely quickly in China and worldwide. Figures 1–4 demonstrated that female oldest-old were disadvantaged as compared to their

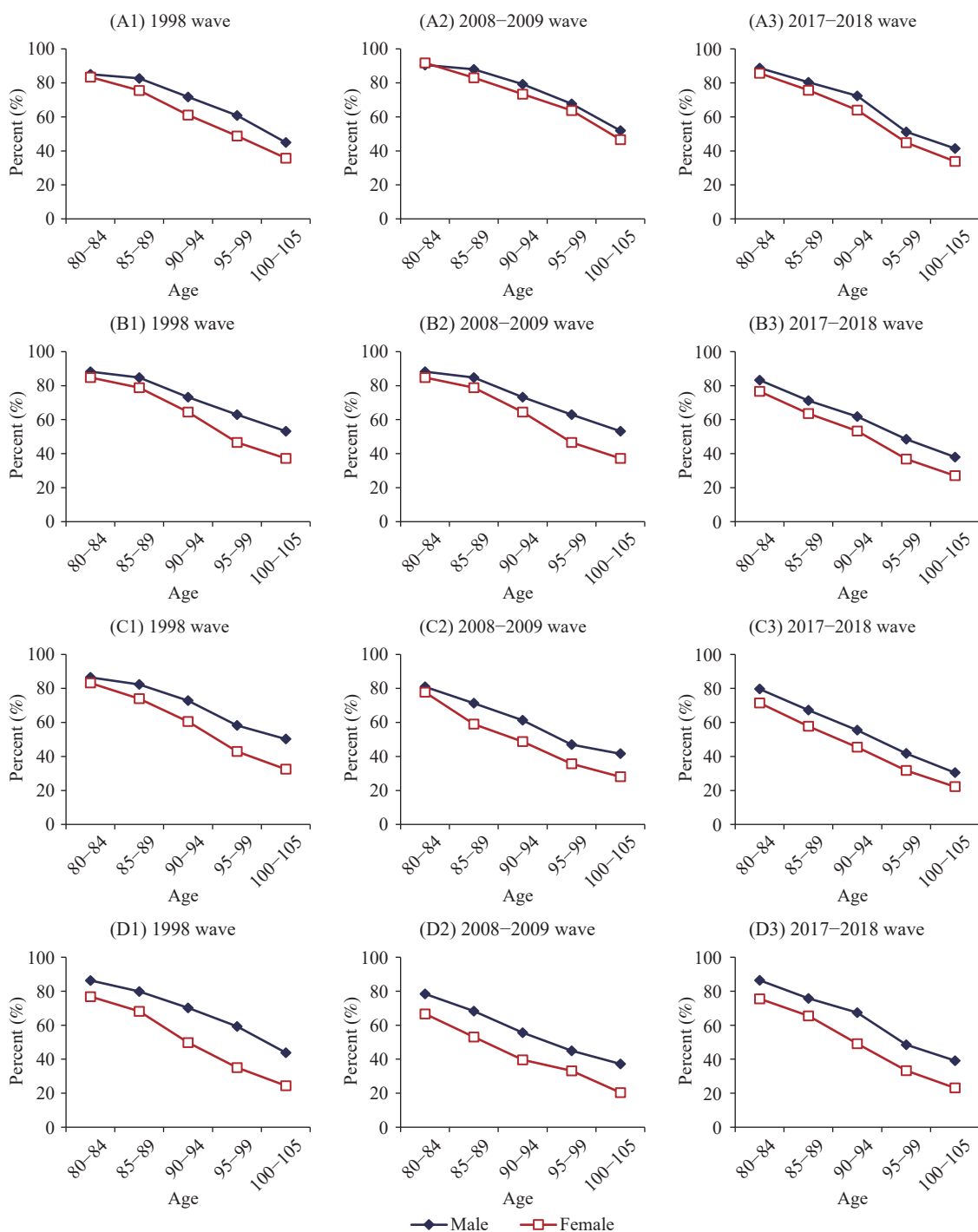


FIGURE 3. Gender differences in functional capacities among the oldest-old in China, 1998–2018. (A) Percent of the oldest-old who were active in activities of daily living (ADL). (B) Percent of the oldest-old who could stand-up from a chair without using their hands. (C) Percent of the oldest-old who could pick-up a book on the floor from standing position. (D) Percent of the oldest-old whose cognitive functional capacity is good.

male counterparts. Oldest-old women were much more likely to live alone as they have higher risk of losing husbands due to higher mortality rates in male oldest-old, while female widows have lower likelihood to remarry. Compared to male oldest-old, the proportion of pension receivers among female oldest-old was much

lower, and they were often less educated, economically more dependent, and more reliant on children for financial support and for care when sick.

Oldest-old women were more likely to be disabled in activities of daily living, physical performances, and cognitive function. Other studies in China (2–3) and

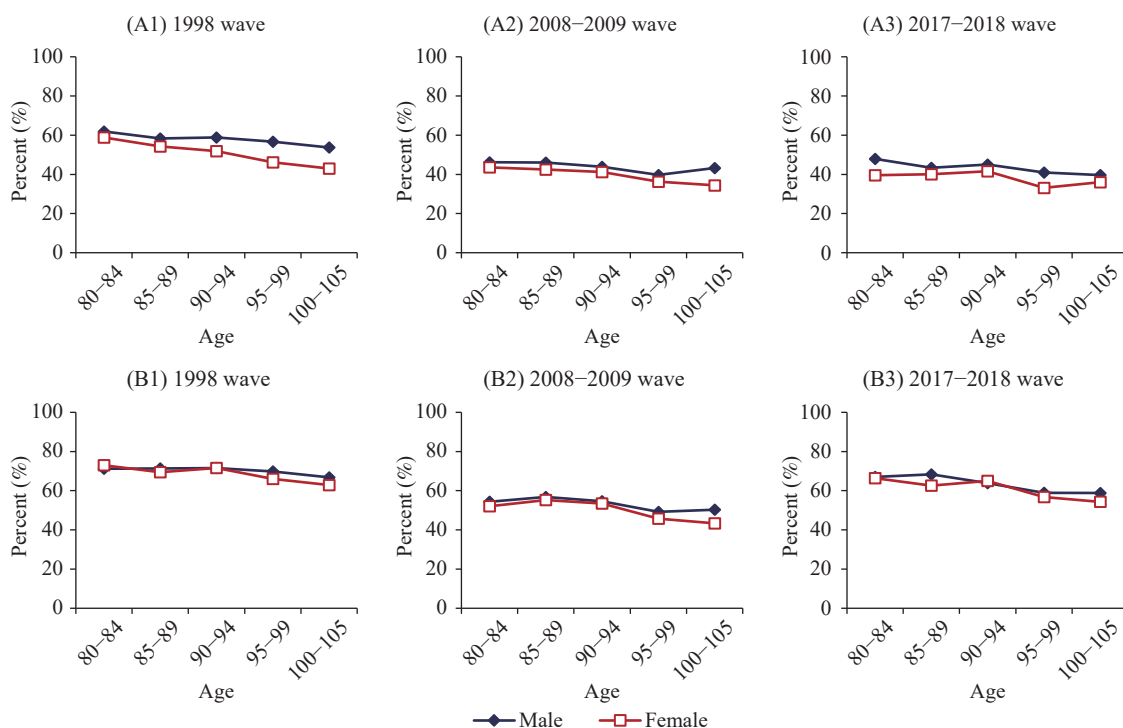


FIGURE 4. Gender differences in self-reported health and life satisfaction among the oldest-old in China, 1998–2018. (A) Percent of the oldest-old who self-reported “good health”. (B) Percent of the oldest-old who self-reported “good life satisfaction”.

elsewhere (4–5) also reported that elderly women were more disabled than men. Self-reported good health did not decline significantly with increase in age, which may be due to declining expectations of health with increasing age among the oldest-old in China and elsewhere (6). Furthermore, gender differences in self-reported life satisfaction among the Chinese oldest-old were mostly negligible as demonstrated in all of the datasets of CLHLS 1998, 2008–2009, and 2017–2018 waves (Figure 4B).

At the same time, however, the oldest-old Chinese women were seriously disadvantaged in marital status, living arrangements, education, pensions, financial resource, ADL, physical performance, and cognitive function as compared to their male counterparts (Figures 1–3). Female oldest-old were also disadvantaged (to a less serious degree) in self-reported health, as shown in Figure 4. Chinese oldest-old women may be more positive in facing life’s challenges and their general expectations in life satisfaction may be lower than their male counterparts. The percentages of self-reported good health and life satisfaction among Chinese male and female oldest-old did not decline or declined only slightly across age groups (Figure 4), while their functional capacities declined quickly with increases in age (Figure 3).

Female oldest-old’s life expectancy at ages 80 and 90

were 18.7% and 16.0% higher, respectively, than that of male oldest-old in China in 2020 (article in submission; email Corresponding Author for more information). These contributed to the well-known “male-female health-survival paradox” (7). Similar gender differentials have also been found in other countries. For example, based on the data from the U.S. Long Term Care Surveys (1982–1994), Manton and Land (8) found that, although American oldest-old women have a longer total life expectancy at the age of 80 and 85, they have significantly shorter active life expectancy as compared to American oldest-old men; such female disadvantages continue to the end of the U.S. health life tables.

Three preliminary explanations may shed light on understanding the “male-female health-survival paradox” and the gender differentials of the familial, socioeconomic and health statuses in China and elsewhere. First, the lifestyle of smoking and drinking strong alcohol was much lower among female oldest-old than male oldest-old in China, which contributed to oldest-old women’s longer lifespan. It was generally considered inappropriate for a woman to smoke or to attend a formal dinner (or banquet) at which the male hosts and participants drank a lot of strong alcohol in the traditional Chinese society. Thus, female Chinese oldest-old were subjected to a substantially lower risk

of smoking and drinking strong alcohol that reduced lifespan.

Second, as compared to their male counterparts, female oldest-old were less likely to perform outdoor physical activities, such as farming, exercising, and fishing. Oldest-old women were also less likely engaged in reading, writing, meetings, and social and cultural activities, as they have lower levels of education and socioeconomic status. Female oldest-old persons' lower frequency of performing outdoor activities and lower education levels and socioeconomic status gave them fewer opportunities to maintain their capacities in activities of daily living, physical performance, cognitive function, and to obtain health services when they were sick.

Third, we recently discovered that genetic associations with longevity benefit females significantly more than males through analyzing datasets of genome-wide association study on 2,178 centenarians and 2,299 middle-age controls of CLHLS participants. This novel discovery was replicated across North and South regions of China and was further reconfirmed by analyses of different datasets of Chinese healthy aging candidate genes with 2,972 centenarians and 1,992 middle-age controls of CLHLS participants (article in submission; email Corresponding Author for more information).

In conclusion, the CLHLS 20-years longitudinal survey observations have consistently demonstrated the oldest-old women's serious disadvantages in familial and socioeconomic statuses, capacities of activities of daily living, physical performance and cognitive function, and self-reported health and life satisfaction. These findings imply that long-term care service programs should take into account the disadvantaged status of the female oldest-old. Government at all levels and society more broadly need to pay attention to enormous gender differentials in pensions and main source of financial support for the oldest-old persons. Very careful attention in policymaking and implementation should be given to ensure that any old age insurance and social service programs be developed or reformed to better prioritize the female oldest-old.

While the present study made significant contributions in providing empirical evidences of gender differences in familial, socioeconomic and health statuses of oldest-old aged 80 years and over in China, it also had limitations. In this paper, we adjusted only for genders and ages to ascertain the factual gender differentials in marital status, living arrangements, socioeconomic status, capacities in activities of daily living, physical performance,

cognitive functions, self-reported health, and life satisfaction. However, other possible confounding factors were not controlled for. For example, as demonstrated in Figure 3D, we discovered that the gender differences in cognitive function among the Chinese oldest-old were extremely large. Due to space limits and the policy analyses nature of the present paper, we did not quantitatively explore which of the complicated factors caused such a large gender gap. We will conduct in-depth investigations on the causal determinants and impact factors of the gender differences in our future academic research articles, through employing the multivariate statistical methods such as sophisticated regression analyses.

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SUPPLEMENTARY MATERIAL

Background Information

The numbers and proportions of oldest-old aged 80 years and over who most likely need care in daily life and health service will increase much faster than the overall elderly populations in China and worldwide. In addition to the continued and significant decline of mortality rates especially at oldest-old ages, the main reason why the number of oldest-old will climb so quickly especially after 2030 is that China's baby boomers, those who were born in the 1950s and the 1960s, will become the "oldest-old" after 2030. Clearly, the oldest-old population is growing much faster than the overall elderly population.

Data Source: The Chinese Longitudinal Healthy Longevity Study (CLHLS), 1998–2018

The first 8 waves of the Chinese Longitudinal Healthy Longevity Study (CLHLS) were conducted in 1998–2018. The 9th wave is being conducted in 2021 and has been expanded into the Chinese Longitudinal Healthy Longevity and Happy Family Study (CLHLS-HF) by adding several family-relevant questions based on CLHLS' initial questionnaire that contained about one-third of family-relevant questions. In this paper, we used the datasets of the CLHLS conducted in 1998–2018, which are summarized here.

The baseline survey of the CLHLS was conducted in 1998 and the follow-up surveys with new recruitments to replace dead participants were conducted in 2000, 2002, 2005, 2008–2009, 2011–2012, 2014, and 2017–2018. The CLHLS surveys were conducted in randomly selected roughly half of the counties and city districts of 23 out of 31 provincial level administrative divisions in China, including Liaoning, Jilin, Heilongjiang, Hebei, Beijing, Tianjin, Shanxi, Shaanxi, Shanghai, Jiangsu, Zhejiang, Anhui, Fujian, Jiangxi, Shandong, Henan, Hubei, Hunan, Guangdong, Guangxi, Sichuan, Chongqing, and Hainan. The survey areas covered 985,000,000 persons in the baseline year 1998 and 1,156,000 persons in the most recent census year 2010, about 85% of the total population of China.

In the 8 waves of the CLHLS conducted in 1998–2018, we have conducted over face-to-face home-based 113,000 interviews, including 19,500 centenarians, 26,800 nonagenarians, 29,700 octogenarians, 25,500 younger elders aged 65–79, and 11,300 middle-aged adults aged 35–64. Data on death dates/age and relatively detailed information of health status, care needs/costs, etc., before dying for the 28,900 elders aged 65–118 who died between waves were collected in interviews with a close family member of the deceased. All of the interviews, basic health exams, and DNA samples were voluntarily collected with standard consensus forms reviewed/signed by the participants (or their direct family members).

All centenarians who voluntarily agreed to participate in the study in the randomly selected roughly half of the counties and city districts of the 23 provincial level administrative divisions were interviewed. For each centenarian, 1 nearby nonagenarian (aged 90–99), 1 nearby octogenarian (aged 80–89), and 1.5 nearby young-old aged 65–79 were interviewed. "Nearby" was loosely defined — it could be in the same village or street if the interviewees of pre-designated age and sex were available, or in the same town or in the same sampled county or city district if not available in the same village or street.

The pre-designated age and sex of the participants used to identify the approximately equal numbers of male and female nonagenarians, octogenarians, and young-old at each of the 5-year age groups from age 65 to 99 were randomly determined, based on the code numbers of the centenarians (*I*). The questionnaire data collected provides information on family structure, living arrangements and proximity to children, activities of daily living (ADL), the capacity of physical performance (picking up a book from the floor; standing up from a chair; and turning 360° without help), self-reported health, self-evaluation of life satisfaction, cognitive functioning and mental health, chronic disease prevalence, care needs and costs, participation in social activities, diet, smoking and drinking behaviors, psychological characteristics, economic resources, and care giving and family support among elderly respondents and their relatives. Information about the health status of the CLHLS participants who were interviewed in the previous wave but died before the current survey was collected by interviewing a close family member. Information provided consists of cause of death, chronic diseases, ADL before dying, frequency of hospitalization or instances of being bedridden from the last interview until death, whether bedridden before death,

length of disability, and suffering before death, etc.

The CLHLS has documented internationally established good data quality, including age reporting, assessments of mortality rates, proxy response, non-response rates, sample attrition, reliability and validity of major health measures, and rates of logically inconsistent answers (2–5). Relatively accurate age reporting of elderly including oldest-old among the Han Chinese (92% of total population of China) has been well-established and re-confirmed by a wide variety of international and domestic studies; this accuracy was due to the cultural traditions of memorizing one's exact date of birth to determine dates of important life events, such as dates of marriage and starting date to build a residential house (6–7).

Measurements of the Health Statuses

Activities of daily living (ADL)

Self-reported six ADL, including eating, dressing, transferring, using the toilet, bathing, and continence, were useful measurements of functional capacity and service needs, as verified in numerous previous studies; ADL was also a significant predictor of mortality (8). Following the widely adopted practice in the literature, if none of the six ADL activities was impaired, the elder was classified as “ADL active”; otherwise, the elder was classified as “ADL impaired”.

Physical performance

Self-reported ADL status may not always be accurate in measuring actual capacity in physical performance of the oldest-old, mainly because ADLs were also affected by household facilities (9). Also, some of the oldest-old may feel ashamed to report difficulties in daily activities such as continence. Therefore, as in other international healthy aging surveys, we conducted objective examinations to measure oldest-old participants' physical performance. We present and discuss in this paper the 1998, 2008, 2017-2018 waves of CLHLS results of gender differentials in the physical performance of standing up from a chair and picking up a book from the floor.

The cognitive functional

The cognitive functional statuses of the Chinese elderly were screened by the Chinese version of the Mini-Mental State Examination (MMSE), which were translated into the Chinese language based on the widely used international standard of the MMSE questionnaire with careful considerations of Chinese cultural and social context, and empirically tested in pilot survey interviews (9). We used the same cutoffs as the MMSE international standard, defining a score of 24+ as “good” cognitive function and a score of <24 as impaired cognitive function (11–12).

Self-reported health and life satisfaction

Self-reported health and life satisfaction were significant and valuable predictors of the functioning and mortality of older adults, as demonstrated in many previous studies (13). In addition to self-reported health, the CLHLS also asked the elderly participants to report “How do you rate your life at the present?” The multiple responses to this question about life satisfaction were “very good; good; so-so; bad; very bad; and not able to answer.” The category of self-reported “good life satisfaction” included those who provided an answer of “very good” or “good” to this question.

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Methods and Applications

The Establishment and Application of Mobile Electronic Surveillance System for Infectious Diseases with the Help of China — Sierra Leone, 2016-Present

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ABSTRACT

Introduction: Infectious disease surveillance has long been a challenge for low-income countries like Sierra Leone. Traditional approaches based on paper and Short Message Service (SMS) were subject to severe delays in obtaining, transmitting, and analyzing information.

Methods: During the China aid operation for fighting Ebola since the end of 2014, a mobile electronic surveillance system for infectious diseases (MESSID) was developed in collaboration with the Republic of Sierra Leone Armed Forces (RSLAF), which comprised an Android-based reporting system and a complementary web-based program designed by Active Server Page.NET (ASP.NET) with the main functions including surveillance, real-time reporting, and risk assessment of infectious diseases.

Results: MESSID was successfully registered in June 2016 and had been used by all medical and health institutions in RSLAF. From June 1, 2016 to July 5, 2021, 34,419 cases were diagnosed with 47 infectious diseases of 5 categories, with a total of 42 clinical symptoms. Compared to traditional approaches based on paper and SMS, the MESSID showed flexibility, high efficiency, convenience, and acceptability.

Discussion: MESSID is an accessible tool for surveillance of infectious diseases in Sierra Leone and possibly in other African countries with similar needs, capable of improving timeliness of disease reporting, thus rendering a timely outbreak detection and response.

low and middle-income countries are more readily afflicted by emerging infectious diseases while lacking such surveillance systems combined with the resources needed for pathogen surveillance (3). During 2014–2015, an outbreak of Ebola virus disease (EVD) swept across parts of West Africa with high incidence and case fatality reported in Sierra Leone. A lack of public health infrastructure in conjunction with delays in laboratory detection and implementation of control interventions have contributed to the widespread transmission of EVD in the country. Major gaps exist for collecting, processing, and transmitting data, primarily due to the lack of adequate reporting tools and limited access to laboratory diagnosis of infectious diseases. The paper and SMS disease reporting systems had been applied by the medical and healthcare system of Republic of Sierra Leone Armed Forces (RSLAF). However, the submission of surveillance forms was affected by poor transport and telecommunication infrastructures, poor electricity facilities, weather conditions, and challenging terrain.

In September 2014, the China Mobile Laboratory Testing Team was dispatched at the request of the Sierra Leone government to support Sierra Leone and to respond to the World Health Organization's (WHO) and the United Nations' (UN) requests to help control the EVD epidemic (4). During this aid operation, Chinese aid experts have designed and implemented a mobile electronic surveillance system for infectious diseases (MESSID) via collaboration with the RSLAF. This article described the design and implementation of the system, presented preliminary data obtained since June 2016, and provided examples of data that are being obtained in Sierra Leone.

INTRODUCTION

Fundamental disease surveillance systems are essential to guide the informed prevention and control of infectious diseases for each country (1–2). However,

METHODS

System Structure

The development of MESSID system was primarily

based on a display center, a service center, a data center, and user authority. A schematic overview of the MESSID is shown in Figure 1.

Display center: MESSID used a web-based graphical interactive interface with C# (version 4.0; Microsoft Corporation; Washington State, U.S.) as the main development programming language, and Visual Studio 2012 (version 2012; Microsoft Corporation; Washington State, U.S.) as the programming IDE (Integrated Development Environment). Microsoft.NET Framework (version 4.0; Microsoft Corporation; Washington State, U.S.) was adopted as the main development framework to build applications with pleasant user experience, seamless communication across technical boundaries, and support for various business types. Model View Controller was adopted for design specifications to map traditional input, processing, and output functions in a logical graphical user interface structure.

Service center: To attain effective data sharing and interaction and statistical analysis, Sever/Brower architecture was adopted, and handheld terminal data collection was using the Android platform and using the Java programming language (version 11; Oracle; California, U.S.). Under this structure, the user interface was implemented through the web browser, and transaction logic was implemented in the front end

(Browser), while the main transaction logic is implemented on the server side (Server), forming the so-called three-tier structure. This greatly simplifies the client-computer load, reducing the cost and workload of system maintenance, upgrades, and the overall cost to end users.

Data center: In order to realize data sharing and interactions between various systems, Microsoft's enterprise-level relational database SQL Server (version 2008 R2; Microsoft Corporation; Washington State, U.S.) was used as the database storage system to build a unified data center to ensure consistency and timeliness of the data collection.

User authority: An extended Role-Based Access Control permission control model was adopted, which combined user permissions and role permissions. In user permissions, users were assigned permissions. During emergencies, there was no need to modify the content of role permissions.

Data Collection and Reporting

Two kinds of questionnaires (symptom surveillance and laboratory data) were designed to collect data from each case, which included date, demography, epidemiological information, clinical syndrome, clinical diagnosis, laboratory testing if applicable, etc.

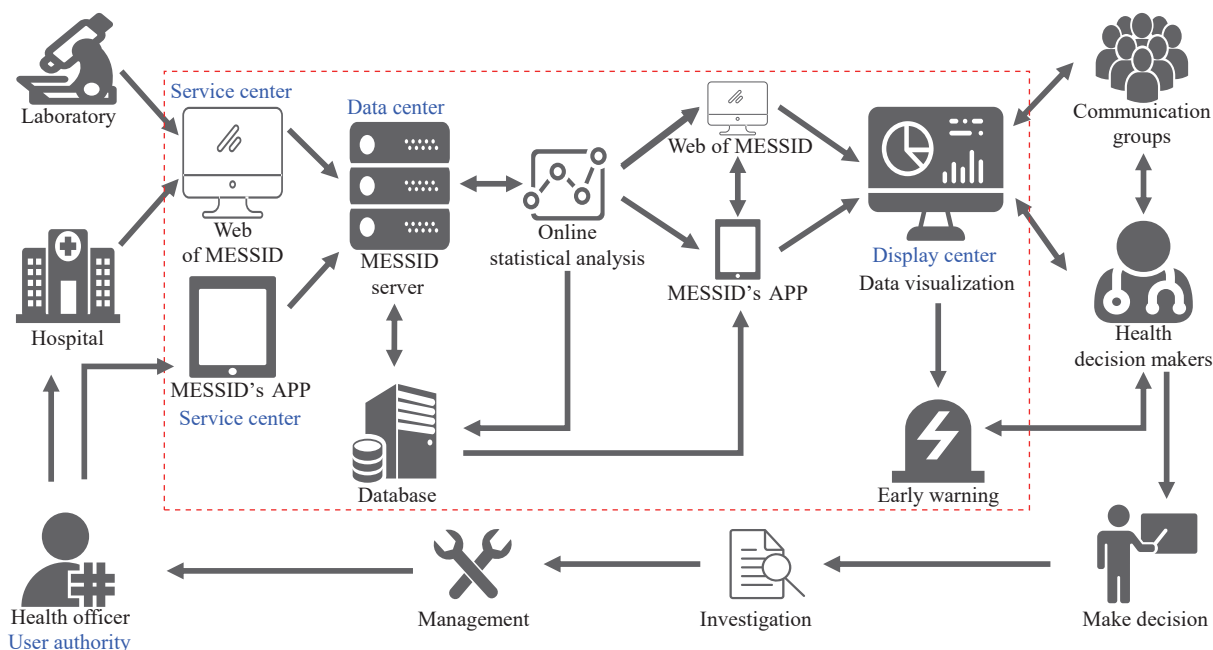


FIGURE 1. A schematic overview of the MESSID.

Note: The display center was used to visualize data, maps, or analyzed results to users; the service center was used for data filling, data transmission and sharing, and data exporting; the data center was used for data storage and management; and user authority was used to assign permissions to users.

Abbreviation: MESSID=mobile electronic surveillance system for infectious diseases.

The location of each survey was also collected with global positioning system, and latitudinal and longitudinal information was integrated into the report data. For data transmission, in addition to reporting through the browser version of the MESSID, a MESSID APP was designed to facilitate the staff to report cases through the mobile terminal. As shown in Table 1, MESSID's APP had most of the functions of the MESSID, except that no data downloading was permitted (Figure 2A–B). Moreover, the intelligent report was used in MESSID APP to improve the efficiency of reporting. At locations covered by mobile telecommunication network, collected data could be submitted real time to the data center at the 34 Military Hospital through the wireless network service of tablet or mobile phone. Under situations when the surveys were performed in remote areas without cellular service, the data would be stored locally, and the MESSID APP would automatically upload the data when the user returned to an area with a mobile telecommunication network.

Data Management and Visualization

There was also pre-stored baseline information in the MESSID for the user's reference, primarily involving the local socioeconomic, geographic, and environmental data at the provincial level. Based on this information, the frequency of cases and their diagnosis and the collected symptom information could be summarized in relation to age, gender, occupation, time duration, region, sentinel clinics, etc.

(Figure 2D). The results could also be exported as an Excel file for further analysis. The spatiotemporal distribution of symptoms, cases, and diagnoses could be summarized and presented by generating spatial distribution maps, epidemic curves, and dynamic statistical graphs by gender, age, and occupation (Figure 2C). Thus, the disease situation could be assessed by health officers and could be customizable to aid the generation of epidemic situation reports in regular (weekly, monthly, and yearly) or irregular (customizable time, region, population, and selected elements) intervals. During data collection and processing, privacy and data security were considered; no personal identifiers were linked to survey submissions and all data were denominated for analysis.

RESULTS

The Application of MESSID

A pilot version of this system was implemented in June 2016 in partnership with all medical and health institutions in RSLAF. The systems were successfully registered and used by medical staff from Joint Medical Units of RSLAF stationed at the 12 districts, which had taken all 31 Medical Inspection Rooms and hospitals in RSLAF.

During the operation period from June 1, 2016 to July 5, 2021 in Sierra Leone, a total of 34,419 cases were diagnosed with 47 infectious diseases, with a total of 42 clinical symptoms. The median age of the

TABLE 1. The functions of MESSID and MESSID APP in comparison with traditional approaches of disease reports based on paper and SMS.

Function	Traditional approach based on paper and SMS paper and SMS reporting	MESSID APP	MESSID
Data collection	Manually collect data	Collect data based on the mobile terminals	Collect data based on the website on users' computers
Data storage	Manually enter data	Data was locally stored and automatically uploaded to the data center when the mobile telecommunication network was available	Automatically uploaded the data to the data center
Data transmission	By paper or SMS report delivery	Automatically data transmission through wireless network service of tablet or mobile phone	Data transmission through network service of users' computers
Data content	Disease species and the number of cases	Demographical, spatiotemporal, clinical, epidemiological, and therapeutic information of patients, as well as laboratory testing information if applicable	Demographical, spatiotemporal, clinical, epidemiological, therapeutic information, and laboratory testing information if applicable
Real-time statistical analysis	Unable to conduct real-time statistical analysis	Query data with simple statistical analysis	Real-time online statistical analysis on the website in client computers
Data visualization	Data visualization requires additional software	Part of the data could be visualized on the app	The data could be visualized on the website in client computers
Real-time risk assessment and early warning	Difficulty for risk assessment and early warning in time	Real-time surveillance and easy risk assessment through the app	The global situation analysis, real-time surveillance and be easy for risk assessment and early warning by health officials

Abbreviations: MESSID=mobile electronic surveillance system for infectious diseases; SMS=short message service.



FIGURE 2. Interface display of MESSID APP in tablet and MESSID in PC. (A) Interface of questionnaire form for data collection in the MESSID APP; (B) Interface of online statistic in MESSID APP; (C) Interface of global situation analysis on the website of MEESID (<http://www.messid.net/userinterface/Login.aspx>); (D) The interface of symptom statistics on the website of MESSID.

Abbreviation: MESSID=mobile electronic surveillance system for infectious diseases.

patients were 41 years old (range: 0–118) and 71.90% males. Geographically, cases were predominantly

reported from Western Area Urban District (9,013 records, 26.19%) and Bombali District (6,922 records,

20.11%). A total of 37,954 clinical diagnoses were submitted, which were related to 47 diseases or their coinfections. The most common diagnosis was malaria (15,647 cases, 45.46%), followed by flu (3,691 cases, 10.72%), typhoid fever (2,794 cases, 8.12%), mycobacteriosis (304 cases, 0.88%). Each syndromic grouping was linked to ways of disease transmission, including vector-borne diseases, zoonotic diseases, respiratory infections diseases, enteric infectious diseases, and blood, sexually, and direct contact transmitted diseases.

Life threatening and severe infections or emerging infectious diseases were alerted and responded to in a timely manner, including yellow fever (10 cases), Rift Valley fever (1 case), anthrax (1 case) and melioidosis (1 case). Notably, the early alert for COVID-19 was identified through MESSID. During the early stages of COVID-19 epidemic in Africa, the reported COVID-19 cases in Sierra Leone totaled at 50 cases as of April 22, 2020 (5), out of which 24 cases received by the military medical and health institutions were recorded by MESSID, which had taken an important part of overall cases in the early days of COVID-19 epidemic in the country. The first COVID-19 patient recorded by MESSID was reported on March 31, 2020, which was 1 day earlier than the official report from WHO (on April 1, 2020).

Comparison Between MESSID and Traditional Approach Based on Paper and SMS

MESSID had particular benefits of convenience,

flexibility, high efficiency, and acceptability, compared to traditional approaches based on paper and SMS (Table 2) (6). The MESSID reporting process was simple and highly efficient, taking only a few minutes to successfully report a case, in contrast with 3–5 days taken for traditional approach based on paper and SMS. A high receptive attitude to the MESSID was obtained from the health workers. A high flexibility of MESSID allows for the update of information collection and organization. For example, COVID-19 was added to the surveillance system when the WHO declared that the COVID-19 outbreak constituted a Public Health Emergency of International Concern (7). The real-time data collection, analysis, and report generation had allowed an early detection of change of infectious diseases.

DISCUSSION

The currently described MESSID offered an integrated solution that comprised surveillance, real-time reporting, and risk assessment, therefore enhancing the approach for authorities to collect baseline data for common infectious diseases or emerging infectious diseases (Table 2). Informed preventive measures could be taken if necessary. The platform could also assist the healthcare sector in planning and control measures such vaccine deployment.

In recent years, various countries and organizations have established electronic surveillance systems of infectious diseases or public health events such as

TABLE 2. Performance and characteristics of MESSID by compared with traditional approach of disease reports based on paper and SMS.

Features	Traditional approach based on paper and SMS	MESSID
Convenience	1. The reporting process is complicated and tedious. 2. Not able to report immediately.	1. The reporting process is clear and simple. 2. Able to report immediately.
Flexibility	1. Due to the tedious reporting process, it takes a long time for health workers to fully grasp the reporting process. 2. Traditional approach based on paper and SMS cannot adapt to changing information needs. 3. Traditional approach based on paper and SMS cannot flexibly change the content of the questionnaire.	1. Due to the simple reporting process, it only takes a few hours for health workers to fully grasp the reporting process. 2. MESSID can adapt to changing information needs if necessary. 3. MESSID can flexibly change the content of the questionnaire if necessary.
Highly efficient	1. Limited information was analyzed and reported. 2. Difficulty for real-time surveillance and risk assessment of outbreaks of infectious diseases.	1. Real-time integration and analysis of demographical, spatiotemporal, clinical, epidemiological, therapeutic, and laboratory testing information. 2. Easy for real-time surveillance and risk assessment of outbreaks of infectious diseases.
Acceptability	1. More additional work in the data input, collection, and analysis. 2. More additional work on the draft of disease report.	1. Almost no additional work in the data collection, analysis. 2. Automatically generate reports on demand.

Abbreviations: MESSID=mobile electronic surveillance system for infectious diseases; SMS=short message service.

Global Public Health Intelligence Network and HealthMap, which are used to collect case or outbreak data, manage case databases, and analyze data thereby promoting the prevention, monitoring, and control of infectious diseases (8). These information systems mainly rely on big data technologies to capture information related to infectious diseases on the Internet to display the status of global emerging or reemerging infectious diseases and provide early warnings for potential disease outbreaks by data integration, analysis, and risk assessment (9). However, this is not suitable for developing countries with the lack of fundamental disease surveillance system based on case information. In addition, building an infectious disease electronic surveillance system requires not only network data transmission capabilities, but a practical infectious disease surveillance framework. MESSID is not only an infectious disease monitoring software, but more importantly, it provides a ready-to-use real-time mobile monitoring solution for infectious diseases in developing countries without electronic reporting tools of infectious diseases, MESSID is a software system independently developed by the Beijing Institute of Microbiology and Epidemiology, which has all intellectual property rights and provides authorization or permission to use. No costly software is required for the installation of the MESSID, which has system-level security to protect key data by using data transmission and storage encryption technology that is helpful for its wide application in other developing countries. In addition, support from authorities has been the most important factor in the successful implementation and operation of MESSID. The system has also enabled group coordination and information sharing among the various entities so decision makers can obtain data in time and transfer information with health officials (10–11).

One of the obstacles to efficient implementation of the MESSID in its current form lies in the low capacity of laboratory diagnosis in Sierra Leone, and the probable misdiagnosis of diseases. These limitations might undermine the reliability and accuracy of data submitted to MESSID. The poor infrastructure and the cost to implement MESSID might also deter efforts of nationwide implementation. Still, it is helpful for some developing countries to establish information systems to meet their particular needs of infectious disease surveillance from this study.

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Notifiable Infectious Diseases Reports

Reported Cases and Deaths of National Notifiable Infectious Diseases — China, June, 2021

Diseases	Cases	Deaths
Plague	0	0
Cholera	3	0
SARS-CoV	0	0
Acquired immune deficiency syndrome	5,978	1,554
Hepatitis	126,681	46
Hepatitis A	1,089	0
Hepatitis B	101,633	39
Hepatitis C	20,937	7
Hepatitis D	23	0
Hepatitis E	2,266	0
Other hepatitis	733	0
Poliomyelitis	0	0
Human infection with H5N1 virus	0	0
Measles	72	0
Epidemic hemorrhagic fever	724	5
Rabies	18	15
Japanese encephalitis	10	1
Dengue	8	0
Anthrax	25	0
Dysentery	6,408	0
Tuberculosis	73,884	104
Typhoid fever and paratyphoid fever	829	0
Meningococcal meningitis	6	0
Pertussis	519	0
Diphtheria	0	0
Neonatal tetanus	0	0
Scarlet fever	4,165	0
Brucellosis	9,670	0
Gonorrhea	10,950	0
Syphilis	47,423	2
Leptospirosis	19	0
Schistosomiasis	4	0
Malaria	109	0
Human infection with H7N9 virus	0	0
COVID-19*	670	0
Influenza	38,772	0
Mumps	12,015	1

Continued

Diseases	Cases	Deaths
Rubella	115	0
Acute hemorrhagic conjunctivitis	2,467	0
Leprosy	36	0
Typhus	112	0
Kala azar	23	0
Echinococcosis	238	0
Filariasis	0	0
Infectious diarrhea [†]	117,015	0
Hand, foot, and mouth disease	224,426	2
Total	683,394	1,730

* The data were extracted from the website of the National Health Commission of the People's Republic of China.

† Infectious diarrhea excludes cholera, dysentery, typhoid fever and paratyphoid fever.

The number of cases and cause-specific deaths referred to data recorded in National Notifiable Disease Reporting System (NNDRS) in China, which includes both clinically-diagnosed cases and laboratory-confirmed cases. Only reported cases of the 31 provincial-level administrative divisions in the mainland of China are included in the table, whereas data of Hong Kong Special Administrative Region, Macau Special Administrative Region, and Taiwan, China are not included. Monthly statistics were calculated without annual verification, which is usually conducted in February of the next year for de-duplication and verification of reported cases in annual statistics. Therefore, 12-month cases could not be added together directly to calculate the cumulative cases because the individual information might be verified via NNDRS according to information verification or field investigations by local CDCs.

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