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Cover Photo: China CDC Staff field sampling for vector in the public health emergency drill, Inner Mongolia, China, September 2023.

Preplanned Studies

Economic Burden of Hand, Foot, and Mouth Disease — Beijing Municipality, China, 2016–2019

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Summary

What is already known about this topic?

Current research regarding hand, foot, and mouth disease (HFMD) has primarily concentrated on the economic impacts, drawing from retrospective or sentinel hospital-based data. This approach often overlooks cases that were either not consulted or were misdiagnosed.

What is added by this report?

This research systematically examined the iceberg phenomenon of HFMD and its economic implications in Beijing. Our findings indicate that each confirmed case represents 9.1 actual infections, imposing financial burdens of 25.58 United States dollars (USD) per unconsulted individual, 265.75 USD per misdiagnosed individual, 366.50 USD per individual with mild cases, and 2355.89 USD per individual with severe cases. The annual economic losses attributed to HFMD in the area range from 7.03 million USD to 13.31 million USD.

What are the implications for public health practice?

This study offers insight into the actual prevalence of HFMD in Beijing, as well as conducting an economic burden analysis on a per-case, per-category basis. This could facilitate a cost-effectiveness analysis of prevention and control strategies for HFMD.

Hand, foot, and mouth disease (HFMD) — predominantly associated with enterovirus infection — is a widespread disease adversely affecting children below the age of five (*1*). Since HFMD's designation as a notifiable infectious disease in 2008, its prevalence has consistently topped the charts in China, evolving into the leading cause of disease-related morbidity (*2*).

However, despite this official classification, a comprehensive understanding of the magnitude of HFMD infections and the economic burden they bear remains elusive. This is largely due to the "iceberg" phenomenon unique to infectious diseases — where the vast majority of HFMD infections exhibit no symptoms, and symptomatic cases might opt against seeking medical treatment at sentinel hospitals, either owing to mild symptoms or financial constraints. This subset constitutes "unconsulted" cases (*3*). Moreover, due to HFMD symptoms' similarity to other medical conditions, misdiagnoses are likely (*4*).

To accurately gauge the economic burden of HFMD in Beijing, our study employs both prospective and retrospective methods to quantify the prevalence and per-person economic strain tied to misdiagnosed and hospital-consulted infections across a range of severity categories. We deployed a Monte Carlo multiplier model to approximate true infection rates.

Our analysis determines that each officially confirmed case of HFMD correlates to 9.1 actual infections [95% confidence interval (*CI*): 4.6–31.5]. The economic burden per person was as follows: 25.58 United States dollars (USD) for unconsulted cases, 265.75 USD for misdiagnosed cases, 366.50 USD for mild cases, and 2355.89 USD for severe cases. The cumulative annual economic loss attributable to HFMD fluctuates between 7.03 million USD and 13.31 million USD.

In April 2017, we undertook a prospective study in Fengtai District to gauge the morbidity and economic impact of HFMD (Figure 1A). Participants included children aged from 6 to 35 months who had resided in the district for a minimum of 6 months, and the observation period extended from April 2017 to October 2018. Seasoned general practitioners recorded symptoms resembling HFMD, medical consultations, clinical diagnoses, and associated costs and collected pharyngeal samples for testing for Enterovirus (EV).

A parallel retrospective study was also initiated in April 2017 to estimate the economic burden of hospitalized cases, incorporating patients from 6 administrative regions within Beijing (Figure 1B). To circumvent recall bias when calculating the expenses related to HFMD, medical practitioners instructed study participants to retain all documentation relating to HFMD-related expenditures.

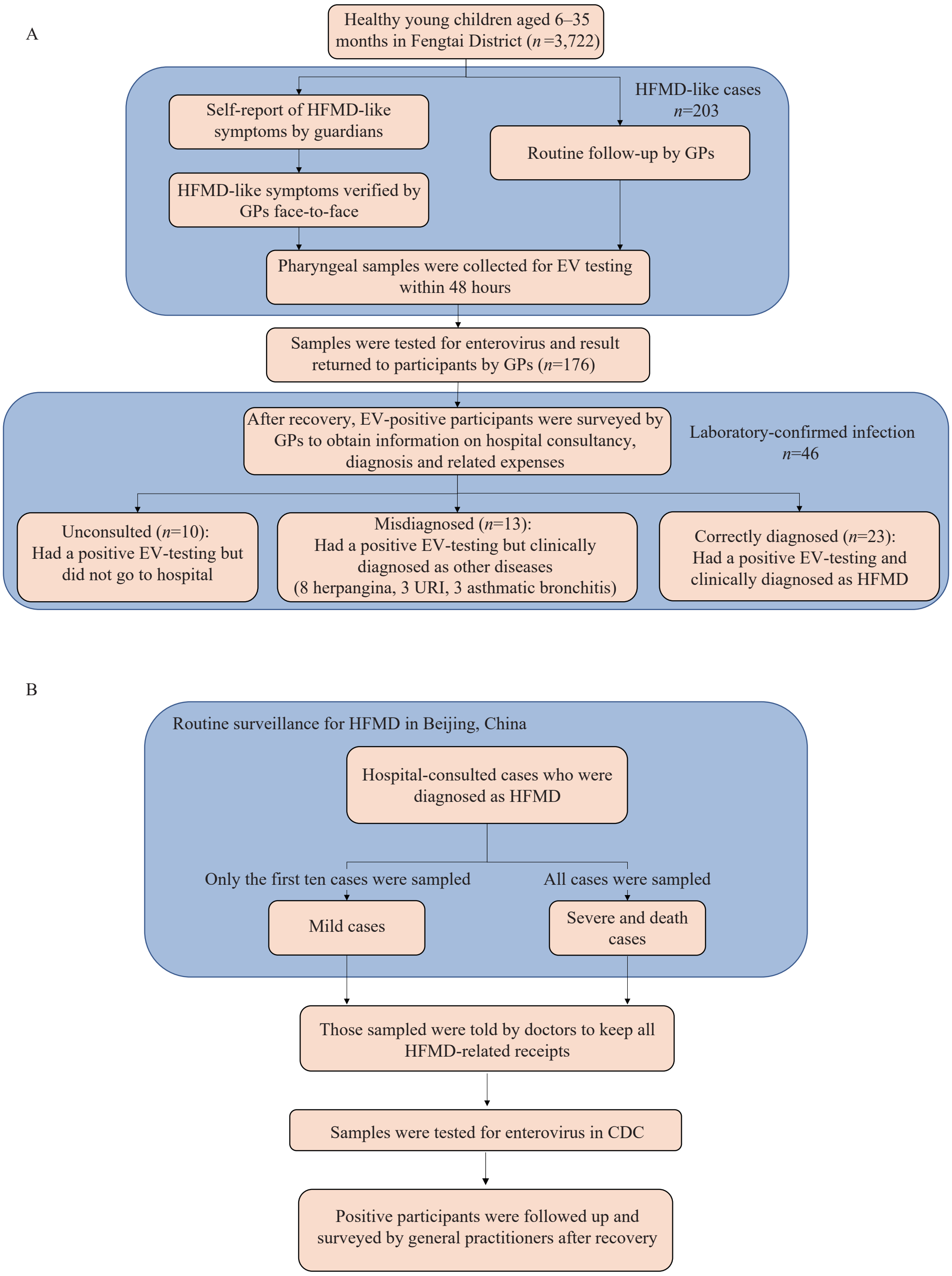

FIGURE 1. Flowchart Illustrating the prospective and retrospective study design. (A) Flowchart for the prospective on the actual prevalence of HFMD; (B) Flowchart for retrospective studies on the unit cost of HFMD.

Note: Figure 1A: In April 2017, a prospective study was conducted in Beijing's Fengtai District, enrolling 3,722 healthy children aged 6 to 35 months, residing in the district for at least six months. Follow-up occurred from April 2017 to October 2018. HFMD-like cases (203) were identified through self-reporting and confirmation by GPs or routine follow-ups. Pharyngeal samples (n=176) were collected within 48 hours of symptom reporting, with 46 testing positive for EV. Post-recovery, GPs surveyed these cases for hospital consultations, diagnoses, and associated costs. Among them, 23 were accurately diagnosed, 13 were misdiagnosed, and 10 did not seek consultation. Figure 1B: This study considered HFMD cases from six sentinel hospitals in Beijing, China. These hospitals collected samples from the initial ten mild HFMD cases each month, or all cases if fewer than ten were reported. Severe and fatal cases were also included. Patients were advised to retain expense receipts for cost calculation. Following positive enterovirus confirmation, patients were monitored and surveyed by community GPs post-recovery to avoid recall bias.

Abbreviation: HFMD=hand, foot, and mouth disease; GPs=General Practitioners; EV=enterovirus.

We employed the Monte Carlo multiplier model to estimate the actual infection levels of HFMD. We considered parameters such as the symptomatic infection rate, consultation rate, diagnosis rate, and EV-positive rate to deduce the actual infections (Supplementary Table S1 and Supplementary Figure S1, available in https://weekly.chinacdc.cn/). The direct economic burden incorporated personal and reimbursement costs, which included direct medical expenses associated with case treatments, as well as direct non-medical costs such as nutritional and transportation expenses incurred by patients during diagnosis and treatment.

Indirect costs factoring in lost labor due to patient care were quantified by multiplying the average daily wage per capita by the average number of days lost. We also considered the economic burden of death cases, accounting for illness-related costs and the loss of societal productivity due to premature death. Cost estimations were performed separately for different infection types.

All statistical analyses were carried out using R software (version 4.2.0, R Foundation for Statistical Computing, Vienna, Austria), and all statistical tests were two-sided with an α value of 0.05.

In April 2017, a prospective study was undertaken in Fengtai District of Beijing. Between September 2017 and August 2018, we recruited 3,722 healthy children into the study. Of this group, 1,965 (53.8%) were male and 1,757 (47.2%) were female. The average age was 1.5 years [standard deviation (SD): 0.6]. After a one-year follow-up period, 203 children presented with symptoms resembling those of HFMD. A total of 176 pharyngeal samples were collected and examined for EV, resulting in 46 (26.1%) positive outcomes. The EV-positive cases consisted of 1 case of EV-A71 (2.2%), 7 cases of coxsackievirus type 16 (CV-A16) (15.2%), 22 cases of CV-A6 (47.9%), and 16 cases of other EV serotypes (34.8%). Of the 46 confirmed infections, 36 (78.3%, 95% *CI*: 65.9%–90.7%) sought medical care at hospitals. Among these, 23 cases (63.9%, 95% *CI*: 47.4%–80.4%) were diagnosed with HFMD. The remaining 13 cases were misdiagnosed: 8 with herpangina, 3 with upper respiratory infection, and 2 with asthmatic bronchitis. Consequently, we estimated a hospital consultation rate of 78.3% and a misdiagnosis rate of 36.1% (Figure 1).

A retrospective study was conducted in six districts in Beijing from April 2017 to October 2018. The study encompassed 697 HFMD cases in children aged five years and younger, including 410 males and 287 females. Of these cases, 547 (78.5%) tested positive for EV; CV-A6 had the highest positivity rate at 46.2%, followed by other EV types at 17.5%, CV-A16 at 11.9%, and EV-A71 at 2.9%. Notably, 88 cases (12.6%) were reported in vaccinated individuals, and none of those vaccinated were infected with EV-A71. The overwhelming majority of cases were mild, accounting for 97.7%, while severe cases represented 2.3%. No fatalities were recorded during the study period.

Based on Monte-Carlo multiplier calculations (*4*–*6*), each confirmed case corresponds to an estimated 9.1 actual infections (95% *CI*: 4.6–31.5). Furthermore, one confirmed case is representative of 2.5 (95% *CI*: 1.9–3.7) actual cases and 2.0 (95% *CI*: 1.5–2.9) consulting cases.

TABLE 1. Summary of economic burden per case in Beijing ($\bar{x}$±SD in USD*).

Infection classification†	Direct burden		Indirect burden	Total
	Medical burden	Non-medical burden		(95% *CI*)
Unconsulted (*n*=10)	3.26±2.12	2.44±2.77	19.88±44.67	25.58 (7.83, 43.37)
Diagnosed as HFMD				
Mild (*n*=681)	75.73±124.64	50.74±99.44	240.03±322.46	366.50 (337.16, 395.86)
Severe (*n*=16)	1415.16±1284.57	261.51±229.88	679.21±405.96	2355.89 (1570.70, 3140.75)
Death	2885.43±3302.65	620.68±754.70	280.75±840.46	3786.87 (2777.97, 4796.97)
Diagnosed as others (*n*=13)	62.61±43.53	34.89±19.07	168.25±88.20	265.75 (212.60, 318.90)

Abbreviation: SD=standard deviation; USD=United States dollars; *CI*=confidence interval; HFMD=hand, foot and mouth disease; CNY=Chinese Yuan; CPI=consumer price index.

* The average exchange rate for USD to CNY was noted as 6.4515 in the year 2021. We adjusted all associated costs in accordance with the 2021 CPI.

† Cost estimates for both unconsulted and misdiagnosed cases were derived from our prospective study. Meanwhile, the cost data associated with both mild and severe cases were ascertained through our retrospective study. As for the cost implications of fatal outcomes, these were referenced to Zheng et al., 2013 (*10*).

In the prospective study, each of the 10 untreated HFMD infections represented an economic burden of 25.58 USD per person, with the direct economic burden contributing 22.3% and the indirect economic burden contributing 77.7% (Table 1). The economic burden of the 13 misdiagnosed infections was higher, at 265.75 USD per person, with direct economic costs accounting for 36.7% and indirect economic costs making up the remaining 63.3% (Table 1). In terms of the retrospective study, the economic burden for mild cases averaged 366.50 USD per person, of which the largest portion was for indirect costs (65.5%), followed by direct medical costs (20.7%) and direct non-medical costs (13.8%). For the 16 severe cases, the average economic burden was significantly higher at 2355.89 USD per person, with direct medical costs contributing 60.1%, direct non-medical costs adding 11.1%, and indirect costs accounting for 28.8%. Median and IQR data are detailed in Supplementary Table S2 (available in https://weekly.chinacdc.cn/).

Annual economic losses attributable to HFMD in Beijing are estimated to range between 7.03 million USD and 13.31 million USD. A mere 2.1% of these losses arise from unconsulted infections. Mild infections consistently account for the largest proportion of these losses, having increased gradually from 65.8% in 2016 to 66.3% in 2018. The contribution of severe infections to the total economic burden varies significantly year by year. Importantly, no deaths were reported in connection with the disease from 2016 to 2019 (Table 2). If calculations are based solely on reported HFMD cases, the 2019 total economic burden would be projected at 0.49 million Chinese Yuan (CNY), thereby underestimating the actual burden by 30%.

DISCUSSION

This study conducted a systematic investigation into the actual morbidity and economic impact of HFMD, revealing an annual economic loss between 7.0 million USD and 13.3 million USD in Beijing, which represents 0.1% of the overall health expenditure. The economic burden attributed to unconsulted cases, mild and severe cases, as well as misdiagnosed cases, remained fairly consistent over the years. The prospective study results indicated that expenditure for each unconsulted HFMD infection averaged 25.58 USD per person, resulting in an anticipated average economic burden of 0.15–0.29 USD million per annum in Beijing. Despite severe HFMD cases resulting in the highest per-person costs among those consulted, they constituted only a minor portion of the overall burden due to their limited prevalence. The research found the economic impact of severe infections to be in line with findings from other regions (*7*–*8*). Although the financial loss per mild infection is only one-seventh of that of a severe case, given their high frequency, mild cases contribute significantly to the overall economic impact of HFMD. The study found that only 64% of cases were correctly diagnosed as HFMD upon hospital visits. The resulting costs of treatment for those misdiagnosed aligned with those of correctly diagnosed cases. It is therefore crucial to recognize that overlooking the economic burden born of approximately 35% of misdiagnosed cases would lead to a considerable underestimation of the financial impact of the HFMD disease.

In milder cases, indirect costs predominated — a pattern that diverged notably from the cost distributions seen in other countries (*9*) and from the nationwide average in China (*10*), where direct medical costs typically held sway. However, economic disparities between different study areas, including patient demographics and the spectrum of disease severity, might contribute to differences in economic costs. When equated with Shanghai, which had a comparable economic status to Beijing (*11*), the

TABLE 2. The estimated morbidity and overall economic burden of HFMD cases in Beijing (10,000 USD*)

Year	Unconsulted (%)	Hospital Diagnosed			Misdiagnosed (%)	Total
		Mild (%)	Severe (%)	Death (%)		
2016	26.6 (2.1)	816.3 (65.8)	12.2 (1)	0 (0)	386.2 (31.1)	1241.4
2017	16.2 (2.1)	498.1 (65.8)	7.3 (1)	0 (0)	235.7 (31.1)	757.2
2018	28.6 (2.1)	877.7 (65.9)	9.9 (0.7)	0 (0)	415.3 (31.2)	1331.5
2019	15.2 (2.2)	466.4 (66.3)	1.2 (0.2)	0 (0)	220.7 (31.4)	703.4

Abbreviation: USD=United States dollars; HFMD=hand, foot and mouth disease; CNY=Chinese Yuan; CPI=consumer price index.
* All costs have been adjusted in accordance with the 2021 CPI. The average exchange rate from USD to CNY in 2021 was 6.4515.

proportion of indirect costs was alike. Furthermore, in both our study and in Shanghai, a significant portion of the indirect cost was attributed to parental work loss, indicating a strong influence by the average income of citizens.

This study is subject to certain limitations. First, despite efforts to minimize recall bias — such as the retention of all HFMD-related receipts by participants for the calculation of HFMD-linked expenses — the potential for recall bias may still endure. Second, the HFMD severity spectrum in Beijing may vary significantly in comparison to other cities. Hence, the extrapolation of economic burden findings from this study to cities exhibiting radically dissimilar economic statuses and disease spectra should be undertaken with considerable caution.

In conclusion, this study elucidates the true morbidity rate of HFMD cases in Beijing and establishes critical parameters for future estimates of HFMD infections. The evaluation of the economic burden per case and by case category could facilitate cost-effectiveness analyses for HFMD prevention and control strategies.

Conflicts of interest: No conflicts of interest.

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SUPPLEMENTAL MATERIALS

Definitions

Hand, foot, and mouth disease (HFMD)-like cases were defined as a rash on any part of the hands, feet, mouths, and buttocks and could clearly exclude other rash-like diseases. The manifestations of the rash include skin color changes, bulging, or blisters on the skin surface. According to patients' severity, cases were diagnosed with HFMD as mild, severe, or death.

Laboratory-confirmed infection was defined as a person exhibiting HFMD-like symptoms and yielding positive results for the Enterovirus (EV) reverse transcription-polymerase chain reaction (RT-PCR) universal test from throat swab samples. Individuals who tested positive for the EV RT-PCR universal test would subsequently have their serotypes identified as either EV-A71, CV-A16, CV-A6, or others.

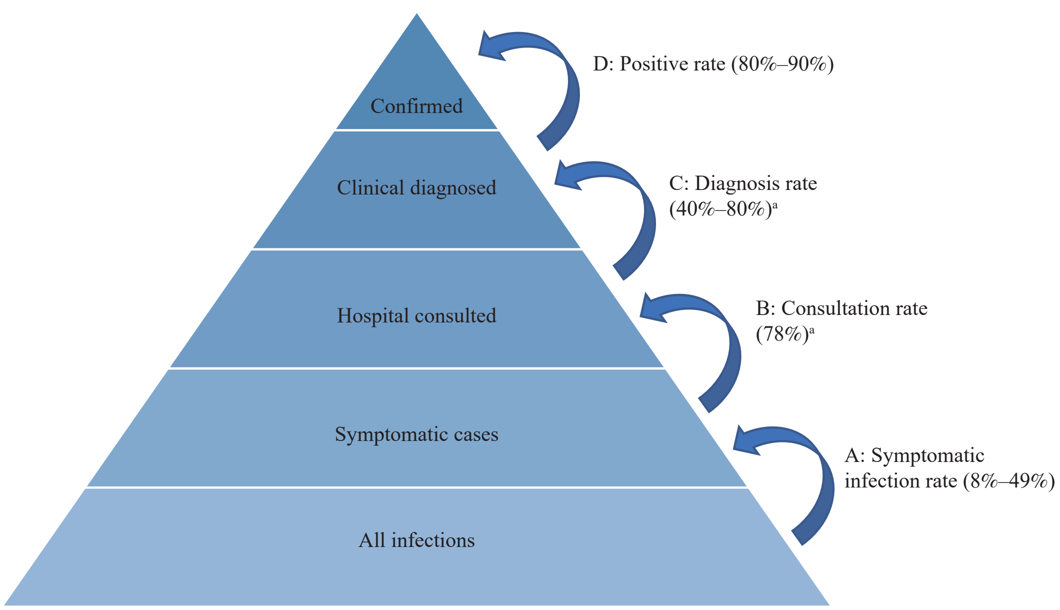
An unconsulted case was identified as an individual afflicted with HFMD infection who did not seek medical consultation at a sentinel hospital. Meanwhile, a misdiagnosed infection referred to an individual presenting with HFMD infection (confirmed by a positive EV test) who sought medical attention at a sentinel hospital but did not receive an accurate HFMD diagnosis.

Estimating Morbidity Rates

The estimation of the true prevalence of infection and morbidity was conducted using the Monte Carlo multiplier model (Supplementary Figure S1). The actual count of infections was inferred from parameters such as the rate of symptomatic infections, consultation rates, diagnostic rates, and the EV positive rate (*1–5*). The multiplier, M, used to scale confirmed cases from the reporting system was defined as follows:

$$M = \frac{1}{A} \times \frac{1}{B} \times \frac{1}{C} \times \frac{1}{D} \quad (1)$$

The following parameters were defined in the context of this research. First, we defined 'A' as the symptomatic infection rate of HFMD, denoting the proportion of patients presenting with hand, foot, and mouth symptoms in relation to total enteroviral infections. 'B' specified the hospital consultation rate of HFMD, indicating the proportion of HFMD cases that required medical consultation at a hospital. We referred to 'C' as the diagnosis rate, deriving from the ratio of symptomatic HFMD patients who sought medical consultation and were clinically



SUPPLEMENTARY FIGURE S1. Parameters for the estimation of actual HFMD infections using the multiplier model.
* Acquired from the prospective study. The symptomatic infection rate and positivity rate were extracted from the existing literature.

identified as having HFMD by healthcare providers. Lastly, 'D' represented the positive rate, which was the proportion of laboratory-confirmed enteroviral infections among those clinically diagnosed with HFMD. The total number of confirmed cases from the surveillance system, *R*, was taken to be

$$R = \sum_{m} N_m P_{ms} \tag{2}$$

$$Actual\ number\ of\ infections = R \times M \tag{3}$$

In this research, Nm refers to the clinically diagnosed cases reported to the surveillance system on a monthly basis, while Pms denotes the rate of positivity across all serotypes of enterovirus.

$$Total\ infections = \frac{\sum_s R_s}{ABCD} \tag{4}$$

$$Total\ morbidities = \frac{\sum_s R_S}{BCD} \tag{5}$$

$$Total\ hospital\ consultations = \frac{\sum_s R_s}{CD} \tag{6}$$

$$Total\ correctly\ diagnosed\ HFMD\ cases = \frac{\sum_s R_s}{D} \tag{7}$$

In the given formula, 's' denotes the number of serotypes, whereas 'Rs' represents the estimated confirmed cases of each serotype as derived from the surveillance system data.

Estimating the Economic Burden

The direct economic impact encompasses both personal expenditures and reimbursed costs. This includes direct medical expenses incurred throughout the treatment process, as well as direct non-medical expenditures such as nutritional supplies, food, and transportation expenses incurred by patients during the stages of diagnosis and treatment.

The indirect economic burden was defined as the social and family economic loss (productivity loss) induced by the patient's illness and the days off work of relatives and friends during the treatment period. The human capital method was employed to evaluate the cost associated with lost labor time for caregivers and those visiting patients (*6*). Accordingly, the indirect economic burden is determined by multiplying the average daily income per capita by the average number of days missed due to the patient's care. Absent work days were gauged through self-reporting, while the average daily income per capita was calculated by dividing the average annual salary by 250 days, as per wage reports in Beijing.

The effect of disability on the social productivity of mild and severe HFMD cases has been overlooked, taking into account the young age of the affected individuals and the abbreviated duration of their illness. Given the significant loss to societal productivity as a result of premature death, the economic burden of mortality cases consists of 1) the economic burden incurred during the period of illness, and 2) the economic burden on social productivity brought about by premature death.

The economic impact was separately assessed, taking into account the cost disparities among various infections.

$$EB_{total} = EB_{visit} \times N_{visit} + EB_{no\ visit} \times N_{no\ visit} \tag{8}$$

In this context, EB_{total} denotes the total economic burden of HFMD, EB_{visit} indicates the average economic burden per hospital visit for HFMD infection, and N_{visit} is the number of hospital visits due to infection. Additionally, $EB_{no\ visit}$ represents the average economic burden for cases that did not warrant a hospital visit, with

SUPPLEMENTARY TABLE S1. Parameters used in the Monte Carlo multiplier.

Parameters	Range	Source
Symptomatic rates (%)	7.9–49.2	Literature (*7–10*)
Consultation rates (%)	78	Results in this study
Diagnosis rates (%)	40–80	Literature and results in this study (*11*)
Sampling success rates (%)	80–90	Literature (*12*)

SUPPLEMENTARY TABLE S2. Summary of economic burden per case in Beijing [Median (IQR) in USD*]

Infection classification†	Direct burden		Indirect burden	Total
	Medical burden	Non-medical burden		
Unconsulted (*n*=10)	2.45 (0, 8.15)	0 (0, 4.08)	0 (0, 0)	8.15 (4.89, 24.46)
Diagnosed as HFMD				
Mild (*n*=931)	54.37 (34.1, 93.93)	8.22 (0, 31.00)	0 (0, 209.97)	134.85 (55.44, 352.81)
Severe (*n*=16)	938.78 (559.63, 1802.38)	171.19 (91.71, 479.33)	662.58 (314.72, 977.3)	2052.47 (1361.42, 2754.39)
Death	1786.61 (1084.05, 3606.79)	329.11 (147.76, 803.3)	52.39 (0, 192.09)	2100.94 (1495.11, 5354.44)
Diagnosed as others (*n*=13)	48.91 (45.16, 73.37)	32.61 (17.93, 48.91)	66.26 (0, 198.77)	266.43 (187.51, 328.68)

Abbreviation: IQR=interquartile range; HFMD=hand, foot and mouth disease; USD=United States dollars; CNY=Chinese Yuan.

* The average exchange rate for USD to CNY was noted as 6.4515 in the year 2021. We adjusted all associated costs in accordance with the 2021 CPI.

† Cost estimates for both unconsulted and misdiagnosed cases were derived from our prospective study. Meanwhile, the cost data associated with both mild and severe cases were ascertained through our retrospective study. As for the cost implications of fatal outcomes, these were referenced to Zheng et al., 2013. (*13*).

$N_{no\ visit}$ reflecting the count of such cases. The economic burden associated with hospital cases was bifurcated into those diagnosed with HFMD and those who were not. Furthermore, the diagnosed cases were further stratified based on the levels of severity. Economic implications for asymptomatic HFMD cases were overlooked, given the absence of symptoms and consequently, the lack of incurred costs.

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Vital Surveillances

Geographic Diversity in the Incidence of Human Prion Diseases — China, 2006–2019

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ABSTRACT

Introduction: Human prion diseases (PrDs) are rare, fatal encephalopathies requiring comprehensive diagnostic analysis. This study examines hospital referral patterns to the Chinese National Surveillance for Creutzfeldt-Jakob Disease (CNS-CJD) from 2006 to 2019.

Methods: We assessed 1,970 PrD cases referred by various hospitals to CNS-CJD. Referral distributions were analyzed based on provincial-level administrative divisions (PLADs). Differences in referral numbers and confirmed cases between monitored and non-monitored PLADs were statistically evaluated.

Results: The study included cases from 344 hospitals across 29 Chinese PLADs. Hospital referrals increased over the surveillance years: from 28.2 hospitals annually during 2006–2010, to 64 in 2011–2015, and 107 in 2016–2019. Of these, 12.2% (42/344) of hospitals reported ≥10 PrD cases, accounting for 70.0% (1,379/1,970) of total cases. Referral numbers varied across PLADs, with the top 5 of Beijing (41), Henan (26), Shanghai (21), Guangdong (21), and Jiangsu (21) leading. Additionally, 12 CJD-surveillance PLADs had more referring hospitals and PrD cases than the other 17 non-surveillance PLADs.

Conclusions: Geographical variations in PrD recognition exist across Chinese PLADs, with certain regions and major cities reporting notably higher case numbers.

Human prion diseases (PrDs) encompass a suite of transmissible spongiform encephalopathies (TSEs) induced by the unwelcome prion pathogen. This set of diseases includes Kuru disease, Creutzfeldt-Jakob disease (CJD), Gerstmann-Sträussler-Scheinker syndrome (GSS), and fatal familial insomnia (FFI) (*1–2*). Human PrDs can manifest in sporadic, genetic, or iatrogenic forms. Among these, sporadic CJD (sCJD) is the most prevalent form of human PrDs, constituting approximately 85%–90% of all PrD cases (*3–4*). The global morbidity for human PrDs is estimated at 1–2 individuals per million annually, with mortality invariably standing at 100% (*2–3*). Clinical manifestations of human PrDs can be diverse; however, rapid progressive dementia typically serves as the primary symptom. The definitive diagnosis of human PrDs currently relies on the neuropathological examination of biopsied brain tissue or postmortem analyses (*1–2,5*).

Recognition and diagnosis of human PrDs in China remained largely absent until the end of the 1980s due to its rarity. Prior to the implementation of the China National Surveillance for Creutzfeldt-Jakob Disease (CNS-CJD) in 2006, only a handful of Chinese CJD cases were reported in scholarly literature (*6–7*). The initiation of the CNS-CJD, however, led to an increase in diagnoses as hundreds of hospitals across China began to recognize and identify PrD cases (*8–10*).

Nonetheless, there was notable variance in both the number of participating hospitals and diagnosed PrD cases between different provincial-level administrative divisions (PLADs) in China (*9*). Utilizing CNS-CJD surveillance data, we conducted an analysis of the relevant factors pertaining to participating hospitals. This analysis was undertaken to evaluate the disparities in PrD recognition capacities across different PLADs.

METHODS

CNS-CJD

The development and execution of the CNS-CJD project has previously been discussed in depth (*10*). To summarize, the CNS-CJD initiative was officially launched in 2006. This project encompasses 12 provincial CDCs and 15 sentinel hospitals, spanning across 12 PLADs, including Beijing, Shanghai, Tianjin, Chongqing, Jilin, Shaanxi, Hubei, Guangdong, Guizhou, Anhui, Henan, and Xinjiang

(*9*–*10*). Surveillance data indicated that clinical records and samples from suspect patients were procured by local hospital clinicians, while pertinent epidemiological data were gathered by provincial CDC personnel. Compiled data and samples [including cerebrospinal fluid (CSF), blood, and brain tissue] were then forwarded to the Chinese CDC's national reference laboratory for CNS-CJD for lab testing and ultimate diagnosis.

Case Definition

The suspected cases of CJD referred to as CNS-CJD were identified and subtyped based on the diagnostic criteria released by the Chinese National Health Commission. This criteria framework was adapted from the diagnostic criteria for CJD developed by World Health Organization (WHO). Patient clinical and epidemiological data were gathered using specially designed questionnaires. A spectrum of clinical examination results were amassed, including magnetic resonance imaging (MRI), electroencephalography (EEG), and routine CSF biochemistry, along with laboratory tests such as CSF 14-3-3, CSF tau, CSF and skin real time-quaking induced conversion assay (RT-QuIC), and *PRNP* PCR and sequencing. A panel of experts consisting of neurologists, neuropathologists, epidemiologists, and laboratory staff were responsible for determining the interim or final diagnosis (*9*).

Data Collection

This study incorporated a total of 1,970 distinct PrD cases, comprising patients with sCJD and a variety of genetic PrDs (gPrD). Hospitals that reported diagnosed cases to CNS-CJD were identified as the referring hospitals in this investigation. Separate counts were maintained for the annual and cumulative totals of PrD cases reported from each hospital. The distribution of referring hospital numbers and their diagnosed PrD cases were established based on the varied PLADs.

Statistical Analysis

The differences in the numbers of the referring hospitals and the diagnosed PrD cases between surveillance and non-surveillance PLADs were assessed by two-tailed Student's t test using the SPSS 22.0 (International Business Machines Corporation, Armonk, New York, USA) statistical package. The data were presented as mean±standard deviation (SD).

RESULTS

The Number of Referring Hospitals for Human PrDs Increased Over the Duration of the Surveillance Years

This study enrolled a total of 1,970 human PrD cases of CNS-CJD from 2006 to 2019, encompassing sCJD, FFI, and various genotypes of gCJD and GSS. These PrD cases derived from 344 distinct hospitals across 29 of the 31 PLADs in Chinese mainland. Remarkably, 89% (308/344) of these referring hospitals represent Grade III class A medical institutions, the highest level according to Chinese standards for hospital classification. The annual tally of both the referring hospitals and the diagnosed PrD cases was compiled for the years 2006 through 2019. Concurrent with the uptick in diagnosed PrD cases was an increase in the number of referring hospitals throughout these surveillance years (Figure 1). The average number of referring hospitals during the first five years (2006–2010) and the second five years (2011–2015) were 28.2 and 64 respectively, this number increased to 107 in the most recent four years (2016–2019). This suggests that an increasing number of hospitals have been identifying and diagnosing human PrD cases over the surveillance period.

A Significant Number of PrD Cases Reported from a Small Subset of Hospitals

The referring hospitals were categorized based on the number of PrD cases they diagnosed (Table 1). Among these, 12.2% (42/344) reported and diagnosed ten PrD cases within the study period, collectively representing 70.0% (1,379/1,970) of all PrD cases. Leading the group was Beijing Xuanwu Hospital, which diagnosed the highest number of PrD cases (163). Moreover, ten additional hospitals referred between 40 and 99 PrD cases, distributed among Beijing (4 hospitals), Henan (2), Guangdong (1), Jilin (1), Shanghai (1), and Sichuan (1). An additional 31 hospitals reported between 10 and 39 cases. Despite this, the majority of the hospitals (263, accounting for 76.5%) reported merely one or a handful of PrD cases (less than 5).

The Referral Hospitals in China Unevenly Distributed Among the PLADs

We evaluated the diversity of the referring hospital

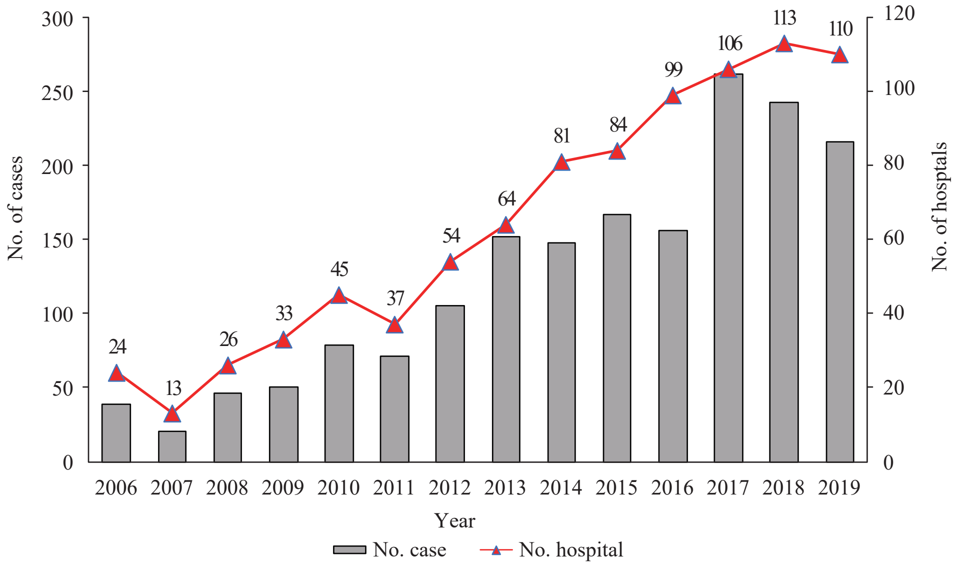

FIGURE 1. Annual number of referred hospitals and PrD cases from 2006 to 2019.
Note: Right Y-axis represents the number of referring hospitals (indicated by red triangles), while the Left Y-axis represents the number of PrD cases (depicted by gray columns).
Abbreviation: PrD=prion disease.

TABLE 1. Distribution of referring hospitals based on the number of diagnosed prion disease cases.

Case	>100	80–99	60–79	40–59	20–39	10–19	5–9	1–4	Total
No. of hospitals (%)	1 (0.3)	1 (0.3)	3 (0.9)	6 (1.7)	10 (2.9)	21 (6.1)	39 (11.3)	263 (76.5)	344
No. of cases (%)	163 (8.3)	95 (4.8)	215 (10.9)	287 (14.6)	262 (13.3)	285 (14.5)	255 (12.9)	408 (20.7)	1,970

distributions within the PLADs, based on the number of referring hospitals and the PrD cases reported in each PLAD. Table 2 indicates that Beijing had the highest number of referring hospitals and diagnosed PrD cases. During the study period, 41 hospitals from Beijing reported 546 PrD cases, constituting 11.9% of the referring hospitals and 27.7% of the total reported PrD cases. Five other PLADs reported equal to or more than 20 referring hospitals: Henan (26), Shanghai (21), Guangdong (21), Jiangsu (21), and Hebei (20). An additional seven PLADs had referring hospital numbers ranging from 10 to 19. The reported cases from these 13 PLADs represented 82.6% of all PrD cases (1,628 out of 1,970). While there was a strong correlation between the numbers of referring hospitals and diagnosed PrD cases, diversities were observed in several PLADs. For instance, Jiangsu and Hubei had a larger number of referring hospitals but a relatively small number of PrD cases, whereas Jilin, with fewer referring hospitals, reported a higher number of PrD cases.

Table 2 further delineates the distribution of hospitals in various PLADs in China that referred 10 or more PrD cases. Of the 29 PLADs reporting PrD cases, 19 had a range of hospitals referring at least 10 PrD cases. The most significant numbers of such hospitals were located in Beijing (11) and Shanghai (5), which reported 472 and 107 PrD cases, respectively. Two provinces, Shandong and Shaanxi, each had three hospitals referring 10 or more PrD cases, and five PLADs — Chongqing, Henan, Guangdong, Hebei, and Zhejiang — each had two hospitals doing the same. Among these, two hospitals in Henan reported notably higher case numbers, with 152 cases. In contrast, 10 PLADs had only one hospital referring 10 or more PrD cases, with the most cases reported in Jilin (49), Sichuan (47), and Fujian (28). These data highlight substantial variation in both the number of referring hospitals and those referring 10 or more PrD cases. Given its unparalleled medical resources, Beijing demonstrates its superior capacity for recognizing and diagnosing PrDs among the varied PLADs.

The Majority of Referring Hospitals Located in Provincial Capital Cities

The disparities in the number of referral hospitals

TABLE 2. Distribution of the numbers of total referring hospitals and the hospitals with 10 diagnosed PrD cases in PLADs.

PLADs	Total		≥10 cases	
	No. of hospitals (%)	No. of cases (%)	No. of hospitals (%)	No. of cases (%)
Beijing Municipality	41 (11.9)	546 (27.7)	11 (26.2)	472 (34.2)
Shanghai Municipality	21 (6.1)	146 (7.4)	5 (11.9)	107 (7.6)
Chongqing Municipality	10 (2.9)	72 (3.7)	2 (4.8)	44 (3.2)
Tianjin Municipality	9 (2.6)	48 (2.4)	1 (2.4)	30 (2.2)
Henan Province	26 (7.6)	205 (10.4)	2 (4.8)	152 (11.0)
Guangdong Province	21 (6.1)	146 (7.4)	2 (4.8)	89 (6.6)
Jiangsu Province	21 (6.1)	44 (2.2)	0 (0.0)	0 (0.0)
Hebei Province	20 (5.8)	62 (3.1)	2 (4.8)	33 (2.4)
Fujian Province	19 (5.5)	59 (3.0)	1 (2.4)	28 (2.0)
Zhejiang Province	18 (5.2)	72 (3.7)	2 (4.8)	45 (3.3)
Shandong Province	17 (4.9)	98 (5.0)	3 (7.1)	73 (5.3)
Hubei Province	13 (3.8)	31 (1.6)	0 (0.0)	0 (0.0)
Shaanxi Province	12 (3.5)	78 (4.0)	3 (7.1)	65 (4.7)
Sichuan Province	12 (3.5)	69 (3.5)	1 (2.4)	47 (3.4)
Xinjiang Uygur Autonomous Region	9 (2.6)	19 (1.0)	0 (0.0)	0 (0.0)
Guizhou Province	8 (2.3)	32 (1.6)	1 (2.4)	18 (1.3)
Anhui Province	8 (2.3)	28 (1.4)	1 (2.4)	12 (0.9)
Liaoning Province	8 (2.3)	21 (1.1)	0 (0.0)	0 (0.0)
Gansu Province	8 (2.3)	20 (1.0)	0 (0.0)	0 (0.0)
Jilin Province	6 (1.7)	58 (2.9)	1 (2.4)	49 (3.5)
Shanxi Province	6 (1.7)	16 (0.8)	0 (0.0)	0 (0.0)
Guangxi Zhuang Autonomous Region	6 (1.7)	6 (0.3)	0 (0.0)	0 (0.0)
Hunan Province	5 (1.5)	23 (1.2)	1 (2.4)	12 (0.9)
Jiangxi Province	5 (1.5)	23 (1.2)	1 (2.4)	10 (0.7)
Yunnan Province	5 (1.5)	21 (1.1)	1 (2.4)	12 (0.9)
Heilongjiang Province	3 (0.9)	15 (0.8)	1 (2.4)	10 (0.7)
Ningxia Hui Autonomous Region	3 (0.9)	6 (0.3)	0 (0.0)	0 (0.0)
Hainan Province	2 (0.6)	4 (0.2)	0 (0.0)	0 (0.0)
Inner Mongolia Autonomous Region	2 (0.6)	2 (0.1)	0 (0.0)	0 (0.0)
Total	344 (100)	1,970 (100)	42 (100)	1,379 (100)

Abbreviation: PLADs=provincial-level administrative divisions; PrD=prion disease.

and reported PrD cases between provincial capital cities and other cities received further analysis. Excluding four municipalities (Beijing, Shanghai, Tianjin, and Chongqing), 146 hospitals from the 25 provincial capital cities reported 947 PrD cases, while 117 hospitals from other cities reported 209 cases (Table 3). Although the overall ratio of referral hospitals in provincial capital cities to those in other cities was not significantly different (55.5% *vs.* 44.5%, *P*=0.359), the ratio of diagnosed PrD cases showed a significant disparity (81.9% *vs.* 18.1%, *P*=0.001). On average, the number of referral hospitals and PrD cases in the 25 provincial capital cities were 5.84 (range: 1–17 hospitals, median: 5) and 37.88 (range: 1–169 cases, median: 21), respectively. Considering the actual number of other prefecture-level cities (281 cities excluding the capital cities) in those 25 PLADs, the average number of referral hospitals was 0.41 (range: 0–17), and the average number of PrD cases was 0.74 (range: 0–36 cases). This discrepancy underlines the predominant role of provincial capital cities in identifying PrD patients.

TABLE 3. Comparison between provincial capital cities and other cities in terms of the number of referring hospitals and PrD cases.

PLADs	No of hospital (%)		No. of case (%)	
	Provincial capital city	Other cities	Provincial capital city	Other cities
Henan Province	9 (34.6)	17 (65.4)	169 (82.4)	36 (17.6)
Guangdong Province	17 (81.0)	4 (19.0)	140 (95.9)	6 (4.1)
Jiangsu Province	7 (33.3)	14 (66.7)	16 (36.4)	28 (63.6)
Hebei Province	4 (20.0)	16 (80)	36 (58.1)	26 (41.9)
Fujian Province	10 (52.6)	9 (47.4)	41(69.5)	18 (30.5)
Zhejiang Province	8 (44.4)	10 (55.6)	59 (81.9)	13 (18.1)
Shandong Province	6 (35.3)	11 (64.7)	64 (66.7)	32 (33.3)
Hubei Province	12 (92.3)	1 (7.7)	30 (96.8)	1 (3.2)
Shaanxi Province	8 (66.7)	4 (33.3)	74 (94.9)	4 (5.1)
Sichuan Province	5 (41.7)	7 (58.3)	59 (85.5)	10 (14.5)
Xinjiang Uygur Autonomous Region	7 (77.8)	2 (23.2)	14 (73.7)	5 (26.3)
Guizhou Province	6 (75.0)	2 (25.0)	30 (93.8)	2 (6.2)
Anhui Province	5 (62.5)	3 (37.5)	25 (89.3)	3 (10.7)
Liaoning Province	3 (37.5)	5 (62.5)	13 (61.9)	8 (38.1)
Gansu Province	6 (75.0)	2 (25.0)	18 (90.0)	2 (10.0)
Jilin Province	4 (66.7)	2 (33.3)	56 (96.6)	2 (3.4)
Shanxi Province	6 (100)	0 (0.0)	16 (100)	0 (0.0)
Guangxi Zhuang Autonomous Region	4 (66.7)	2 (33.3)	4 (66.7)	2 (33.3)
Hunan Province	3 (60.0)	2 (40.0)	21 (91.3)	2 (8.7)
Jiangxi Province	3 (60.0)	2 (40.0)	16 (69.6)	7 (30.4)
Yunnan Province	5 (100)	0 (0.0)	21 (100)	0 (0.0)
Heilongjiang Province	2 (66.7)	1 (33.3)	14 (93.3)	1 (6.7)
Ningxia Hui Autonomous Region	3 (100)	0 (0.0)	6 (100)	0 (0.0)
Hainan Province	2 (100)	0 (0.0)	4 (100)	0 (0.0)
Inner Mongolia Autonomous Region	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)
Total	146 (55.5)	117 (44.5)	947 (81.9)	209 (18.1)

Abbreviation: PLADs=provincial-level administrative divisions; PrD=prion disease.

A Greater Number of Referring Hospitals Found in the Surveillance PLADs Compared to the Non-surveillance PLADs

Evaluation of the numerical differences between referring hospitals and diagnosed PrD cases in both surveillance and non-surveillance PLADs was undertaken. A mean of 15.3 referring hospitals were counted in the 12 surveillance PLADs (range 6.0–41.0), above the average of the 17 non-surveillance PLADs (9.9 hospitals, range 2.0–21.0); however, the observed discrepancy did not reach statistical significance (P=0.073). Conversely, diagnosed PrD cases in surveillance PLADs presented a noticeable average increase, with 117.4 cases (range 31.0–516.0) compared to the 34.9 cases (range 2.0–98.0) of non-surveillance PLADs (P=0.028) (Figure 2A).

Assessing the historic data spanning 2006–2019, calculations of hospitals referring 10 cases and their corresponding PrD diagnoses were performed. Surveillance PLADs averaged 2.4 hospitals referring a minimum of 10 cases (range 0.0–11.0) and their corresponding average PrD diagnoses were 86.4 (range 0.0–472.0), significantly greater compared to non-surveillance PLADs. Non-surveillance PLADs averaged at 0.8 for hospitals referring 10 cases (range 0.0–3.0, P=0.042), with an average of 15.9 PrD diagnoses (range 0.0–78.0, P=0.036) (Figure 2B).

Moreover, within the timeframe of investigation, it was recorded that in 47.1% of non-surveillance PLADs

(8/17) and 16.7% (2/12) of surveillance PLADs, no hospital had diagnosed 10 cases. The results highlight a comparatively robust capacity in the recognition and diagnosis of PrDs within the surveillance PLADs.

DISCUSSION

In the present study, we have analyzed the annual- and geographic-distributions and case reporting frequencies of the hospitals diagnosed and referred human PrDs in China in the past 15 years. Accompanying with the increase of the annual diagnosed PrD cases, more and more hospitals referred PrD cases to CNS-CJD actively, particularly in the last four year that the numbers of referring hospitals are over 100 continually. Notably, some local and small hospitals (below Grade III) started to report PrD cases actively in recent years. It implies that the awareness and recognition of human PrDs in the medical institutions in China have been gradually improved in the past 15 years.

There is a notable disparity in the frequency of case reporting across referring hospitals, characterized by a majority of diagnosed PrD cases originating from a limited number of these institutions. The majority of PrD cases are referred by a select few — primarily university hospitals boasting robust neurology departments — amongst the top 20 referring hospitals. Conversely, the majority (over 75%) of referring hospitals reported a relatively low number of PrD cases (less than 5), with 168 (48.8%) of these hospitals having only reported a single case in the last 15 years. These findings suggest a significant variation in the recognition capacity for human PrDs among hospitals in China.

Our findings suggest a significant geographic disparity in the distribution of both referring hospitals and PrD cases. Expectedly, the eastern region of China records a higher number of referring hospitals and PrD cases than its western counterparts. The four municipalities directly governed by the central government — Beijing, Shanghai, Chongqing, and Tianjin — report high rates of referring hospitals and PrD cases. Notably, Beijing, the capital city, reports a significantly higher number with 4 out of the top 10 hospitals reporting the most cases situated there. Conversely, PLADs such as Inner Mongolia, Hainan, Ningxia, and Heilongjiang, located in the border regions and characterized by lower population density and underdeveloped economies, report fewer referring hospitals and/or PrD cases. Notably, the PLADs of Qinghai and Xizang have no medical institutions actively reporting any PrD cases. This geographic disparity, to some extent, reflects the variable

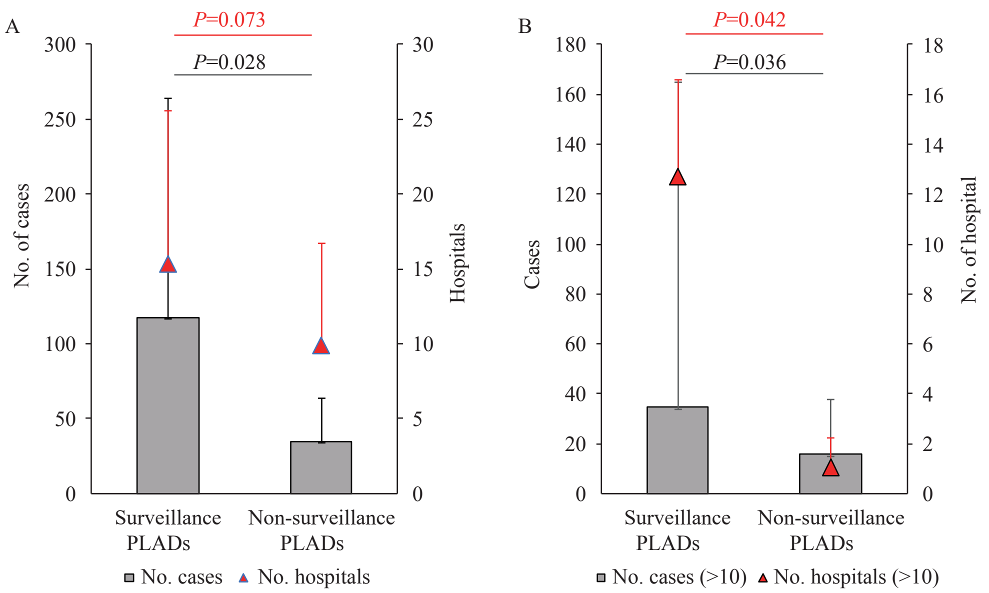

FIGURE 2. Comparison of the number of referring hospitals and PrD cases between CJD-surveillance and non-surveillance PLADs. (A) Total numbers. (B) Number of hospitals diagnosing 10 cases.
Note: Right Y-axis: number of referring hospitals (red triangle). Left Y-axis: number of PrD cases (grey column). *P* values indicating differences in hospital numbers (red) and case numbers (grey) between surveillance and non-surveillance PLADs are displayed above the graphs.
Abbreviation: PrD=prion disease; CJD=Creutzfeldt-Jakob disease; PLAD=provincial-level administrative division.

provincial-level capacity for recognizing human PrDs in China.

A prominent trend observed is the elevated detection of human PrD cases heavily concentrated in larger, central cities. Aside from the four municipalities, the incidence of reported PrD cases in provincial capital cities significantly surpasses the cumulative incidents from other cities. Aside from these four municipalities, the overwhelming majority of hospitals with at least ten reported PrD cases in PLADs are situated in provincial capitals. This disparity in PrD detection between major, central cities and smaller, outlying regions is strongly linked to variances in access to medical resources and economic proficiency. Predominantly, large, reputable hospitals — particularly university-affiliated hospitals — are located within provincial capital cities.

We have found a significant difference in the PrD recognition capacity between CJD surveillance and non-surveillance PLADs, especially notable during the first and second five-year periods of surveillance. In addition to the available medical resources, we attribute this disparity to the more established CJD surveillance activities, annual human PrD training courses and workshops, as well as relatively active academic exchanges concerning human PrDs and other neurodegenerative diseases, organized by various local entities. This significantly bolsters PrD recognition and diagnostic capacity within the surveillance PLADs. This is exceedingly pronounced in Beijing and Shanghai where all Grade III hospitals have been incorporated into their local CJD surveillance systems (*11*). Moreover, an increasing number of provincial CDCs and medical institutions from non-surveillance PLADs are being included in the annual workshops and other activities hosted by CNS-CJD in recent years. We believe this is a positive step towards enhancing PrD recognition capacity in these non-surveillance PLADs.

Despite significant improvements in PrD recognition capacity in China, largely due to the implementation of CNS-CJD since 2006, the yearly case count remains underestimated compared to data from numerous countries in Europe and North America (*12*–*14*). This is the case even in large, developed central cities. Even though the China CDC implemented a diagnostic protocol for CJD surveillance in 2006, and the National Health Commission issued diagnostic criteria for CJD in 2017, most PrD patients only receive their final diagnoses after being transferred multiple times between hospitals, typically from smaller local facilities to larger central institutions. As PrDs represent a rare set of neurological diseases lacking specific clinical manifestations, misdiagnoses are frequent (*15*). Increased awareness and recognition of human PrDs are warranted, particularly in smaller cities. Key strategies for improvement include the widespread promotion and implementation of CJD diagnostic criteria among clinicians, the sequential development of training programs on prions and PrDs for clinicians, public health personnel, and laboratory staff, and an emphasis on related scientific literacy and health education for the general public.

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Outbreak Reports

Dichloromethane-Induced Poisoning from Acrylic Paint Cleaner — Shenzhen City, Guangdong Province, China, 2023

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Summary

What is already known about this topic?

Dichloromethane (DCM) is a colorless and transparent organic solvent that commonly causes poisoning during occupational contact.

What is added by this report?

Unknown to teachers and students, they were utilizing an acrylic paint cleaner that contained DCM. At the time of the poisoning incident, the art room was occupied beyond its capacity with inadequate local ventilation. The primary cause of the incident was determined to be the students' inhalation of DCM during the cleaning process.

What are the implications for public health practice?

The unclear composition of environmental cleaning products available for purchase online presents a major obstacle for consumers trying to assess their toxicity. It is imperative that robust regulatory measures and proactive public education campaigns are implemented to mitigate instances of poisoning.

At 20:00 on June 9, 2023, the Nanshan CDC in Shenzhen City received an incident report from a local hospital. It stated that several students from a nearby school began experiencing discomfort after cleaning an art room with an acrylic paint cleaner. Five of these students were treated in the emergency department upon suspicion of organic solvent poisoning. In response, the CDC swiftly assembled a team comprised of professional staff and members of the Shenzhen Field Epidemiology Training Program to investigate the incident. An amalgamation of epidemiological inquiries, laboratory tests, and field hygiene investigations indicated that the poisoning was due to the use of an acrylic paint cleaner containing dichloromethane (DCM) during the cleaning process, and subsequent inhalation of the DCM.

INVESTIGATION AND RESULTS

Investigators established the incidence of exposure in this incident via multiple routes: consultation with the hospital's outpatient records, interviewing relevant doctors, school physicians, class teachers, as well as students, and the distribution of questionnaires to the affected individuals. The case definition criteria were as follows: Exposure was defined as any faculty member or student who entered the art room from 15:10 to 15:50 on June 9, 2023. Suspected cases were those presenting with symptoms such as dizziness, headache, nausea, vomiting, or upper respiratory tract irritation within a short time following the exposure, given that other causes could be excluded. Clinically diagnosed cases were those amongst the suspected pool that received a diagnosis of "accidental poisoning of chemical products and harmful substances".

As of June 12, the CDC had identified 44 exposed individuals with a total of 34 cases, involving 28 suspected and 6 clinically diagnosed infections. All identified cases were from the same classroom, boasting an equal distribution of males to females and an age range of 10–11 years. The attack rate stood at 77.3% (34/44). As delineated in Table 1, the predominant clinical symptoms were dizziness (58.8%), headache (55.9%), nausea (50.0%), fatigue (32.4%), eye irritation (29.4%), and upper respiratory tract mucosal irritation (26.5%). Symptoms became evident within 20 minutes of commencing cleaning procedures, with the earliest narrative of symptoms observed at 15:20 on June 9, and the latest by 16:35 on the same day. For four of the affected students, the specific time of symptom onset was not ascertainable, reflecting an average incubation period (median) of 15 minutes. Symptom duration varied between 10 minutes and two days (Figure 1). The clinical manifestations and corresponding duration for the six clinically diagnosed cases are illustrated in Supplementary Table S1 (available in https://weekly.chinacdc.cn/). However, no

TABLE 1. The clinical manifestations of 34 cases of acrylic paint cleaner poisoning in a school in Shenzhen City, Guangdong Province, China, 2023.

Symptoms	No. of cases	Percentage (%)
Dizziness	20	58.8
Headache	19	55.9
Nausea	17	50.0
Fatigue	11	32.4
Irritation in the eyes	10	29.4
Mouth and nose irritation/pharyngeal foreign body sensation	9	26.5
Abdominal pain	9	26.5
Vomiting (≥1 time)	7	20.6
Skin irritation (burning and numbness)	6	17.6
Syncope	2	5.9
Cold limbs	1	2.9
Rapid heartbeat	1	2.9

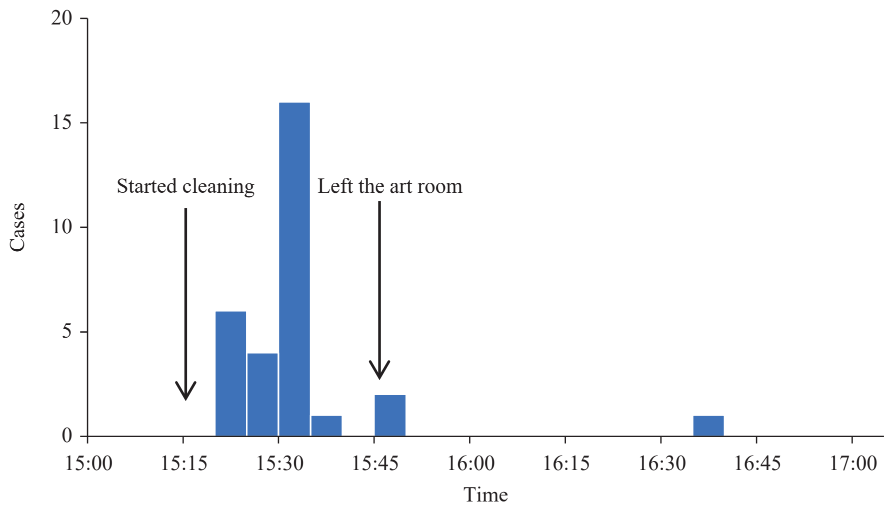

FIGURE 1. The onset times of 30 cases of acrylic paint cleaner poisoning in a school in Shenzhen City (5-minute intervals), Guangdong Province, China, 2023.

abnormalities were observed in blood electrolytes, liver function, myocardial enzymes, routine blood tests, or electrocardiograms. Following oxygen administration and milk consumption, symptomatic relief was reported among all affected cases, with no severe cases or fatalities noted.

A field investigation, alongside interviews with the art teacher and students, unveiled the specifics of the cleaning process, the ventilation conditions of the room, and the source of the paint cleaner used. Around 15:15 on June 9, students initiated the cleanup process in the art room, applying the paint cleaner to stains on the sink and floor, subsequently scouring them with steel wool balls. Roughly five minutes into the process, the room field with a pungent odor and accompanying irritants. Shortly thereafter, several students began reporting symptoms of discomfort, notably dizziness and nausea.

The field hygienic investigation revealed that the art room, situated on the third floor of Building B, encompasses a north-south oriented space measuring 10.8 meters in length and 8.6 meters in width, totaling an area of 92.9 square meters. The room's ceiling height reaches 3.3 meters.

The south-facing side of the ground-level corridor features two doors and three windows, beneath which sit rows of cupboards with hinged door panels. These cupboards held several plastic paint bottles. On the north side, a single window overlooks a rectangular hand-washing sink fitted with three faucets. The art room's ceiling features a north-south oriented timber framework, with split wall-mounted air conditioning units installed in both the northeast and northwest ceiling corners. The air conditioner's outlet is located approximately 2.9 meters above the floor level.

At the time of the investigated incident, the art room's air conditioner was operating. Both the front and back doors were open, whereas the classroom windows were closed. Most students were crouched to clean the floor, situating their respiratory belts roughly 50 cm above the floor and away from the air conditioner vents. Despite the congregation of individuals, the site's overall ventilation was deemed adequate.

However, a localized poor ventilation issue was observed in the vicinity of the hand-washing sink, which sits away from the door. The details of this scenario can be seen in Figure 2.

A total of eight bottles of an inferior cleaning product were purchased from an online retailer. During the incident at hand, five and a half bottles, equivalent to 5.5 liters, were utilized. Furthermore, the retailer only supplied sky-blue, flimsy gloves devoid of any product identification on the exterior packaging; there were no masks or comprehensive instructions provided for chemical safety.

Professionals collected 20 mL of acrylic paint cleaner on site for qualitative analysis of its volatile components and to determine its peak area percentage. Meanwhile, simulated field air sampling was performed. Briefly, after pouring approximately 20 mL of the acrylic paint cleaner in the sink and the ground for 10 minutes, 6 L of air samples were collected in activated carbon tubes for the detection of the presence

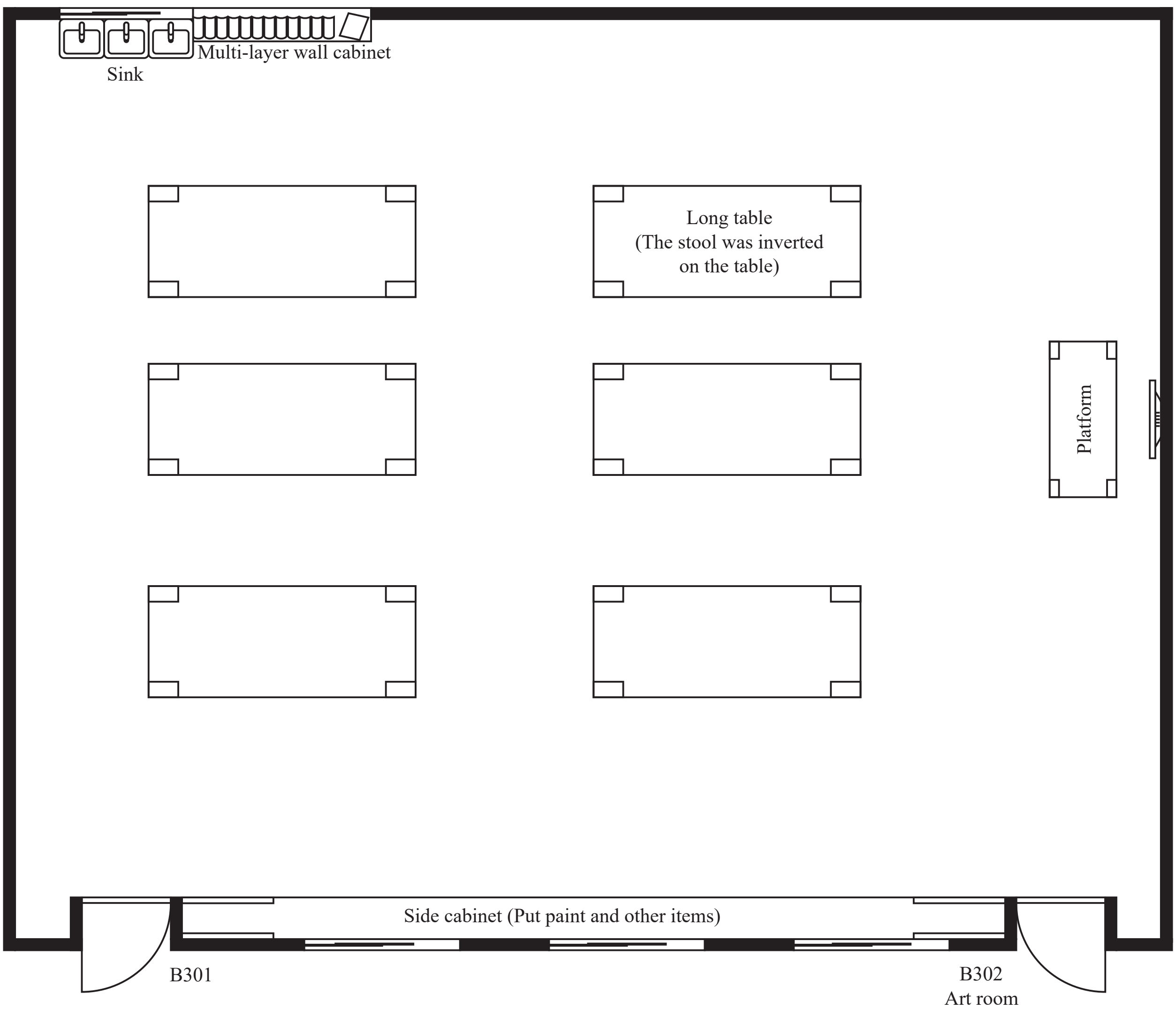

FIGURE 2. The art classroom floor plan in a school in Shenzhen City, Guangdong Province, China, 2023.

of chemical toxicants. The analysis revealed that the peak area percentage of air was 25.37%, while the peak area percentage of DCM was 73.14% (Supplementary Table S2, available in https://weekly.chinacdc.cn/). The primary toxic substance detected in the air samples was DCM.

DISCUSSION

Masked as eco-friendly cleaning solutions, online paint cleaner retailers are selling counterfeit and substandard products. These vendors neglect to provide adequate safety instructions for the chemical products, and they often fail to supply appropriate protective equipment for consumers. This negligence increases the risk of poisoning when unsuspecting consumers utilize these products. Therefore, corresponding government departments ought to intensify their investigations and manage the unlawful sale of chemicals occurring on online retail platforms. Available art pigments and pigment cleaners on the market must include explicit instructions regarding their composition and concentration, along with appropriate usage cautions. Pertinent authorities need to amplify public outreach and education initiatives to enhance public awareness on the topic of chemical safety.

Instances of acute and chronic DCM poisoning are not uncommon (*1*–*3*) and can potentially be fatal (*4*–*5*). Research has suggested that DCM could be linked to an increased risk of diseases such as liver cancer, pediatric germ cell tumors, teratomas, acute myeloid leukemia, and bile duct cancer (*6*–*8*). In Europe, the sale and utilization of paint strippers containing DCM levels of 0.1% or higher have been prohibited (*9*), however, no similar regulation exists in China.

The application of DCM as a paint remover in the art field has not been extensively studied. Through qualitative analysis of volatile organic components in acrylic paint cleansers, it has been discovered that DCM represents a peak area percentage of 73.14%. When users such as art students directly pour DCM, which has a volatile nature at room temperature, onto surfaces like sinks and floors, it accelerates the volatilization process.

This practice, combined with inadequate ventilation in the art studio and direct inhalation of DCM by the students during cleaning, led to this poisoning incident. It's noteworthy this incident took place in an educational institution, implicating the environmental health of the school and the safety of its students, and thus, warrants particular concern.

Conflicts of interest: No conflicts of interest.

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SUPPLEMENTARY MATERIALS

SUPPLEMENTARY TABLE S1. The clinical manifestations and their duration in six clinically diagnosed cases of poisoning in a school in Shenzhen, China, 2023.

Case No.	Sex	Age (years)	Symptoms	Duration (hours)
1	Female	11	**Dizziness**, headache, nausea, vomiting, pharyngeal foreign body sensation, numbness in the right hand, and rapid heartbeat	48
2	Male	11	**Dizziness**, nausea, vomiting, abdominal pain, unsteady gait, and syncope	3
3	Male	10	**Dizziness**, headache, fatigue, nausea, vomiting, **eye and nose irritation**, pharyngeal foreign body sensation, abdominal pain, syncope	3.5
4	Male	11	**Dizziness**, fatigue, nausea, **eye and nose irritation**, and abdominal pain	5.5
5	Female	10	Dizziness, headache, **fatigue**, eye irritation, skin irritation, and cold limbs	48
6	Male	10	**Dizziness**, irritation of the mouth and nose, and numbness of the right hand	0.4

Note: Bold font indicates the first symptom of that particular case.

SUPPLEMENTARY TABLE S2. The peak area percentage of volatile components in the acrylic paint cleaner.

No.	Retention time (min)	Peak area	Peak area percentage (%)	Name of component
1	4.658	183,050,585	25.37	Air
2	5.074	2,845,801	0.39	Water
3	8.087	1,718,782	0.24	Dimethoxymethane
4	8.587	527,680,423	73.14	Dichloromethane
5	11.036	91,043	0.01	N-hexane
6	20.018	6,120,725	0.85	Dimethylformamide

Note: The peak area of each component was normalized to obtain its percentage.

Notifiable Infectious Diseases Reports

Reported Cases and Deaths of National Notifiable Infectious Diseases — China, July 2023*

Diseases	Cases	Deaths
Plague	0	0
Cholera	4	0
SARS-CoV	0	0
Acquired immune deficiency syndrome†	4,854	1,749
Hepatitis	151,809	148
Hepatitis A	1,053	0
Hepatitis B	125,116	34
Hepatitis C	22,326	114
Hepatitis D	14	0
Hepatitis E	2,620	0
Other hepatitis	680	0
Poliomyelitis	0	0
Human infection with H5N1 virus	0	0
Measles	97	0
Epidemic hemorrhagic fever	344	1
Rabies	9	11
Japanese encephalitis	33	0
Dengue	1,604	0
Anthrax	51	1
Dysentery	4,684	0
Tuberculosis	66,989	330
Typhoid fever and paratyphoid fever	657	0
Meningococcal meningitis	3	0
Pertussis	2,767	0
Diphtheria	0	0
Neonatal tetanus	2	0
Scarlet fever	2,237	0
Brucellosis	9,164	1
Gonorrhea	10,104	0
Syphilis	58,247	2
Leptospirosis	25	0
Schistosomiasis	5	0
Malaria	289	1
Human infection with H7N9 virus	0	0
Influenza	48,848	0
Mumps	9,280	0
Rubella	99	0

Continued

Diseases	Cases	Deaths
Acute hemorrhagic conjunctivitis	13,425	0
Leprosy	36	0
Typhus	169	0
Kala azar	30	0
Echinococcosis	342	0
Filariasis	0	0
Infectious diarrhea§	119,375	0
Hand, foot and mouth disease	457,212	0
Total	962,794	2,244

* According to the National Bureau of Disease Control and Prevention, coronavirus disease 2019 (COVID-19) is not included.

† The number of deaths of acquired immune deficiency syndrome (AIDS) is the number of all-cause deaths reported in the month by cumulative reported AIDS patients.

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

The numbers of cases and cause-specific deaths refer to data recorded in National Notifiable Disease Reporting System in China, which includes both clinically-diagnosed cases and laboratory-confirmed cases. Only reported cases of the 31 provincial-level administrative divisions in Chinese mainland 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 are 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 National Notifiable Disease Reporting System according to information verification or field investigations by local CDCs.

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