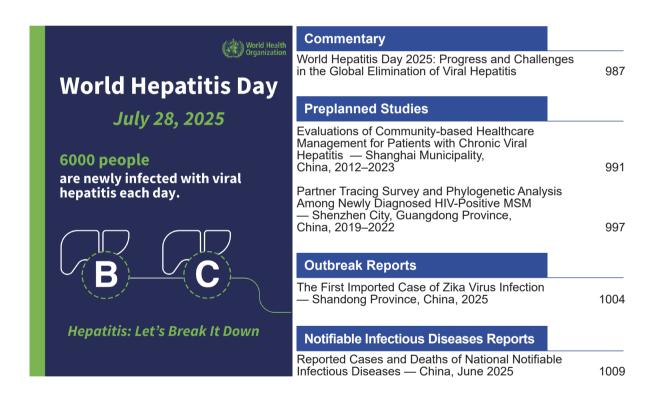
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Commentary

World Hepatitis Day 2025: Progress and Challenges in the Global Elimination of Viral Hepatitis

Minghui Li^{1,2,3,#}; Weihua Cao¹; Yao Xie^{1,2,3}

ABSTRACT

The year 2025 marks the 15th anniversary of World Hepatitis Day, a milestone that has witnessed remarkable progress in global viral hepatitis prevention and treatment. This article systematically examines the establishment and evolution of World Hepatitis Day, emphasizing the latest achievements in hepatitis control through 2025. Current data demonstrate that global hepatitis B vaccine coverage has surpassed the 90% target, while a cumulative 12,748,000 hepatitis C patients received direct-acting antivirals (DAAs) treatment from 2014 to 2023. Despite these advances, persistent challenges, including suboptimal diagnosis rates and pronounced regional disparities continue to impede progress toward the 2030 elimination the objectives. from Drawing most recent epidemiological data, this article presents targeted recommendations to accelerate global elimination efforts.

Background and Establishment of World Hepatitis Day

Viral hepatitis remains a major global public health threat. Five principal types of hepatitis viruses designated A, B, C, D, and E — each cause liver disease but differ significantly in transmission routes, clinical severity, and prevention strategies. Chronic infections from hepatitis B and C viruses represent the leading causes of cirrhosis, hepatocellular carcinoma, and viral hepatitis-related mortality. According to World Health Organization (WHO) estimates (1), approximately 254 million people were living with chronic hepatitis B in 2022, with 50 million affected by hepatitis C (Figure 1). The estimated number of new viral hepatitis infections declined from 3 million in 2019 to 2.2 million in 2022 (2-3), including 1.2 million hepatitis B cases and nearly 1 million hepatitis C cases. By the end of 2022, nearly 7 million patients were receiving hepatitis B treatment, while 12.5 million had undergone hepatitis C therapy (2–3). Nevertheless, viral hepatitis still caused around 1.3 million deaths annually (Figure 1) (4), with low- and middle-income countries bearing the heaviest burden — accounting for over 85% of global hepatitis-related mortality.

July 28, 2025 marks the 15th anniversary of World Hepatitis Day. World Hepatitis Day was established through Resolution WHA63.18 at the 63rd World Health Assembly in 2010. July 28 was chosen to honor Dr. Baruch Blumberg's birthday, the scientist who discovered the hepatitis B virus. The establishment of World Hepatitis Day aimed to unify regional hepatitis awareness campaigns under a single global observance. This decision carried profound significance: 1) Consolidating previously fragmented regional hepatitis awareness initiatives; 2) Creating a platform for coordinated global action; 3) Catalyzing the inclusion of hepatitis elimination in the Sustainable Development Goals (SDGs). Today, World Hepatitis Day stands as 1 of the most influential global public health advocacy campaigns, engaging over 100 countries annually. The theme for World Hepatitis Day 2025 is "Hepatitis: Let's Break It Down", which urges immediate measures to eliminate economic, societal, and structural obstacles — including stigma — that hinder the eradication of hepatitis and prevention of liver cancer.

Key Strategies and Activities of World Hepatitis Day Across Different Phases

Awareness Building Phase (2010–2015) This initial phase concentrated on establishing foundational education initiatives and comprehensive awareness campaigns. The primary objective was to create a unified global advocacy framework that could effectively disseminate hepatitis knowledge through diverse communication channels. A pivotal achievement occurred in 2012 when WHO launched its inaugural Global Hepatitis Strategy, formally incorporating hepatitis prevention and control

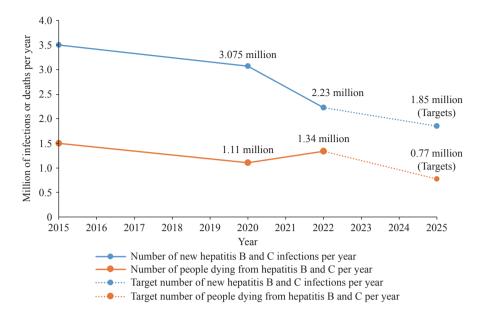


FIGURE 1. Trends in incidence and mortality of hepatitis B and C, 2015–2025.

measures into the international health agenda.

Strategy Implementation Phase (2016–2021) The Global Health Sector Strategy established ambitious 2030 elimination targets, catalyzing significant global progress. Key achievements during this period included: 1) Global three-dose hepatitis B vaccine coverage increased substantially from 82% to 87%; 2) Direct-acting antivirals (DAAs) demonstrated remarkable efficacy with cure rates exceeding 95% for C; 3) Thirty countries developed hepatitis comprehensive national elimination plans aligned with the 2030 goals of achieving a 90% reduction in new infections and 65% reduction in mortality (5).

Acceleration Phase (2022-2025)The period following 2021 witnessed unprecedented momentum in global hepatitis elimination efforts (Figure 2), marked by several transformative breakthroughs: 1) WHO's updated treatment guidelines in 2023 streamlined clinical protocols and enhanced treatment accessibility; 2) Egypt achieved a historic milestone by becoming the first country to receive WHO elimination certification in 2024; 3) Gavi's expanded funding cycle launched in 2024 propelled global hepatitis B vaccine coverage beyond the critical 90% threshold by 2025 (6). The cumulative impact of these initiatives is reflected in treatment scale-up: between 2014 and 2023, an estimated 12,748,000 hepatitis C patients received DAAs treatment (7).

Current Progress

Enhanced Prevention Efforts Global hepatitis B

surface antigen (HBsAg) prevalence among children under 5 years has achieved the 2025 target of \leq 0.5% (2,8); universal coverage of safe injection practices has been attained (9); mother-to-child transmission prevention demonstrates success rates exceeding 97% (8).

Improved Treatment Accessibility DAAs treatment costs have decreased to \$75 per capita in low- and middle-income countries (4); novel hepatitis B therapeutics, including RNA interference (RNAi) therapies, are advancing through Phase III clinical trials; cumulative global hepatitis C treatments continue to increase annually. By 2025, the estimated cumulative number of individuals treated for hepatitis C worldwide reaches approximately 23–25 million.

Innovation and Scale-up of Diagnostic Technologies

High-sensitivity point-of-care testing (POCT) tools have gained widespread adoption, substantially improving screening efficiency in primary care settings. For instance, the enhanced sensitivity of HBsAg testing technologies has established this marker as a critical surveillance indicator for hepatitis B infection in pediatric populations. Multiple countries have implemented comprehensive national hepatitis registries and databases, integrating epidemiological surveillance data with treatment records. These systems facilitate real-time monitoring of elimination progress through validated mathematical models (e.g., the WHO framework), providing robust evidence for policy refinement and strategic adjustments.

Strengthened Policy Support An increasing number of countries are implementing comprehensive national

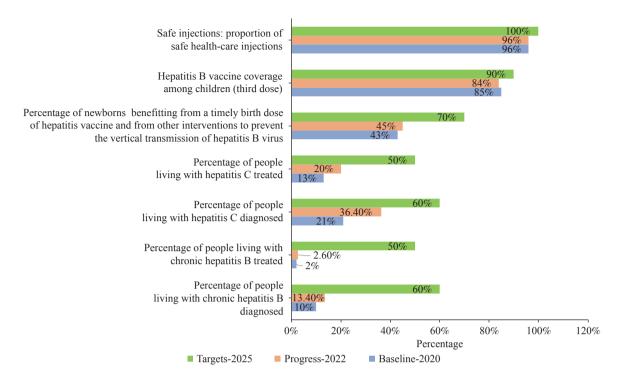


FIGURE 2. Progress towards global viral hepatitis targets.

elimination plans; hepatitis testing is progressively being incorporated into national health insurance coverage systems.

Existing Challenges

Suboptimal Diagnosis Rates Global diagnosis rates remain critically below established targets. As of 2022, only 13% of chronic hepatitis B cases worldwide had received a diagnosis (2). Between 2015 and 2022, merely 36% of hepatitis C cases were identified globally (3), representing a substantial shortfall from the 2030 target of 90%. Low-income countries face particularly severe diagnostic capacity constraints, with polymerase chain reaction (PCR) testing available in only a limited number of healthcare facilities. Testing access remains inequitable: rural and marginalized populations encounter significant barriers to diagnostic services, with cost, geographic distance, and social stigmatization serving as primary obstacles.

Uneven Treatment Coverage Treatment accessibility geographic demonstrates stark and disparities. While coverage rates remain relatively high in high-income countries, patients in low- and middleincome countries (LMICs) face substantial barriers to medication access. By the end of 2022, only 3% of chronic hepatitis B patients globally had received antiviral therapy. Similarly, just 20% of hepatitis C underwent curative patients treatment during

2015–2022. Primary barriers include prohibitive drug pricing, supply chain disruptions, and insufficient capacity within primary healthcare delivery systems.

Inadequate Adoption of Innovative Technologies

Novel diagnostic tools demonstrate limited penetration at the primary care level. Portable technologies such as POCT and dried blood spot (DBS) sampling remain poorly integrated into national procurement systems, with healthcare facilities continuing to rely on traditional laboratory-based approaches. Digital followup systems show inadequate coverage: Long-term patient management frequently depends on paperbased records, resulting in elevated loss-to-follow-up rates. Artificial intelligence (AI)-assisted screening tools have not been incorporated into primary healthcare systems. Technology deployment faces significant barriers: Constraints in electrical infrastructure, internet connectivity, and training resources impede the implementation of innovative technologies in resource-limited settings.

Recommendations for the Future

The theme for China's 2025 World Hepatitis Day — "Societal Co-governance for Hepatitis Elimination" — addresses core challenges through targeted solutions: 1) Diagnosis-Treatment Gap: Establishing an integrated 'Screening-Diagnosis-Treatment-Management' system through efficient

screening protocols and tiered clinical management. 2) Immunization Protection Gap: Implementing precision interventions targeting high-risk adult Therapy populations. 3) Innovative Accelerating functional cure protocols by expediting novel drug approvals and establishing clinical cure clinic networks. 4) Stigma Elimination & Social Mobilization: Advancing the 'co-governance' paradigm through multi-stakeholder engagement. 5) Policy Safeguards: Integrating hepatitis B virus (HBV) innovative therapies and hepatocellular carcinoma (HCC) early detection into national insurance coverage, establishing unified electronic hepatitis registries for real-time surveillance, and prioritizing grassroots resource allocation.

Aligned with the global 2025 theme "Hepatitis: Let's Break It Down", strategic recommendations emphasize dismantling structural barriers through 1) Innovative Screening Approaches: Establishing coordinated networks between community self-testing and centralized screening, promoting community selftesting technologies, optimizing centralized screening processes, and implementing a "three-step screening" collaborative mechanism (community initial screening, institutional fine screening, and hierarchical management); 2) Optimized Treatment Strategies: Advancing from pan-genotypic drugs to hepatitis B cure, optimizing pan-genotypic DAAs for hepatitis C research and application, and developing innovative functional cure protocols for hepatitis B; 3) Improved Resource Allocation: Constructing distribution systems for regional collaboration and international cooperation, establishing mechanisms for regional drug reserves and sharing, and innovating international cooperation through expanded drug patent pools, North-South cooperation production models, crossborder medical collaboration networks, and integrated diagnostic and treatment assistance; 4) Enhanced Technological Innovation: Developing rapid diagnostic equipment suitable for primary care settings, including portable non-invasive diagnostic devices, microfluidic chips and biosensing technology for grassroots applications, and artificial intelligence-assisted diagnostic systems; 5) Robust Monitoring and Evaluation: Constructing real-time dynamic monitoring systems, establishing multidimensional effectiveness evaluation frameworks, implementing quality continuous improvement mechanisms through "evaluation-feedback-optimization" cycles, ensuring close integration between monitoring, evaluation, and policy adjustments.

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Preplanned Studies

Evaluations of Community-based Healthcare Management for Patients with Chronic Viral Hepatitis — Shanghai Municipality, China, 2012–2023

Hong Ren¹,&; Di Xu²,&; Lingxiao Qu³,&; Xin Shen¹; Kaiyun Chen¹; Qichao Pan¹; Jiayu Hu¹; Yang Shi¹; Jian Li²,#; Xin Chen¹,#

Summary

What is already known about this topic?

Current strategies for chronic viral hepatitis prevention and control include immunization, prevention of mother-to-child transmission, expanded testing, antiviral therapy, and national drug price negotiations. To advance high-quality, integrated prevention and treatment services, a decentralized service delivery approach may be beneficial.

What is added by this report?

The chronic viral hepatitis community-based healthcare management program in Shanghai comprehensive service packages across 4 categories encompassing 10 distinct interventions, including epidemiological investigation, health education, free dispensing testing, community services, immunization to family caregivers. The enrolled patients increased substantially from baseline, and antiviral treatment utilization rates reached 64.5% and 58.2% in 2019 and 2023 from 24.5% in 2012. Concurrently, abnormality rates for hepatitis B virus deoxyribonucleic acid (HBV DNA), aminotransferase (ALT), total bilirubin (TBIL), and hepatic fibrosis indices decreased significantly. The 2023 aMAP score demonstrated a significant reduction in hepatocellular carcinoma risk among patients under management. Additionally, community dispensing services were accessed by 14.1% (2019) and 18.2% (2023) of enrolled patients.

What are the implications for public health practice?

The community-based healthcare management program could effectively decentralize hepatitis-related testing and treatment services, and create a favorable environment for the viral hepatitis elimination efforts.

ABSTRACT

Introduction: Current strategies for chronic viral

hepatitis prevention and control include immunization, prevention of mother-to-child transmission, expanded testing, antiviral therapy, and national drug price negotiations. To achieve this effectively, Shanghai has implemented a community-based pilot program that integrates public health and clinical care for chronic viral hepatitis management.

Methods: This study evaluated the effectiveness of Shanghai's community-based healthcare program at three time points (2012, 2019, and 2023), assessing key indicators including antiviral treatment rates and disease status changes and risk of hepatocellular carcinoma. Data were managed using EpiData 3.1, with descriptive statistics and chi-square tests performed using SPSS 29.0.

Results: The study enrolled 1,478, 1,901, and 7,714 patients in 2012, 2019, and 2023, respectively. During the management period, the number of enrolled patients increased substantially from baseline. The antiviral treatment rates in 2019 and 2023 reached 64.5% and 58.2%, with both significantly higher than the baseline rate of 24.5% in 2012. Concurrently, abnormality rates for hepatitis B virus deoxyribonucleic acid (HBV DNA), alanine aminotransferase (ALT), total bilirubin (TBIL), and fibrosis indices decreased significantly in 2019 and 2023. The 2023 aMAP score further revealed a decline in hepatocellular carcinoma risk among managed patients (32.2% vs. 26.3%). With enhanced community healthcare capacity, 14.1% (2019) and 18.2% (2023) of patients accessed community dispensing services, aligning with the strategy to decentralize testing and treatment for disease elimination.

Conclusions: Community-based healthcare management for chronic hepatitis in Shanghai provides patients with decentralized hepatitis-related testing and treatment services, creating an effective environment for chronic viral hepatitis prevention and control and would favorable for the viral hepatitis elimination efforts.

To reduce the burden of disease caused by viral hepatitis, the World Health Organization (WHO) adopted the Global Health Sector Strategy on Viral Hepatitis 2016-2021 (GHSS) in 2016, which explicitly set out to achieve "a 90% reduction in incidence (95% for Hepatitis B virus and 80% for Hepatitis C virus) and 65% reduction in mortality by 2030, compared with a 2015 baseline" (1). In response to this goal, integrating the Hepatitis B vaccine (HepB) for children into the Expanded Programme on Immunization (EPI) (2) and the prevention of motherto-child transmission (MTCT) have reduced the HBsAg carrier rate in China noticeably Additionally, "China Viral Hepatitis Prevention and Control Program (2017-2020)" and "National Action Plan for Eliminating Hepatitis C as a Public Health Threat (2021-2030)" were issued in 2017 and 2021, respectively (4). The National Reimbursement Drug List (NRDL) of healthcare insurance incorporated regular direct-acting antiviral agents (DAAs) (4). To deliver high-quality services, the WHO recommended providing hepatitis patients with accessible tests and treatments through decentralization of care to lowerlevel facilities at this stage (5).

To standardize the management of patients with chronic hepatitis and reduce the morbidity and mortality of hepatitis-related diseases, the communitybased healthcare management pilot called "Love Deliver" was initiated in 2012 in Shanghai. Based on reported information from the Nationally Notifiable Disease Report System (NNDRS), community physicians provided service packages of 4 categories measures, including epidemiological investigation, disinfection, health education, longtime follow-up, free testing, and immunization to family caregivers who had given informed consent. In 2019, with the achievement of national health insurance negotiation and Volume-based procurement (VBP) both causing a significant reduction in drug prices of hepatitis, the expansion of basic medical care comprising hepatitis-related testing, referral, extended dispensing, and treatment in the community health centers (CHCs) was added to the pilot service package (Figure 1). By the end of 2023, 7,714 chronic hepatitis patients were contracted in the real-world study. This study aimed to evaluate the effectiveness of community-based healthcare management for chronic hepatitis patients, with public health and clinical care

Investigation

- 1- Epidemiological investigation, disinfection, and long-time follow up
- 2- Psychological Measurement



Care

- 3- Free testing for patients
- 4- Free testing for high risk population
- 5- Free adult immunization



The Community-based Healthcare Management for Patients with Chronic Viral Hepatitis

Health education

- 6- Patient education
- 7- High risk population education



Treatment

- 8- Hierarchical medical system
- 9- Decentralized treatment with community dispensing
- 10-National negotiation drugs and banded purchasing in community



FIGURE 1. The concrete measures of community-based healthcare management, 2012–2023.

Note: The community-based healthcare management for patients with chronic viral hepatitis comprised 10 measures in 4 categories. Measures 1–7 were executed over the past decade, and measures 8 to 10 of "Treatment" were added to the pilot service package between 2019 and 2023. Since 2020, the addition of first-line antiviral medications for hepatitis B patients and DAAs for hepatitis C patients to the list of medicines covered by the national medical insurance system has significantly improved their accessibility and affordability.

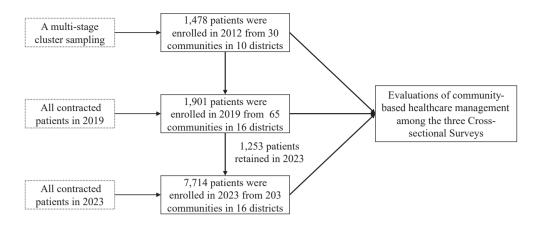


FIGURE 2. Flow chart and sampling methodology for three cross-sectional surveys on the community-based healthcare management.

integration, and to provide a basis for the development of public health service strategies for chronic hepatitis B and C eliminations.

Data was obtained from three cross-sectional surveys of a real-world study conducted in Shanghai, where patients could join or withdraw according to their preferences (Figure 2). In 2012, viral hepatitis patients from 30 communities were randomly selected from 5 central urban districts and 5 suburban districts using a multi-stage cluster sampling method, which served as the baseline as described in the "Study of disease burden of chronic hepatitis B and C patients in Shanghai based on Bronfenbrenner's ecological systems theory: a community-based survey" and explained in the Disclosure statement (6). For the 2019 and 2023 surveys, patient information was drawn entirely from the "Love Deliver" pilot follow-up database, with all community-managed patients enrolled. All three used identical questionnaires demographics, health status, treatment information, and the utilization of antiviral drugs and Hepatitis B vaccination among caregivers. The age-male-ALBIplatelets (aMAP) score was identified as the most prospective of all hepatocellular carcinoma (HCC) prediction models (7). The database was established using the EpiData Association (version 3.1 for Windows; Odense, Denmark), with descriptive statistical analysis and chi-square tests performed using SPSS Statistics (version 29.0 for Windows; IBM, Armonk, US). All statistical tests were two-sided, with a P value of <0.05 considered statistically significant.

In this study, 1,478, 1,901, and 7,714 patients were recruited in 2012, 2019, and 2023, respectively. The mean age of patients across the three survey points increased progressively from 51.5±13.3 years in 2012 to 57.2±12.2 years in 2019, and 58.7±13.4 years in

2023 (Table 1).

Among the 7,714 patients followed in 2023, 6,956 had chronic hepatitis, 32 had cirrhosis, and 16 had HCC, indicating a significant decline in cirrhosis and HCC rates compared to 2012 (ratio 124.7:8.6:1.0). Antiviral treatment rates increased substantially from a baseline of 24.5% in 2012 to 64.5% in 2019 and 58.2% in 2023. Concurrently, abnormality rates for HBV DNA, ALT, TBIL, and fibrosis indices decreased significantly in 2019 and 2023. The 2023 aMAP scores revealed fewer individuals in high-risk HCC groups compared to 2019. Following the implementation of community dispensing services in 2019, 173 patients (14.1%, 173/1,226) in 2019 and 818 patients (18.2%, 818/4,486) in 2023 utilized these services. Additionally, hepatitis B vaccination rates among family members of hepatitis B patients increased compared to baseline levels (Table 1).

Furthermore, 1,253 patients managed in 2019 continued in the program through 2023. These patients showed significant improvements in clinical parameters, including reduced abnormality rates for HBV DNA (11.2% vs. 25.5%), ALT (3.4% vs. 10.7%), TBIL (2.8% vs. 5.7%), and fibrosis indices (15.3% vs. 18.0%), as well as higher rates of hepatitis B vaccination and community dispensing service utilization after five years of follow-up care. Analysis of patients lost to follow-up revealed that 10% (66/648) had died between 2019 and 2023 according to the Vital Statistics System. Additionally, 63% (410/648) of surviving patients who were lost to follow-up primarily resided in urban areas and may have relocated to their hometowns due to the coronavirus disease 2019 (COVID-19) pandemic.

The study consistently demonstrated the therapeutic

TABLE 1. Comparing the demographics and laboratory test results of chronic hepatitis patients in 2012, 2019, and 2023.

Variables	2012, n (%)	2019, n (%)	2023, n (%)	X ²	P
Overall	1,478	1,901	7,714		
Gender				17.376	<0.001
Male	951 (64.3)	1,155 (60.8)	3,935 (51.0)		
Female	527 (35.7)	746 (39.2)	3,779 (49.0)		
Age, years/mean±SD	51.5±13.3	57.2±12.2	58.7±13.4	21.558	<0.001
<40	314 (21.2)	195 (10.3)	891 (11.6)		
40–49	283 (19.1)	288 (15.1)	1,095 (14.2)		
50–59	493 (33.4)	512 (26.9)	1,584 (20.5)		
≥60	388 (26.3)	906 (47.7)	4,144 (53.7)		
HBV DNA [†]				199.374	<0.001
Positive	233 (53.3)	82 (25.5)	454 (20.8)		
Negative	204 (46.7)	240 (74.5)	1729 (79.2)		
anti-HCV [†]				262.614	<0.001
Positive	78 (15.3)	65 (13.3)	558 (25.6)		
Negative	432 (84.7)	424 (86.7)	1,622 (74.4)		
Alanine aminotransferase (ALT) [†]				583.812	<0.001
Positive	413 (27.9)	166 (10.7)	436 (6.6)		
Negative	1,065 (72.1)	1,385 (89.3)	6,170 (93.4)		
⁻otal Bilirubin (TBIL) [†]				150.485	<0.001
Normality	834 (85.6)	1,477 (94.3)	5,136 (95.1)		
Mild jaundice	125 (12.9)	87 (5.5)	252 (4.7)		
Moderate jaundice	13 (1.3)	1 (0.1)	9 (0.2)		
Severe jaundice	2 (0.2)	1 (0.1)	1 (0.0)		
iver Ultrasound [†]				548.594	<0.001
Normality	904 (61.2)	975 (82.0)	3,634 (84.9)		
Mild fibrosis	534 (36.1)	136 (11.4)	477 (11.2)		
Severe fibrosis	28 (1.9)	40 (3.4)	108 (2.5)		
Nodular changes	12 (0.8)	38 (3.2)	60 (1.4)		
Hepatitis B vaccination of caregivers				610.153	<0.001
Full vaccination	369 (25.0)	535 (28.1)	3,820 (49.5)		
Partial vaccination	753 (50.9)	587 (30.9)	1,943 (25.2)		
Unvaccinated	312 (21.1)	615 (32.4)	1,951 (25.3)		
Unknow	44 (3.0)	164 (8.6)	0 (0)		
reatment				655.103	<0.001
Yes	362 (24.5)	1,226 (64.5)	4,486 (58.2)		
No	1,116 (75.5)	675 (35.5)	3,228 (41.8)		
Community dispensing services*	, ,	. ,	, ,	11.418	<0.00
Prescriptions dispensed in CHCs	1	173 (14.1)	508 (11.3)		
Others	1	0 (0)	310 (6.9)		
No	1	1,053 (85.9)	3,668 (81.8)		
aMAP score [†]		. (/		10.146	0.006
Low risk	1	142 (25.0)	1,371 (25.4)		3.500
Medium risk		243 (42.8)	2,610 (48.3)		
High risk	1	183 (32.2)	1,418 (26.3)		

Abbreviation: aMAP=age-male-ALBI-platelets; CHCs=community health centers; SD=standard deviation.

^{*} Indicates the proportion of patients receiving various "community dispensing services" among those on antiviral therapy.

[†] Refers to patients who received relevant laboratory testing as part of management services.

effectiveness of antiviral therapy across all three surveys. Using the 2023 results as a reference, treated patients showed higher HBeAg (χ^2 =33.996, P<0.05) and HCV RNA (χ^2 =20.664, P<0.05) positivity rates compared to untreated patients. Conversely, HBV DNA positivity rates were significantly lower in treated patients (χ^2 =19.924, P<0.05). The aMAP scores indicated that treated patients had a lower proportion of individuals at high risk for HCC (χ^2 =13.982, P<0.05). Overall, aMAP scores revealed that 1,899 (24.6%) of managed patients remained at high risk for HCC, highlighting the importance of continued HCC surveillance and treatment services for this population.

DISCUSSION

With the continuous refinement of the pilot strategy and gradual expansion of services, the communitybased healthcare management package has been delivered to 7,714 patients across 203 communities in all 16 districts of Shanghai by 2023. Our findings indicate that antiviral treatment rates among contracted patients in 2019 and 2023 increased significantly from baseline levels. However, a slight decline was observed as the number of contracted patients expanded to approximately four times that of 2019. Additionally, in 2023, community physicians received enhanced training on the Guidelines for the Prevention and Treatment of Chronic Hepatitis B (version 2022), improving their knowledge of antiviral therapy drugs compared to 2019 (8). This may have led community physicians to exclude patients taking hepatoprotective drugs or other non-antiviral medications. Despite a twelve-year aging trend among patients (from 2012 to 2023), their clinical conditions improved. For instance, abnormality rates in laboratory indices including HBV DNA, ALT, TBIL, and fibrosis were reduced. The likelihood of developing HCC, as indicated by aMAP scores, also decreased. These results were consistent with outcomes observed in the 1,253 patients followed in both 2019 and 2023, suggesting that long-term management can increase treatment rates and lead to effective clinical improvements for contracted patients.

In contrast to baseline (2012), when antiviral treatment and testing services were primarily provided by specialists, a significant portion of contracted patients accepted prescriptions from community general practitioners after project implementation. Community dispensing, which provided high reimbursement rates, demonstrated that

decentralization can be effectively aligned with broader healthcare strategies. Moreover, free adult vaccination rates for caregivers were significantly higher than at baseline, demonstrating that community-contracted management can enhance adult immunization and basic public health services for caregivers. In the Global Hepatitis Report 2024, WHO proposed four strategic directions and ten actions to advance a public health approach in low and middle-income countries (9) with a key direction being the delivery of high-quality, evidence-based, people-centered services. healthcare management pilot in Shanghai, which decentralized management of patients to community health centers, provided patients with extended prescriptions, accessible and affordable drugs, HCV RNA testing, and free hepatitis B vaccination for caregivers. This community-based health services package effectively responds to the WHO's decentralization strategy (5).

Compared to untreated patients, those receiving antiviral therapy in the community demonstrated lower HBV-DNA positivity rates and reduced risk of developing HCC, particularly among males under 60 years of age. Previous clinical studies have confirmed that antiviral therapy effectively delays liver fibrosis progression and reduces HCC incidence in patients with HBV and HCV (10), findings that our study further validates. Additionally, patients who do not currently meet treatment criteria should be monitored annually for disease progression, ALT levels, and HBV DNA levels as recommended by clinical guidelines. Timely intervention should be provided for patients who have previously deferred treatment (11).

Several limitations of this study should be acknowledged. First, this research was conducted in a real-world setting where patients could freely enter or exit the management program in pursuit of higherquality services. Natural mortality, excess deaths, and relocation (60% of lost patients were not local residents) due to the COVID-19 pandemic resulted in approximately 34% attrition between 2019 and 2023. While survivor bias likely exists, its magnitude is difficult to estimate. Second, although laboratory results were obtained using standardized thresholds established by secondary and tertiary medical institutions, minor variations may have occurred depending on test reagent brands and methodologies. Third, the quasi-ecological design of this study makes it difficult to determine whether the service packages played a decisive role compared to the broader medical environment. In the next phase, our research team plans to compare disease progression, complication incidence, treatment outcomes, and quality of life between managed and unmanaged patients reported in NNDRS to more accurately evaluate the effectiveness of community health management services.

In conclusion, the community-based healthcare management pilot for patients with chronic viral hepatitis — which includes community dispensing, nationally negotiated drugs, volume-based procurement at the community level, hepatitis-related testing, and free hepatitis B vaccination for adults provides a reference model for establishing decentralized testing, care, and treatment approaches for chronic viral hepatitis patients. This model effectively combines access to care and treatment with a comprehensive public health approach.

Disclosure statement: This study shared part of the results from 2012 with another study published in Chinese entitled "Study of disease burden of chronic hepatitis B and C patients in Shanghai based on Bronfenbrenner's ecological systems theory: community — based survey" authored by Dr. Hong Ren. That study attempted to establish a novel public health strategy for chronic hepatitis patients based on community engagement and communication between medical institutions and public health departments. In contrast, the current study evaluated the effectiveness of a community-based healthcare management model for chronic hepatitis patients between 2012 and 2023, with an extension of basic medical care added in 2019 that comprised hepatitis-related testing, referral, extended dispensing, and treatment in the community.

Conflicts of interest: No conflicts of interest.

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Preplanned Studies

Partner Tracing Survey and Phylogenetic Analysis Among Newly Diagnosed HIV-Positive MSM — Shenzhen City, Guangdong Province, China, 2019–2022

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Summary

What is already known about this topic?

Partner tracing (PT) represents an established public health strategy for identifying undiagnosed individuals with human immunodeficiency virus (HIV) infection and contributes to controlling sustained HIV transmission.

What is added by this report?

Partner tracing among newly diagnosed HIV-infected men who have sex with men (MSM) demonstrates effectiveness in identifying undiagnosed infected individuals, with regular sexual partners showing higher likelihood of HIV-positive detection. However, phylogenetic analysis revealed that only a small proportion of epidemiologically linked pairs exhibited genetic linkage.

What are the implications for public health practice?

Sustained implementation and broader application of partner tracing may serve a critical role in HIV epidemic control by facilitating early identification of undiagnosed infections and interrupting potential transmission chains. Integrating partner tracing with phylogenetic analysis enhances the capacity to distinguish actual transmission chains from coincidental behavioral associations, thereby improving transmission linkage identification accuracy and informing more targeted intervention strategies.

ABSTRACT

Introduction: In China, the proportion of men who have sex with men (MSM) among newly diagnosed human immunodeficiency virus (HIV) infections is continuously increasing. This study aimed to identify undiagnosed HIV-infected patients in Shenzhen MSM through partner tracing (PT) and to explore potential transmission linkages using phylogenetic analysis.

Methods: From 2019 to 2022, newly diagnosed HIV-positive MSM were recruited as index cases to participate in PT by convenience sampling. Data were collected through offline questionnaires and the National HIV/AIDS Surveillance Database. Phylogenetic analysis using the maximum likelihood method was conducted based on HIV Pol region gene sequences to determine genetic associations.

Results: Of the 486 index cases, a total of 579 sexual partners were traced, of whom 19.9% tested positive for HIV. Among these HIV-positive partners, 83.9% were newly diagnosed infections, and 33.3% were recent infections. Only 8.9% of epidemiologically linked index cases — HIV-positive partner pairs showed genetic associations. Index cases with regular partners were significantly more likely to identify HIV-positive partners [adjusted odds ratio (a*OR*)=1.81; 95% confidence interval (*CI*): 1.02–3.23].

Conclusion: PT is effective in identifying undiagnosed HIV infection and is recommended for further promotion in the MSM population. However, only parts of the epidemiologically linked infected pairs also exhibited genetic association. Therefore, combining PT with phylogenetic analysis can help to more accurately identify the actual transmission network and inform more targeted intervention strategies.

Men who have sex with men (MSM) represent the population at highest risk for human immunodeficiency virus (HIV) infection, with the proportion of newly diagnosed HIV cases attributed to homosexual transmission steadily increasing in China. Surveillance data reveal that homosexual transmission accounts for more than 60% of new HIV cases in Shenzhen. Understanding partnership networks is essential for identifying transmission links among

MSM and disrupting potential transmission chains. Partner tracing (PT) serves as a behavioral surveillance strategy that encourages HIV-infected individuals to refer their sexual partners for HIV testing and treatment (1). Research has demonstrated that PT increases HIV testing rates and condom use among key populations (2). More importantly, PT can identify undiagnosed infections before further transmission occurs and detect potential clusters of cases before they expand (3). To identify additional undiagnosed HIVpositive MSM and explore transmission associations, study implemented PΤ combined phylogenetic analysis among newly diagnosed individuals.

From 2019 to 2022, we recruited newly diagnosed HIV-positive MSM in Shenzhen through convenience sampling to participate in PT. We employed three PT modalities — passive, contractual, or provider notification — to trace sexual partners and provide HIV testing services. After the initial tracing round, HIV-positive sexual partners continued to participate as index cases for a second round of PT. We collected data through offline questionnaires and the China Comprehensive HIV/Acquired Immunodeficiency Syndrome (AIDS) Prevention and Control Data Information System.

We identified recent infections using the HIV-1 limiting-antigen avidity enzyme immunoassay. Sequence acquisition and HIV-1 subtyping methods followed protocols described in previous studies (4). We constructed a sexual partner network using Cytoscape (version 3.10.1, Cytoscape Consortium, Santiago, Chile). We built phylogenetic trees using the Maximum Likelihood (ML) method based on the Kimura 2-parameter model in MEGA (version 6.0, Mega Limited, Auckland, New Zealand) software, with 1,000 bootstrap replicates. We considered sequences that clustered with bootstrap values greater than 95% as genetically linked. We performed statistical analysis using the chi-square test and binary logistic regression.

Between 2019 and 2022, a total of 4,880 newly diagnosed HIV-positive MSM were identified in Shenzhen, of whom 486 participated in PT as index cases. The demographic characteristics of the index cases did not differ significantly from those of the overall population (*P*>0.05) (Table 1). Among the 475 index cases who successfully referred sexual partners, 579 partners were identified, with 19.9% (115/579) testing HIV-positive. Subsequently, 9.6% (11/115) of the HIV-positive sexual partners agreed to serve as new index cases for the second round of PT, referring an

additional 13 sexual partners, of whom 23.1% (3/13) tested HIV-positive. The complete sexual contact network comprised 614 edges and 1,067 cases, with 593 individuals (475 index cases and 118 sexual partners) confirmed as HIV-infected MSM. Among the 118 HIV-positive sexual partners, 83.9% (99/118) were newly diagnosed cases. Of the 108 HIV-positive sexual partners whose samples were available for recent infection analysis, 33.3% (36/108) were determined to have recent infections. Logistic regression analysis revealed that index cases with regular sexual partners (aOR=1.81, 95% CI: 1.02, 3.23) were significantly more likely to have HIV-positive sexual partners identified through tracing (Table 2).

Pol gene sequences were successfully obtained from 92.2% (448/486) of index cases. The predominant HIV-1 subtypes were CRF07 BC (48.4%, 217/448), CRF01 AE (28.3%, 127/448), and CRF55 01B (16.3\%, 73/448), with other subtypes comprising 6.9% (31/448). The subtype distribution among index cases did not differ significantly from that of the overall HIV-positive MSM population (P>0.05). Among the 121 contact pairs traced between 119 index cases and 118 HIV-positive sexual partners, pol sequences were obtained for 83.5% (101/121) of pairs. However, only 8.9% (9/101) of these epidemiologically linked pairs demonstrated genetic linkage in addition to their behavioral associations. The 101 index cases who successfully traced HIV-positive sexual partners showed the following subtype distribution: 51.5% CRF07 BC, 26.7% CRF01 AE, 11.9% CRF55 01B, and 9.9% other subtypes, which did not differ significantly from the overall HIV-positive MSM population (P>0.05). Genetic linkage rates varied substantially by HIV-1 subtype: 7.7% (4/52) for CRF07_BC-infected index cases, 3.7% (1/27) for CRF01 AE-infected cases, 25.0% (3/12)CRF55_01B-infected cases, and 10.0% (1/10) for other subtypes (Figure 1). Fisher's exact test revealed index cases infected with that CRF55 01B demonstrated significantly higher rates of genetic association with their HIV-positive sexual partners compared to those infected with CRF07_BC and CRF01_AE (*P*=0.034).

DISCUSSION

Following extensive behavioral interventions, the MSM population in Shenzhen has demonstrated declining trends in both HIV incidence and clustering rates within molecular transmission networks (4). By

TABLE 1. Demographic characteristics of index cases and total newly diagnosed HIV-infected MSM from 2019 to 2022.

Variable	Total newly diagnosed HIV-infected MSM, n (%)	Index cases, n (%)	P
Age (years)			0.155
16–25	1,456 (29.8)	130 (26.7)	
≥26	3,424 (70.2)	356 (73.3)	
Census registration			0.308
Shenzhen City	811 (16.6)	88 (18.1)	
Guangdong Province except Shenzhen City	936 (19.2)	103 (21.2)	
Others*	3,133 (64.2)	295 (60.7)	
Ethnicity			0.525
Han	4,552 (93.3)	457 (94.0)	
Non-Han	328 (6.7)	29 (6.0)	
Education			0.093
Below senior high school	1,228 (25.2)	102 (21.0)	
Senior high school or technical secondary school	1,539 (31.5)	154 (31.7)	
College or university	2,113 (43.3)	230 (47.3)	
Marital status			0.190
Unmarried	3,940 (80.7)	383 (78.8)	
Divorced or widowed	370 (7.6)	33 (6.8)	
Married	570 (11.7)	70 (14.4)	
Recent infection			0.187
Yes	1,612 (35.2)	174 (38.3)	
No	2,965 (64.8)	280 (61.7)	
HIV subtype			0.144
CRF01_AE	987 (26.0)	127 (28.3)	
CRF07_BC	1,881 (49.6)	217 (48.4)	
CRF55_01B	553 (14.6)	73 (16.3)	
Others	375 (9.9)	31 (6.9)	

Abbreviation: HIV=human immunodeficiency virus; MSM=men who have sex with men.

2022, the HIV-positive rate among MSM in Shenzhen reached 2.78%, substantially lower than the 5.4% rate reported in national MSM sentinel surveillance data. However, the positive rate among sexual partners identified through PT reached 19.9% in this study, significantly exceeding rates from MSM surveillance conducted through respondent-driven sampling (5.2%) or time-location sampling (2.8%) during the same period in Shenzhen (P<0.001). These findings demonstrate that PT represents a highly effective method for detecting HIV-positive MSM with compared superior efficiency conventional to surveillance approaches. The substantial proportion of new diagnoses (83.9%) among HIV-positive partners further underscores PT's effectiveness in identifying previously undiagnosed HIV-infected MSM. These results strongly support the broader implementation

and expansion of PT across diverse settings, which would significantly contribute to achieving the first 95% target of the UNAIDS strategy.

Consistent with previous research (5), we observed a higher proportion of HIV positivity among regular sexual partners of index cases, which likely reflects behavioral and psychological factors. Stronger emotional bonds, greater mutual trust, and reduced perceived infection risk characterize these relationships. In certain contexts, condom use may be perceived as indicating mistrust, thereby increasing the likelihood of unprotected sexual encounters. Additionally, the and continuity inherent in regular stability partnerships may create cumulative risk effects, where frequent and prolonged unprotected sexual activity in the absence of consistent protective measures substantially increases overall infection probability.

^{*} Provinces and cities other than Guangdong Province.

China CDC Weekly

TABLE 2. Sociodemographic and behavioral characteristics of index cases successfully traced to HIV-positive sexual partners.

Variable	Successfully traced to sexual	Index cases successfully traced to HIV-positive sexual partners		_ P aOR
	partners, <i>n</i> (<i>N</i> =486)	n	%	- 「 (95% C
Age (years)				0.873
16–25	128	31	24.2	
≥26	353	88	24.9	
Census registration				0.961
Shenzhen	88	22	25.0	
Guangdong except Shenzhen	102	24	23.5	
Others*	295	73	24.7	
Ethnicity				0.197
Han	457	109	23.9	
Non-Han	29	10	34.5	
Education				0.734
Below senior high school	101	22	21.8	
Senior high school or technical	154	40	26.0	
secondary school College or university	227	57	25.1	
Employment status	221	31	25.1	0.591
Employed	400	96	24.0	0.591
	86	23	26.7	
Unemployed	60	23	20.7	0.374
Annual income (10,000 CNY)	00	24	26.7	0.374
<60,000	90			
60,000–120,000	251	56	22.3	
>120,000	111	32	28.8	0.540
Residence time in Shenzhen (years)	05	0	04.0	0.518
≤0.5	25	6	24.0	
0.6–1.0	23	5	21.7	
1.1–2.0	66	12	18.2	
>2.0	330	88	26.7	
Marital status				0.441
Unmarried	379	89	23.5	
Divorced or widowed	33	9	27.3	
Married	69	21	30.4	
Method of finding sexual partners				0.862
Offline	37	10	27.0	
Online	294	73	24.8	
Both	105	24	22.8	
Orug use				0.448
Yes	37	11	29.8	
No	431	104	24.1	
Number of sexual partners				0.086
≤2	142	40	28.2	
3–5	288	65	22.6	

Continued

Variable	Successfully traced to sexual partners, n (N=486)	Index cases successfully traced to HIV-positive sexual partners		_ P	aOR
		n	%	- •	(95% CI)
6–9	34	12	35.3	-	
≥10	22	2	9.1		
With regular sexual partners				0.041	
Yes	222	63	28.4		1.81 (1.02–3.23)
No	106	19	17.9		1
Condomless anal intercourse				0.755	
Yes	209	53	25.4		
No	249	60	24.1		
Recent infection				0.437	
Yes	174	46	26.4		
No	280	65	23.2		

Abbreviation: aOR=adjusted odds ratio; CI=confidence interval; CNY=Chinese Yuan.

A striking finding of this study is the remarkably low proportion of genetic linkage between index cases and their HIV-positive sexual partners, which was substantially lower than previously reported in Zhejiang Province (8.9% vs. 50.8%) (6). Several factors may account for this significant discrepancy. Shenzhen, as China's largest migrant city, had only 16.6% of HIV-positive MSM in this study being local residents. Previous research has demonstrated that HIV epidemics in Shenzhen are predominantly driven by the migrant population (7). High population mobility substantially increases individuals' exposure to diverse sexual networks and elevates the likelihood of acquiring HIV from genetically unrelated sources, resulting in fragmented transmission chains and disrupted social networks. Additionally, 67.5% of cases in this study were identified as late diagnoses with CD4 counts below 350 cells/µL, suggesting that many infections occurred more than four years earlier (8), likely prior to migration to Shenzhen. In chronic HIV infections, the absence of proofreading mechanisms during prolonged viral replication leads to the accumulation of genetic mutations, which may obscure detectable genetic relatedness even when true transmission has occurred. Furthermore, 70.8% of index cases reported having more than three sexual partners in the past six months, substantially increasing the probability that both the index case and their HIVpositive partners acquired infections independently from different sources. Moreover, the widespread use of online dating platforms — reported by over 90% of index cases — facilitates casual and transient sexual encounters (9), potentially leading to partnerships

between individuals infected by unrelated sources who are not part of the same transmission chain. The fragile and anonymous nature of these relationships also impedes effective partner tracing and mutual reporting, thereby limiting the identification of transmission links. Nonetheless, when index cases were infected with CRF55_01B, a regional hotspot strain originating from the Shenzhen MSM community (10), they demonstrated significantly higher likelihood of genetic linkage with their HIV-positive sexual partners. This finding suggests that PT may be more effective in detecting local transmission networks.

This study presents two primary limitations. First, we employed convenience sampling for participant recruitment. Although comparisons kev demographic characteristics between our study sample and the target population revealed no statistically significant differences, the potential for selection bias cannot be entirely eliminated, which may limit the generalizability of our findings. Second, our analysis utilized Sanger sequencing methodology, which lacks the capability to detect multiple concurrent infections. This technical constraint may compromise the accuracy of genetic linkage assessments and could potentially underestimate the complexity transmission dynamics within the study population.

In conclusion, partner tracing demonstrates significant effectiveness in identifying undiagnosed HIV infections and remains a cornerstone strategy for HIV prevention and control efforts. To maximize overall efficiency, partner tracing should be integrated with complementary surveillance approaches. Furthermore, partner tracing must be combined with

^{*} Provinces and cities other than Guangdong Province.

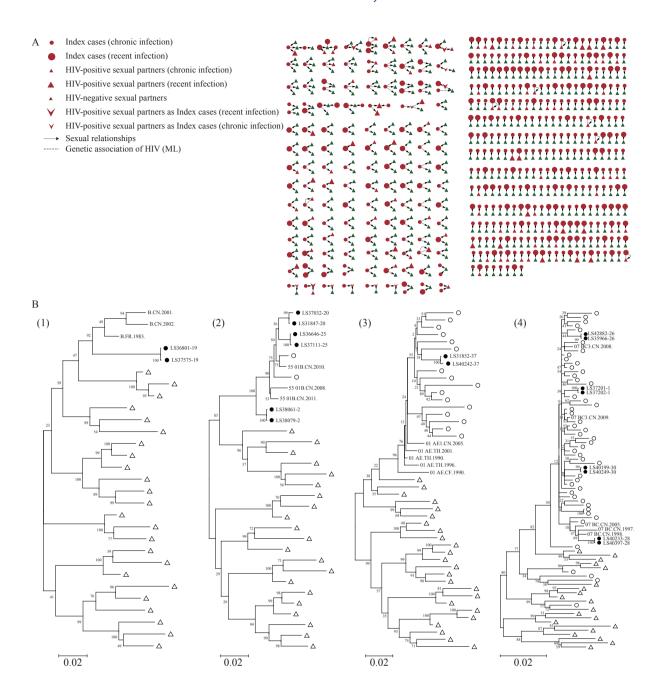


FIGURE 1. Social network of index cases and their partners, with a phylogenetic analysis of HIV-positive partners. (A) Sexual network of Index cases of traced partners and sexual partners; (B) ML tree of subtype B; (C) ML tree of CRF55_01B; (D) ML tree of CRF01_AE; (E) ML tree of CRF07_BC.

Note: For (B)–(E), ML trees were created with the same HIV subtype of index case-HIV-positive partner pairs. \bullet means with both epidemiologic and genetic association; \circ means with only epidemiologic association, and \triangle means reference sequences of subtype A, B, C, D, F, and G.

Abbreviation: HIV=human immunodeficiency virus; ML=maximum likelihood.

both epidemiologic and molecular evidence to accurately infer transmission associations and assess local HIV prevalence patterns, ensuring that transmission dynamics are precisely characterized and intervention strategies appropriately targeted.

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Outbreak Reports

The First Imported Case of Zika Virus Infection — Shandong Province, China, 2025

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Summary

What is already known about this topic?

Zika virus (ZIKV) is transmitted primarily through mosquito vectors, including *Aedes albopictus* and *Aedes aegypti*, both of which are distributed across multiple provinces in China. Approximately 80% of ZIKV infections remain asymptomatic, while symptomatic cases typically manifest as mild, self-limiting illnesses lacking pathognomonic features. Common clinical presentations include maculopapular rash, low-grade fever, conjunctivitis, arthralgia, and myalgia.

What is added by this report?

The clinical manifestations of ZIKV infection are nonspecific and may closely mimic other febrile illnesses, complicating differential diagnosis. This study documents the first laboratory-confirmed ZIKV infection case in Shandong Province. The patient exhibited fever accompanied by extensive subcutaneous petechiae, predominantly distributed across the chest and upper extremities.

What are the implications for public health practice?

This investigation provides comprehensive epidemiological analysis and phylogenetic characterization of a ZIKV infection case imported from Thailand. In accordance with China's Border Health and Quarantine Law, international port cities must strengthen surveillance and diagnostic testing for imported infectious diseases. For cases presenting with diagnoses, healthcare providers prioritize obtaining detailed 30-day travel histories to evaluate potential exposure risks of imported infectious diseases.

ABSTRACT

Introduction: On March 20, 2025, a suspected Zika virus (ZIKV) case departed Thailand and flew to Nanning Wuxu International Airport before transiting to Jinan. Upon receiving notification, local CDCs

immediately initiated comprehensive epidemiological investigations, laboratory testing, and preventive control measures.

Methods: We collected urine, sputum, and blood samples from the patient for analysis. Quantitative real-time reverse-transcription polymerase chain reaction (qRT-PCR) was employed to detect ZIKV nucleic acid. Metagenome Next-Generation Sequencing (mNGS) was performed on the urine sample to obtain complete viral genome sequences. Phylogenetic analysis was subsequently constructed using the obtained sequences to determine the origin, genotype, and mutation profile of this imported case.

Results: The qRT-PCR analysis confirmed ZIKV presence in the patient's urine, sputum, and serum samples. The mNGS successfully generated the complete ZIKV genome sequence. Phylogenetic analysis demonstrated that the ZIKV strain belonged to the Asian lineage, exhibiting 99.57% nucleotide homology with a ZIKV strain from Bangkok, Thailand (GenBank accession no. OR264645.1).

Conclusion: Based on the patient's epidemiological history, clinical presentation, and nucleic acid test results from multiple specimens, this case was confirmed as the first imported ZIKV infection documented in Shandong Province, with the infection source traced to Thailand.

On March 21, 2025, the Shandong CDC received an assistance request from Guangxi CDC regarding a suspected ZIKV infection case in a male patient. Upon receiving this notification, Shandong CDC, Jinan CDC, and Tianqiao District CDC immediately initiated case verification procedures, conducted comprehensive epidemiological investigations, and collected sputum, urine, and blood specimens from the patient. Laboratory analysis of the collected samples was performed by Shandong CDC, yielding positive

results for ZIKV nucleic acid. Subsequently, on March 23, 2025, China CDC provided official confirmation of the patient's ZIKV infection status.

Investigation and Results

On February 9, 2025, this 68-year-old male patient traveled alone to Bangkok, Thailand. On March 20, he departed from Thailand and flew to Nanning Wuxu International Airport before connecting to Jinan City, Shandong Province. During thermal screening at the airport, his body temperature measured 37.4°C, and subcutaneous hemorrhagic spots were observed on his chest and arms. He exhibited no arthralgia, myalgia, rash, headache, conjunctival congestion, facial flushing, chest erythema, or neurological symptoms. During his stay in Thailand, the patient reported no sexual activities or blood transfusions, though his history of mosquito bites remained unknown. The patient subsequently returned to his residence in Jinan City on March 21.

On March 20, 2025, airport personnel collected a throat swab on-site at Nanning Airport, which yielded negative results for both the severe acute respiratory syndrome coronavirus 2 antigen test and rapid dengue virus test. Subsequently, throat swabs and blood samples were collected and sent to the Guangxi International Travel Healthcare Center for further validation. On March 21, laboratory demonstrated that the patient tested positive for ZIKV through quantitative real-time reverse-transcription polymerase chain reaction (qRT-PCR). On March 22, urine, sputum, and blood samples from this patient were collected, and qRT-PCR testing by Shandong CDC confirmed positive ZIKV results in all samples. China CDC Laboratory validated these findings on March 23. The patient was then admitted to the Shandong Provincial Public Health Clinical Center for treatment. On March 23 and 24, qRT-PCR testing of the patient's urine and sputum samples for ZIKV yielded consistently positive results. However, on March 25 and 26, only the urine samples tested positive for ZIKV, while sputum and blood samples returned negative results. On March 27, qRT-PCR testing indicated that the urine sample remained positive for ZIKV, whereas the sputum sample tested negative. According to the Zika Virus Disease Diagnosis and Treatment Protocol (2nd Edition, 2016), the patient met discharge criteria as blood samples had tested negative for two consecutive Consequently, the patient was discharged on March 27. On March 28 and 31, qRT-PCR testing of urine

TABLE 1. Laboratory test results of biological samples from the patient.

Time	ZIKV tested by qRT-PCR (Ct)			
rime	Urine	Urine Sputum		
March 22	(+) 31.24	(+) 32.50	(+) 34.53	
March 23	(+) 33.40	(+) 30.05	N	
March 24	(+) 32.52	-	N	
March 25	(+) 22.57	-	-	
March 26	(+) 31.62	-	-	
March 27	(+) 32.59	-	N	
March 28	-	-	N	
March 31	-	-	N	

Note: "+" indicates positive result; "-" indicates negative result; "N" indicates no sample collected.

Abbreviation: ZIKV=Zika virus; qRT-PCR=Quantitative real-time reverse-transcription polymerase chain reaction.

samples returned negative results for ZIKV (Table 1).

On March 23, 2025, Shandong CDC conducted whole genome sequencing of the patient's urine sample using Metagenome Next-Generation Sequencing (mNGS) and obtained the complete ZIKV genome sequence. Additionally, we successfully isolated ZIKV from urine samples using Vero (African green monkey kidney) cells, designating the isolate Shandong China Mar-2025. Phylogenetic analysis revealed that this ZIKV strain belongs to the Asian lineage and demonstrates close genetic relatedness to the ZIKV strain from Bangkok, Thailand (GenBank accession no. OR264645.1) (Figure 1), sharing 99.57% nucleotide identity. This ZIKV strain harbors mutations D683E, V763M, and T777M within the open reading frame. Furthermore, an A188V substitution was identified in the NS1 protein.

Public Health Response

Following confirmation of ZIKV infection, Shandong CDC, Jinan CDC, and Tianqiao District CDC implemented coordinated control measures. Comprehensive disinfection was conducted on the patient's residence and personal belongings. Vector surveillance was performed in the surrounding environment, revealing no adult mosquitoes or evidence of local transmission. Community residents received instructions on eliminating mosquito breeding sites and implementing personal protective measures.

DISCUSSION

ZIKV has been sporadically documented in

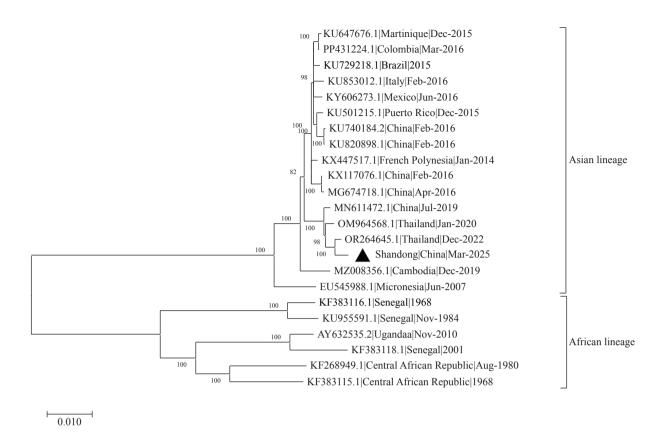


FIGURE 1. Phylogenetic analysis of Shandong|China|Mar-2025 ZIKV whole-genome sequences using the Neighbor-Joining method.

Note: ▲ Shandong|China|Mar-2025 represents viral strain of the first imported ZIKV case in Shandong Province. Abbreviation: ZIKV=Zika virus.

northern Africa and Southeast Asia for decades, with only isolated cases reported historically. However, beginning in May 2015, Brazil experienced the largest ZIKV outbreak on record, which rapidly spread throughout multiple South American countries. These outbreaks demonstrated the virus's widespread potential to cause pregnancy complications, including miscarriage and severe birth defects such microcephaly. In adults, ZIKV infection can trigger neurological complications, particularly Guillain-Barré syndrome (1). According to the World Health Organization (WHO), 89 countries and territories had reported ZIKV cases as of February 2022 (2). The combination of global population growth, rapid urbanization, and insufficient vector control measures has resulted in an increasing number of countries reporting imported ZIKV cases. These imported cases significantly increase transmission risk in regions where competent vectors, particularly Aedes aegypti and Aedes albopictus, are established.

China confirmed its first imported ZIKV case in Jiangxi Province in February 2016, subsequently followed by additional imported cases in Guangdong Province, Zhejiang Province, Yunnan Province, and other regions (3). On March 21, 2025, Nanning Customs notified Shandong CDC of a suspected ZIKV case involving an individual who had returned from Thailand via Nanning before reaching Jinan. Laboratory confirmation by Shandong CDC and subsequent verification by China CDC established ZIKV infection in this patient, representing the first imported ZIKV case documented in Shandong Province.

Shandong Province, with its dense population in northern China, maintains extensive exchanges in travel, trade, and labor with Southeast Asia. These interactions significantly increase the risk of importing tropical vector-borne diseases. The primary vectors for ZIKV transmission are *Aedes aegypti*, followed by *Aedes albopictus*. In Shandong, *Aedes albopictus* represents the predominant species, typically emerging from late April to early May. When this imported ZIKV case was identified, spring temperatures in Shandong were rising rapidly, with sporadic mosquito activity observed indoors. Consequently, the patient was immediately isolated and treated upon confirmation of infection.

Comprehensive disinfection was performed on the patient's residence and personal belongings. During this process, no adult *Aedes* mosquitoes were detected, and no local secondary transmission cases were identified.

Most ZIKV cases or asymptomatic carriers typically test negative for ZIKV in serum by the time of detection. This patient's serum sample demonstrated weakly positive ZIKV nucleic acid results upon entry, indicating the waning phase of viremia. Daily nucleic acid testing of urine, sputum, and blood samples was conducted over one week. The results revealed that ZIKV remained detectable in urine for days 1–6 postonset, in saliva for days 1–2, and in blood only on day 1. These findings indicated higher viral loads and prolonged shedding in urine compared to saliva and blood, consistent with previous international research (4).

ZIKV is a positive-sense RNA virus belonging to the Flavivirus genus, classified into African and Asian genotypes (5). The molecular evolution of ZIKV correlates closely with its geographical distribution patterns. All documented ZIKV cases in China have been imported from endemic regions, including South America, Oceania, and Southeast Asia. Phylogenetic analysis confirmed that the strain identified in this Shandong case belonged to the Asian lineage, demonstrating the highest degree of homology with reference sequence OR264645.1, which originated from Bangkok, Thailand. This molecular evidence provides definitive support for the conclusion that the patient acquired ZIKV infection during travel in Thailand. Whole-genome sequencing revealed mutations (D683E, V763M, T777M) that have been associated with potential teratogenic effects, including congenital Zika syndrome (6). Additionally, an NS1 protein mutation (A188V) was detected, which may enhance viral transmission capacity and infectivity (6). However, the S139N mutation, previously linked to prolonged neuroinflammation and modulation, was absent in this strain (7).

Beyond mosquito-borne transmission, recent years have witnessed an increasing number of documented sexual transmission cases (8), further emphasizing the critical importance of comprehensive ZIKV prevention and control strategies. This case underscores the imperative to strengthen port quarantine measures, particularly during peak travel seasons to Southeast Asian destinations. Essential strategies must be implemented to prevent imported cases through enhanced temperature screening protocols and

expanded laboratory testing capabilities for returning travelers at key entry points. Furthermore, during periods of active mosquito activity in southern China, vector surveillance and control efforts require particular intensification. Public education campaigns targeting travelers returning from epidemic regions should be expanded to promote improved personal protective measures. Pregnant women should be specifically advised to avoid travel to ZIKV-affected areas to minimize the risk of congenital anomalies. The successful management of this outbreak demonstrates the effectiveness of close collaboration among health departments, cross-regional disease control agencies, and customs authorities, enabling timely detection of Shandong's first imported ZIKV case and successfully preventing epidemic spread. This experience reinforces the necessity of establishing normalized multi-sectoral coordination mechanisms that facilitate data sharing and develop real-time infectious disease early warning systems, thereby creating a comprehensive infectious disease prevention and control network that provides robust protection for public health and safety.

Conflicts of interest: No conflicts of interest.

Ethical statement: Approval by the Ethics Committee of Shandong Center for Disease Control and Prevention, China (approval number: 2021-24).

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Notifiable Infectious Diseases Reports

Reported Cases and Deaths of National Notifiable Infectious Diseases — China, June 2025*

Diseases	Cases	Deaths
Plague	0	0
Cholera	2	0
SARS-CoV	0	0
Acquired immune deficiency syndrome [†]	4,783	1,641
Hepatitis	126,144	336
Hepatitis A	1,803	0
Hepatitis B	105,033	38
Hepatitis C	15,898	297
Hepatitis D	19	0
Hepatitis E	2,820	1
Other hepatitis	571	0
Poliomyelitis	0	0
Human infection with H5N1 virus	0	0
Measles	156	0
Epidemic hemorrhagic fever	354	1
Rabies	23	20
Japanese encephalitis	1	0
Dengue	225	0
Anthrax	32	1
Dysentery	3,670	0
Tuberculosis	53,180	296
Typhoid fever and paratyphoid fever	564	0
Meningococcal meningitis	7	1
Pertussis	3,590	0
Diphtheria	0	0
Neonatal tetanus	0	0
Scarlet fever	8,718	0
Brucellosis	7,187	0
Gonorrhea	10,011	0
Syphilis	52,760	7
Leptospirosis	18	0
Schistosomiasis	1	0
Malaria	437	0
Human infection with H7N9 virus	0	0
COVID-19	333,229	8
Monkey pox [§]	102	0
Influenza	92,292	1

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Continued

Diseases	Cases	Deaths
Mumps	9,406	0
Rubella	53	0
Acute hemorrhagic conjunctivitis	2,819	0
Leprosy	22	0
Typhus	135	0
Kala azar	23	0
Echinococcosis	285	0
Filariasis	0	0
Infectious diarrhea [¶]	154,704	1
Hand, foot and mouth disease	150,557	0
Total	1,015,490	2,313

^{*} According to the National Bureau of Disease Control and Prevention.

The number 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 the 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 were 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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[†] 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..

[§] Since September 20, 2023, Monkey pox was included in the management of Class B infectious diseases.

[¶]Infectious diarrhea excludes cholera, dysentery, typhoid fever and paratyphoid fever.

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