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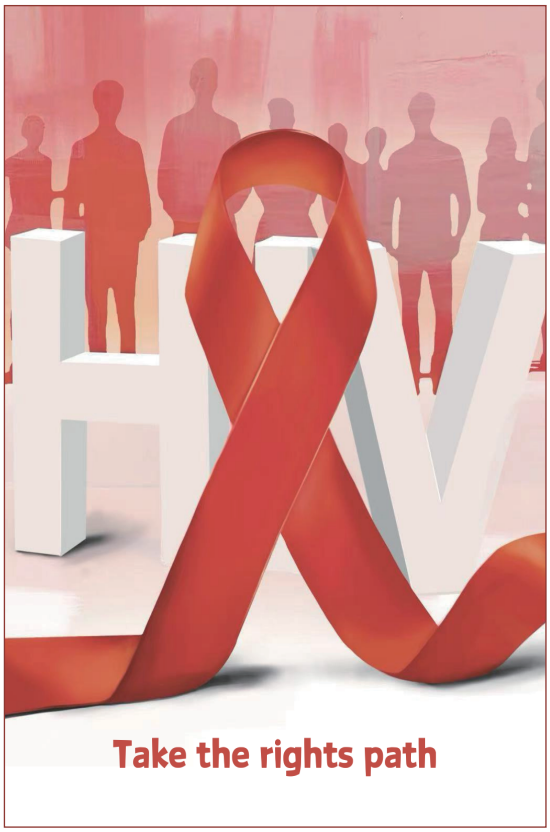

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Vital Surveillances

Pretreatment HIV Drug Resistance to Integrase Strand Transfer Inhibitors Among Newly Diagnosed HIV Individuals — China, 2018–2023

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ABSTRACT

Introduction: The widespread adoption of integrase strand transfer inhibitors (INSTIs) has led to the emergence of INSTI-associated drug-resistance mutations. This cross-sectional study conducted a comprehensive national survey to investigate the prevalence of pretreatment drug resistance (PDR) to INSTIs among newly diagnosed human immunodeficiency virus (HIV) individuals in China.

Methods: The study enrolled 10,654 individuals from 31 provincial-level administrative divisions between 2018 and 2023. All participants underwent integrase region genotypic resistance testing. PDR to INSTIs was analyzed using the Stanford HIV drug resistance database, and molecular transmission networks were constructed using HIV-TRACE.

Results: The overall PDR prevalence of INSTIs was 0.95%. The predominant major and accessory mutations identified were E138K/A (*n*=19) and G163R/K (*n*=29), respectively. Multivariable logistic regression analysis revealed that age ≥50 years [adjusted odds ratio (a*OR*)=1.87, 95% confidence interval (*CI*): 1.03, 3.42] and HIV subtype B (a*OR*=3.87, 95% *CI*: 1.97, 7.58) were significant risk factors for PDR. Molecular network analysis showed that 1,257 (26.0%) CRF07_BC sequences formed 432 transmission clusters, while 811 (27.6%) CRF01_AE sequences were associated with 335 clusters. The identified drug-resistance mutations included E138K/A, R263K, Y143H, G163R/K, E157Q, and T97A.

Conclusions: The current prevalence of PDR to INSTIs in China remains low. However, given the increasingly widespread use of INSTIs, continuous surveillance of drug resistance emergence and transmission patterns is essential.

In 2022, approximately 39 million people were living with human immunodeficiency virus (HIV) globally (*1*), with 29.8 million receiving antiretroviral therapy (ART) to suppress HIV-1 replication. While China's National Free Antiretroviral Treatment Program (NFATP) was fully implemented in 2004, a significant increase in transmitted drug resistance has been observed. The prevalence of resistance to overall treatments, non-nucleoside reverse transcriptase inhibitors, efavirenz, and nevirapine rose from 2.6%, 1.8%, 1.6%, and 1.8%, respectively, during 2004–2007 to 7.8%, 6.7%, 6.3%, and 6.7% during 2020–2022 (*2*). Integrase strand transfer inhibitors (INSTIs) represent a new class of antiretroviral drugs with high genetic barriers to resistance. The World Health Organization now recommends dolutegravir (DTG) as a component of first-line ART and advocates for genotyping both reverse-transcriptase and integrase regions of HIV-1 (*3*). In China, INSTI-containing regimens were recommended as first-line treatment in 2018 (*4*), and DTG was incorporated into the NFATP for conditional use in 2023 (*5*). Regional surveys of pretreatment drug resistance (PDR) in various provincial-level administrative divisions (PLADs) have reported prevalence rates of 0.53% in Beijing (*6*), 1.7% in Jiangsu (*7*), and 0.71% in Chongqing (*8*). However, these studies were geographically limited with small sample sizes, and no large-scale national investigation of INSTI PDR has been conducted in China. To prevent drug resistance emergence a comprehensive understanding of INSTI PDR prevalence is crucial for developing second-line therapeutic strategies and maintaining vigilance against potential increases in resistance.

Molecular transmission network analysis enables the identification of active transmission clusters through

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genetic analysis. While HIV-1 *pol* gene sequences are commonly used for transmission network characterization, some researchers have successfully employed integrase (*int*) gene sequences (*9*). However, no large-scale national studies have utilized *int* sequences to investigate INSTI PDR in China.

This study aimed to conduct a comprehensive national survey to determine the prevalence of INSTI PDR and characterize viral mutations among newly diagnosed HIV individuals in China, while also examining transmission networks associated with INSTI drug resistance.

METHODS

A cross-sectional study was conducted following the World Health Organization protocol for HIV pretreatment drug resistance surveillance across China's regions. Based on HIV incidence, PLADs were stratified into high-, moderate-, and low-prevalence regions. Clinics were randomly selected within each study area, and patients were sequentially enrolled at these sites during the study period. Sample sizes for each PLAD are detailed in Supplementary Table S1 (available at https://weekly.chinacdc.cn/). To assess the prevalence of PDR to INSTIs before their widespread implementation in China, we analyzed all available *int* sequences from 2018, 2022, and 2023. Inclusion criteria comprised: age ≥18 years; confirmed HIV-1 diagnosis in 2018, 2022, or 2023; *int* sequence length ≥500 bp (HXB2 positions 4230-5096); and provided informed consent. Exclusion criteria were age <18 years or prior ART exposure. This study received approval from the Ethics Committee of the National Centre for AIDS/STD Control and Prevention, China CDC (approval number X140617334).

Viral RNA extraction was performed using the QIAsymphony platform, followed by integrase fragment amplification and sequencing using an in-house PCR protocol. Sequences were aligned and filtered using BioEdit, excluding those shorter than 500 nucleotides. HIV-1 subtypes were determined through phylogenetic analysis using IQ-Tree. Drug susceptibility predictions for five INSTIs [first-generation: raltegravir (RAL), elvitegravir (EVG); second-generation: dolutegravir (DTG), bictegravir (BIC), and cabotegravir (CAB)] were generated using the Stanford HIV Database genotypic resistance interpretation system.

Molecular transmission networks were constructed using the Tamura-Nei 93 model in HIV-TRACE. Each node in the network represented an HIV-infected individual with corresponding epidemiological data. Given the slower evolutionary rate of the *int* gene compared to the *pol* gene, nodes were connected using a genetic distance threshold of 0.5% substitutions per site. Network visualization was performed using web-based tools (https://veg.github.io/hivtrace-viz/) following established technical guidelines for HIV transmission network monitoring and intervention.

Statistical analyses were conducted using SAS (version 9.4, SAS Institute Inc, Cary, NC, USA). Factors associated with drug resistance were analyzed using logistic regression, with statistical significance set at $P<0.05$.

RESULTS

Among the 10,654 HIV-1-infected individuals recruited over the three-year study period, 41.9% were aged ≥50 years. The study population was predominantly comprised of men (79.0%) and individuals of Han ethnicity (83.3%). Most participants (60.1%) had educational attainment at or below junior high school level, and 35.2% were single. Heterosexual transmission was the primary route of infection (61.8%). The vast majority (98.3%) had no prior antiretroviral exposure, and 68.9% presented with CD_4 cell counts between 200–499 cells/mm^3 before initiating treatment. The HIV-1 subtype distribution showed CRF07_BC (45.4%), CRF01_AE (27.6%), CRF08_BC (8.9%), CRF55_01B (1.1%), and subtype B (3.0%) as the predominant strains (Table 1).

Among the 10,654 HIV-1 individuals in our study, the overall prevalence of PDR to INSTIs was 0.95% (*n*=101). The PDR of RAL, EVG, DTG, BIC, and CAB were 0.91% (*n*=97) for RAL, 0.87% (*n*=93) for EVG, 0.21% (*n*=22) for DTG, 0.15% (*n*=16) for BIC, and 0.34% (*n*=37) for CAB. We identified nine major and six accessory INSTI-related drug resistance mutations (DRM). The E138K/A mutation, conferring low-level resistance to RAL and EVG, was the most frequent major mutation (*n*=19). Eight cases harbored the R263K mutation, which causes low-level resistance to RAL and intermediate-level resistance to EVG, DTG, BIC, and CAB. The combination of S147G and Q148K mutations resulted in high-level resistance to RAL, EVG, and CAB. The G163R/K accessory mutation, detected in 29 cases, conferred low-level resistance to RAL and EVG (Table 2).

Multivariate analysis revealed that individuals with

TABLE 1. Demographic and clinical characteristics of newly diagnosed HIV individuals in China.

Variable	2018		2022		2023		Total	
	N	Prevalence (%)	*N*	Prevalence (%)	*N*	Prevalence (%)	*N*	Prevalence (%)
Total	905	100.0	2,757	100.0	6,992	100.0	10,654	100.0
Age (years)								
18−29	231	25.5	629	22.8	1,630	23.3	2,490	23.4
30−49	459	50.7	1,012	36.7	2,175	31.1	3,646	34.2
≥50	215	23.8	1,116	40.5	3,138	44.9	4,469	41.9
Unknown	0	−	0	−	49	0.7	49	0.5
Sex								
Male	743	82.1	2,212	80.2	5,458	78.1	8,413	79.0
Female	162	17.9	545	19.8	1,470	21.0	2,177	20.4
Unknown	0	−	0	−	64	0.9	64	0.6
Ethnicity								
Han	744	82.2	2,252	81.7	5,876	84.0	8,872	83.3
Others	161	17.8	502	18.2	1,063	15.2	1,726	16.2
Unknown	0	−	3	0.1	53	0.8	56	0.5
Education								
Junior high school or blew	386	42.7	1,679	60.9	4,334	62.0	6,399	60.1
Senior high school	249	27.5	405	14.7	972	13.9	1,626	15.3
College and above	174	19.2	653	23.7	1,612	23.1	2,439	22.9
Unknown	96	10.6	20	0.7	74	1.1	190	1.8
Marital status								
Single	369	40.8	987	35.8	2,389	34.2	3,745	35.2
Married or cohabiting	410	45.3	1,227	44.5	2,975	42.5	4,612	43.3
Divorced or widowed	112	12.4	520	18.9	1,554	22.2	2,186	20.5
Unknown	14	1.5	23	0.8	74	1.1	111	1.0
Risk								
Heterosexual	460	50.8	1,699	61.6	4,424	63.3	6,583	61.8
Homosexual	402	44.4	925	33.6%	2,327	33.3	3,654	34.3
Intravenous drug use	21	2.3	28	1.0	32	0.5	81	0.8
Others	2	0.2	4	0.1	1	0.0	7	0.1
Unknown	20	2.2	101	3.7	208	3.0	329	3.1
Prior ARV exposure								
No	905	100.0	2,616	94.9	6,947	99.4	10,468	98.3
Yes	0	−	76	2.8	38	0.5	72	0.7
Unknown	0	−	65	2.4	7	0.1	114	1.1
CD4 cell count before ART (cell/mm^3)								
<200	292	32.3	1,010	36.6	206	2.9	1,508	14.2
200–499	433	47.8	1,404	50.9	5,504	78.7	7,341	68.9
≥500	148	16.4	302	11.0	1,282	18.3	1,732	16.3
Unknown	32	3.5	41	1.5	0	−	73	0.7
Subtype								
CRF07_BC	319	35.2	1,305	47.3	3,208	45.9	4,832	45.4

Continued

Variable	2018		2022		2023		Total	
	N	Prevalence (%)	*N*	Prevalence (%)	*N*	Prevalence (%)	*N*	Prevalence (%)
CRF01_AE	290	32.0	712	25.8	1,940	27.7	2,942	27.6
CRF08_BC	135	14.9	245	8.9	566	8.1	946	8.9
CRF55_01B	8	0.9	49	1.8	65	0.9	122	1.1
B	34	3.8	70	2.5	217	3.1	321	3.0
URFs	38	4.2	161	5.8	395	5.6	594	5.6
Others	81	9.0	215	7.8	601	8.6	897	8.4

Abbreviation: ART=antiretroviral therapy; ARV=antiretroviral drugs; HIV=human immunodeficiency virus; CRF=circulating recombinant form; URFs=unique recombinant forms.

TABLE 2. Prevalence and patterns of HIV integrase strand transfer inhibitor resistance mutations among newly diagnosed individuals in China.

Antiretroviral drug	Prevalence, *N*	% (95% *CI*)	HIV drug resistance mutations and combination of mutations, *n* (%)
INSTIs	101	0.95 (0.76, 1.11)	Major mutations
Raltegravir	97	0.91 (0.73, 1.09)	E138K/A : 19
Elvitegravir	93	0.87 (0.69, 1.05)	E138K+L74I : 1
Dolutegravir	22	0.21 (0.12, 0.29)	E138K+E92Q+R263K : 1
Bictegravir	16	0.15 (0.08, 0.22)	R263K : 8
Cabotegravir	37	0.34 (0.24, 0.46)	R263K+A128T :1
			Y143S/C/H : 8
			T66A/I : 4
			T66I+E157Q : 1
			N155S/T : 3
			N155H+Q95K+E157Q : 1
			Q146P/R/L : 3
			Q146R+S153A : 1
			Q148R : 2
			Q148K+S147G : 1
			S147G : 1
			G140R : 1
			Accessory mutations
			G163R /K: 29
			G163R+E157Q : 3
			S230R : 6
			S230R+S153F : 1
			H51Y : 4
			V151A : 2
			S153F : 2
			E157Q+T97A : 1

Abbreviation: HIV=human immunodeficiency virus; *CI*=confidence interval.

HIV-1 subtype B had significantly higher odds of drug resistance compared to those with CRF07_BC [adjusted odds ratio (a*OR*)=3.87, 95% confidence interval (*CI*): 1.97, 7.58]. Additionally, individuals aged ≥50 years showed increased odds of drug resistance compared to those aged 18–29 years (a*OR*=1.87, 95% *CI*: 1.03, 3.42) (Table 3).

Molecular transmission network analysis, using a

TABLE 3. Risk factors associated with integrase strand transfer inhibitor resistance among newly diagnosed HIV individuals in China.

Variable	*N*	PDR, *n* (%)	*OR* (95% *CI*)	*P*	a*OR* (95% *CI*)	*P*
Total	10,654	101 (0.95)				
Age (years)						
18–29	2,490	14 (0.56)	1.00			
30–49	3,646	37 (1.01)	1.81 (0.98, 3.36)	0.059	1.80 (0.97, 3.35)	0.062
≥50	4,469	49 (1.10)	1.96 (1.08, 3.56)	0.027	1.87 (1.03, 3.42)	0.041
Unknown	49	1 (2.04)	3.69 (0.48, 28.59)	0.211	3.71 (0.45, 29.08)	0.212
Sex						
Male	8,413	79 (0.94)	1.00			
Female	2,177	22 (1.01)	1.08 (0.67, 1.73)	0.760		
Unknown	64	0 (0.00)	–	–		
Ethnicity						
Han	8,872	85 (0.96)	1.00			
Others	1,726	13 (0.75)	0.79 (0.44, 1.41)	0.417		
Unknown	56	3 (5.36)	5.85 (1.79, 19.09)	0.003		
Education						
Junior high school or blew	6,399	64 (1.00)	1.00			
Senior high school	1,626	17 (1.05)	1.05 (0.61, 1.79)	0.870		
College	2,439	18 (0.74)	0.74 (0.44, 1.24)	0.253		
Unknown	190	2 (1.05)	1.05 (0.26, 4.33)	0.943		
Marital status						
Single	3,745	34 (0.91)	1.00			
Married or cohabiting	4,612	50 (1.08)	1.20 (0.77, 1.85)	0.422		
Divorced or widowed	2,186	15 (0.69)	0.75 (0.41, 1.39)	0.364		
Unknown	111	2 (1.80)	2.00 (0.48, 8.44)	0.344		
Risk						
Heterosexual	6,583	64 (0.97)	1.00			
Homosexual	3,654	32 (0.88)	0.90 (0.59, 1.38)	0.628		
IDU	81	0 (0.00)	–	–		
Others	7	0 (0.00)	–	–		
Unknown	329	5 (1.52)	1.57 (0.63, 3.93)	0.334		
Prior ARV exposure						
No	10,468	101 (0.96)	1.00			
Yes	72	0 (0.00)	–	–		
Unknown	114	0 (0.00)	–	–		
CD4 cell count before ART (cell/mm^3)						
<200	1,508	12 (0.80)	1.00			
200–499	7,341	73 (0.99)	1.25 (0.68, 2.31)	0.472		
≥500	1,732	15 (0.87)	1.09 (0.51, 2.33)	0.826		
Unknown	73	1 (1.37)	1.73 (0.22, 13.50)	0.600		
HIV subtype						
CRF07_BC	4,832	44 (0.91)	1.00			
CRF01_AE	2,942	22 (0.75)	0.82 (0.49, 1.37)	0.449	0.84 (0.50, 1.41)	0.510

Continued

Variable	*N*	PDR, *n* (%)	*OR* (95% *CI*)	*P*	a*OR* (95% *CI*)	*P*
CRF08_BC	946	10 (1.06)	1.16 (0.58, 2.32)	0.669	1.10 (0.55, 2.20)	0.799
CRF55_01B	122	0 (0.00)	–	–	–	–
B	321	11 (3.43)	3.86 (1.98, 7.55)	<0.001	3.87 (1.97, 7.58)	<0.001
URF	594	7 (1.18)	1.30 (0.58, 2.89)	0.524	1.33 (0.60, 2.98)	0.481
Others	897	7 (0.78)	0.86 (0.38, 1.91)	0.703	0.87 (0.39, 1.93)	0.723
Diagnosed year						
2018	905	7 (0.77)	1.00			
2022	2,757	26 (0.94)	1.22 (0.53, 2.82)	0.640		
2023	6,992	68 (0.97)	1.26 (0.58, 2.75)	0.562		

Note: *P* values <0.05 were considered statistically significant.
"–" means not available.
Abbreviation: ART=antiretroviral therapy; ARV=antiretroviral drugs; IDU=intravenous drug use; CRF=circulating recombinant form; URFs=unique recombinant forms; HIV=human immunodeficiency virus; *CI*=confidence interval; a*OR*=adjusted odds ratio.
* *P* values were calculated using Pearson's Chi-squared test.

genetic distance threshold of 0.5% substitutions per site, identified 1,257 (26.0%) CRF07_BC sequences forming 432 clusters (size range 2–217) among 4,832 analyzed sequences. Within these clusters, 11 drug-resistant sequences were distributed across 8 clusters, harboring mutations including E138K, Y143H, E157Q, G163R/K/S, and R263K. Notably, Cluster 1 contained two nodes sharing E157Q and G163R mutations, while Cluster 2 comprised three individuals with G163R (Figure 1A). Analysis of 2,942 CRF01_AE sequences revealed 811 (27.6%) sequences forming 335 clusters (size range 2–15), with two drug-resistant strains carrying E138K/A mutations distributed across two clusters (Figure 1B).

DISCUSSION

In China, the PDR to INSTIs was 0.95%, which aligns with previous reports (*10*). This prevalence is marginally higher than surveys from six Chinese PLADs (0.80%) (*11*), Beijing (0.53%) (*6*), and Chongqing (0.71%) (*8*), yet slightly lower than reports from Jiangsu (1.7%) (*7*), Shenzhen (1.77%) (*12*), and Taiwan (2.6%) (*13*). The observed rates are notably lower than those reported in European and American regions, including Italy (1.5%) (*14*), Mediterranean Europe (2.33%) (*15*), Spain (2.5%) (*16*), and Chile (8.0%) (*17*). The higher PDR prevalence in Western countries likely reflects their earlier and more extensive INSTI implementation, exemplified by Chile, where approximately 60% of HIV patients receive INSTI-based therapy (*17*). According to WHO's qualitative classification, China's PDR prevalence of INSTIs remains at a low level.

The predominant DRM sites identified were E138, R263, Y143, T66, N155, G140, Q146, S147, and Q148. E138K/A emerged as the most frequent mutation, representing a non-polymorphic alteration that typically confers high-level resistance to RAL and EVG while inducing intermediate-level resistance to DTG. We also identified eight cases harboring the R263K mutation, a non-polymorphic variant selected in vitro by EVG, DTG, BIC, and CAB, which reduces susceptibility to all INSTIs (*18*). The prevalence of E138 and R263 as the two primary major mutations corresponds with findings from Italian studies (*14*). Among accessory DRMs, we detected G163, S230, H51, S153, E157, and T97. The G163R/K mutation, a non-polymorphic variant primarily selected by RAL, contributes to low-level resistance against first-generation INSTIs. This G163 mutation has also been frequently documented in other regions, including Italy, Ghana, and Chile (*14–19*). Continued surveillance and monitoring remain crucial for tracking the dissemination of resistant strains.

Multivariable analysis revealed that patients with subtype B had 3.87 times greater odds of PDR compared to those with subtype CRF07_BC, consistent with previous findings in China (*14*). This association likely stems from the initial deployment of INSTIs in Europe and the United States, where subtype B predominates. Additionally, individuals aged ≥50 years demonstrated 1.87 times greater odds of PDR compared to those aged 18–29 years. Research has indicated that older populations play a significant role in drug resistance transmission (*21*).

Our construction of subtype-specific molecular transmission networks using *int* sequences of

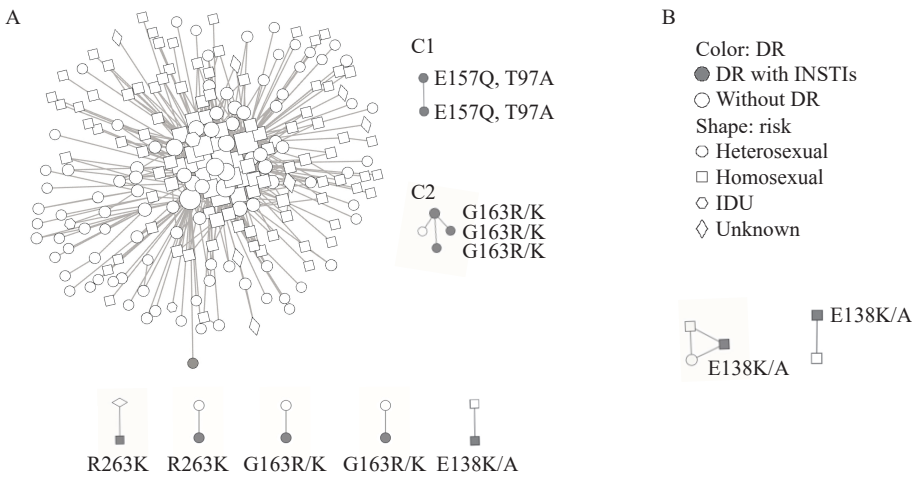

FIGURE 1. Molecular transmission clusters containing pretreatment drug resistance to INSTIs. (A) Resistance mutations identified in HIV-1 subtype CRF07_BC; (B) Resistance mutations identified in HIV-1 subtype CRF01_AE.

CRF07_BC and CRF01_AE revealed notable patterns. Within the CRF07_BC network, we identified two resistance strains in Cluster 1 and three in Cluster 2. Both nodes in Cluster 1 exhibited E157Q and G163R mutations, while all three nodes in Cluster 2 displayed G163R mutations. The presence of identical DRMs within single molecular clusters suggests strong transmission relationships among these HIV-positive individuals, though additional epidemiological investigations are necessary to confirm direct transmission links.

This study has several limitations. First, incomplete information from drug-resistant individuals may have affected the analytical accuracy. Second, the use of Sanger sequencing limited detection to drug-resistant variants present at frequencies above 20%. Additionally, the slower evolutionary rate of the HIV *int* gene compared to the *pol* gene necessitates further methodological evaluation for molecular transmission network construction using integrase sequences.

In conclusion, the prevalence of PDR to INSTIs in China remains low. While INSTIs represent a relatively new and effective class of antiretroviral drugs, patients harboring resistant strains will maintain these mutations indefinitely and potentially transmit them to others, thereby compromising therapeutic efficacy. Given the increasingly widespread use of INSTIs, continuous surveillance of these individuals is essential to provide optimal preventive interventions and therapeutic strategies. Furthermore, achieving the global objective of eliminating AIDS as a public health threat by 2030 requires coordinated national and provincial efforts in regular PDR surveillance.

Conflicts of interest: No conflicts of interest.

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SUPPLEMENTARY MATERIALS

SUPPLEMENTARY TABLE S1. Distribution of HIV-positive individuals across 31 PLADs in China, 2018, 2022, and 2023.

PLAD	2023		2022		2018		Total	
	N	Prevalence (%)	*N*	Prevalence (%)	*N*	Prevalence (%)	*N*	Prevalence (%)
Total	6,992	68 (0.97)	2,757	26 (0.94)	905	7 (0.77)	10,654	101 (0.95)
Beijing	195	0 (0)					195	0 (0)
Tianjin	78	0 (0)					78	0 (0)
Hebei	136	2 (1.47)	86	1 (1.16)			222	3 (1.35)
Shanxi	132	3 (2.27)					132	3 (2.27)
Inner Mongolia	124	1 (0.81)					124	1 (0.81)
Liaoning	150	1 (0.67)					150	1 (0.67)
Jilin	123	1 (0.81)	196	5 (2.55)			319	6 (1.88)
Heilongjiang	141	0 (0)			150	1 (0.67)	291	1 (0.34)
Shanghai	143	0 (0)					143	0 (0)
Jiangsu	362	2 (0.55)	341	2 (0.59)			703	4 (0.57)
Zhejiang	231	4 (1.73)	383	3 (0.78)	134	1 (0.75)	748	8 (1.07)
Anhui	230	2 (0.87)					230	2 (0.87)
Fujian	259	1 (0.39)					259	1 (0.39)
Jiangxi	274	5 (1.82)					274	5 (1.82)
Shandong	136	1 (0.74)					136	1 (0.74)
Henan	209	4 (1.91)					209	4 (1.91)
Hubei	126	2 (1.59)	373	3 (0.80)			499	5 (1.00)
Hunan	487	0 (0)			142	0 (0.00)	629	0 (0)
Guangdong	185	1 (0.54)			50	0 (0.00)	235	1 (0.43)
Guangxi	319	2 (0.63)			153	1 (0.65)	472	3 (0.64)
Hainan	67	0 (0)					67	0 (0)
Chongqing	307	6 (1.95)	390	4 (1.03)			697	10 (1.43)
Sichuan	1,111	12 (1.08)	348	4 (1.15)	128	2 (1.56)	1,587	18 (1.13)
Guizhou	357	2 (0.56)					357	2 (0.56)
Yunnan	455	5 (1.10)	377	1 (0.27)	148	2 (1.35)	980	8 (0.82)
Xizang	39	0 (0)					39	0 (0)
Shaanxi	189	4 (2.12)					189	4 (2.12)
Gansu	118	1 (0.85)					118	1 (0.85)
Qinghai	51	1 (1.96)					51	1 (1.96)
Ningxia	64	1 (1.56)					64	1 (1.56)
Xinjiang	194	4 (2.06)	263	3 (1.14)			457	7 (1.53)

Abbreviation: PLAD=provincial-level administrative division.

Preplanned Studies

Characteristics and Predictors of Interprovincial Migration Following HIV Diagnosis Among Men Who Have Sex with Men — China, 2016–2022

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Summary

What is already known about this topic?

Men who have sex with men (MSM) are highly vulnerable to human immunodeficiency virus (HIV) infection and demonstrate significant mobility patterns. Understanding post-diagnosis migration patterns among HIV-positive MSM is crucial for targeted case management, yet comprehensive data from China remains limited.

What is added by this report?

Among 204,394 HIV-positive MSM, 20,117 (9.8%) migrated after diagnosis, with primary movement from economically developed regions like Guangdong Province and Shanghai Municipality to less developed provincial-level administrative divisions such as Sichuan Province and Anhui Province. Key predictors of migration included age under 50 years, unmarried status, lower educational attainment, employment as commercial staff or student status, and diagnosis before 2020.

What are the implications for public health practice?

Enhanced healthcare resources, strengthened case management systems, and targeted HIV-related services are essential to ensure consistent treatment access and improved health outcomes for migrant HIV-positive MSM.

Migration, as defined by the World Health Organization (WHO) as the movement of people from one area to another for varying periods, has significant public health implications (*1*). Men who have sex with men (MSM) in China are particularly vulnerable to HIV infection and are more likely to migrate due to widespread stigma and discrimination (*2*). Post-diagnosis migration of human immunodeficiency virus -positive (HIV-positive) MSM presents unique challenges for maintaining consistent care, tracking epidemic patterns, and ensuring equitable healthcare access — making it more consequential than other forms of migration within the HIV care continuum. Currently, the interprovincial movement patterns of HIV-positive MSM after diagnosis in China remain poorly understood. Therefore, a comprehensive analysis of interprovincial migration was conducted to identify where HIV-infected or at-risk individuals require services and to strategically focus HIV management efforts. The findings reveal that approximately 10% of HIV-positive MSM migrated post-diagnosis, predominantly from affluent to less developed provincial-level administrative divisions (PLADs), highlighting the need for enhanced resources, improved case management, and tailored HIV services to support these migrants.

Data were extracted from the National Integrated HIV/AIDS Control and Prevention Data System. Study inclusion criteria were: 1) MSM; 2) age ≥15 years; 3) confirmed HIV-positive status through confirmatory testing; 4) experience of interprovincial migration. Participants were classified as MSM migrants if their follow-up addresses differed from their baseline addresses at diagnosis, while those with unchanged addresses were categorized as non-migrants (*3*). For cases with multiple address changes, the first change was considered as the inflow location. Data analysis was performed using R software (version 4.3.0; R Core Team, Vienna, Austria). Univariable logistic regression was employed to calculate odds ratios (*OR*s) and their 95% confidence intervals (*CI*) for potential factors associated with migration among HIV-positive MSM. Subsequently, multivariable logistic regression analysis was conducted through stepwise elimination to calculate adjusted *OR*s. The Ethics Review Board of the National Center for AIDS/STD Control and Prevention, and the Chinese Center for Disease Control and Prevention approved this study.

Among the 204,394 MSM diagnosed with HIV during the study period, 20,117 (9.8%) were identified as migrants based on post-diagnosis relocation.

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Significant demographic differences emerged between migrant and non-migrant MSM. Migrants were predominantly younger (36.4% *vs.* 27.2% aged 15–24), more likely to be unmarried (71.1% *vs.* 64.4%), and had lower educational attainment (60.8% *vs.* 56.0% with senior high school education or below). Occupationally, migrants showed higher proportions of commercial staff (27.2% *vs.* 22.9%) and students (9.9% *vs.* 7.9%). Migration rates decreased substantially during 2020–2022 (21.8%) compared to 2016–2019 (37.6%) (Table 1). Furthermore, migrant MSM demonstrated lower treatment initiation rates compared to non-migrants [91.3% (18,360/20,117) *vs.* 95.0% (174,998/184,277)] (χ^2=485.7, P<0.001). Among migrants, 57.0% (1,467/20,117) initiated treatment before relocation, 33.8% (6,801/20,117) began treatment after relocation, and 9.2% (1,849/20,117) remained untreated.

The migration patterns of HIV-positive MSM predominantly involved key out-migrating and in-migrating PLADs. Among the 20,117 HIV-positive MSM who migrated, 10,244 (50.9%) were initially diagnosed in economically developed PLADs. The PLADs with the highest numbers of out-migrating cases were Guangdong, Shanghai, Zhejiang, Beijing, and Jiangsu (Figure 1A). Analysis of migration destinations revealed that 86.4% (8,854/10,244) of these individuals relocated to PLADs corresponding to their household registration place for follow-up. Specifically, of 21,974 MSM diagnosed in Guangdong, 2,376 (10.8%) migrated to other PLADs, with 2,063 (86.8%) returning to their household registration place. Among 6,907 MSM diagnosed in Shanghai, 2,208 (32.0%) relocated, with 2,028 (91.8%) returning to their household registration place. Of 11,790 MSM diagnosed in Zhejiang, 2,085 (17.7%) migrated, with 1,808 (86.7%) returning to their household registration place. For 11,521 MSM diagnosed in Beijing, 1,956 (17.0%) migrated, with 1,604 (82.0%) returning to their household registration place. Among 14,823 MSM diagnosed in Jiangsu, 1,619 (10.9%) migrated, with 1,351 (83.4%) returning to their household registration place. The PLADs with the highest proportion of out-migrating cases were Shanghai (2,208/6,907, 32.0%), Zhejiang (2,085/11,790, 17.7%), Beijing (1,956/11,521, 17.0%), Tianjin (530/3,483, 15.2%), and Fujian (632/4,645, 13.6%) (Figure 1B). The top five PLADs receiving in-migrating cases were Sichuan (1,532 cases), Anhui (1,497 cases), Henan (1,486 cases), Guangdong (1,268 cases), and Hunan (1,116 cases), collectively accounting for 34.3% of all migrant MSM (Figure 1C). The PLADs with the highest proportion of in-migrating cases were Jiangxi (888/3,372, 26.3%), Anhui (1,497/7,803, 19.2%), Guangxi (704/4,688, 15.0%), Hunan (1,116/7,888, 14.2%), and Henan (1,486/11,527, 12.9%) (Figure 1D). Notable migration corridors with over 300 cases included Beijing-Hebei (474 cases), Shanghai-Anhui (434 cases), Jiangsu-Anhui (410 cases), Guangdong-Hunan (409 cases), Guangdong-Guangxi (397 cases), and Zhejiang-Anhui (300 cases).

Analysis of migration-related factors revealed several significant associations. Compared to those aged ≥50 years, individuals aged 15–24 years had a higher likelihood of migration [adjusted odds ratio (a*OR*)=2.29, 95% *CI*: 2.13, 2.47], as did those aged 25–49 years (a*OR*=1.63, 95% *CI*: 1.53, 1.73). Being unmarried was associated with increased migration (compared to married individuals, a*OR*=1.21, 95% *CI*: 1.16, 1.27). Lower education levels showed a clear gradient effect, with primary school and below (a*OR*=1.89, 95% *CI*: 1.76, 2.02), junior high school (a*OR*=1.61, 95% *CI*: 1.54, 1.68), and senior high school (a*OR*=1.21, 95% *CI*: 1.16, 1.25) all showing higher migration rates compared to college education and above. Occupation also influenced migration patterns, with commercial staff (a*OR*=1.49, 95% *CI*: 1.37, 1.63) and students (a*OR*=1.38, 95% *CI*: 1.25, 1.51) more likely to migrate than government employees. Additional risk factors included having STD history (a*OR*=1.16, 95% *CI*: 1.12, 1.21), being identified through testing among key populations (a*OR*=1.18, 95% *CI*: 1.12, 1.24), and being diagnosed between 2016–2019 (a*OR*=2.13, 95% *CI*: 2.06, 2.21) (Figure 2).

DISCUSSION

This study reveals significant patterns of post-HIV diagnosis migration among MSM in China, characterized by initial diagnosis in economically developed regions followed by return migration to household registration locations in central and western PLADs for follow-up care. Key factors associated with post-diagnosis migration include age under 50, unmarried status, lower educational attainment, employment as commercial staff or student status, STD history, and diagnosis before 2020.

The findings indicate that approximately 10% of HIV-positive MSM relocated between diagnosis and follow-up, exceeding the migration rate of the general

TABLE 1. Demographic characteristics of HIV-positive MSM categorized by provincial-level migration status in China, 2016–2022.

Characteristics	Non-migrant MSM *N* (%) (*n*=184,277)	Migrant *N* (%) (*n*=20,117)	Chi-square	*P*
Age group (years)			1,029.04	<0.001
15–24	50,084 (27.2)	7,325 (36.4)		
25–49	112,478 (61.0)	11,446 (56.9)		
50–65	18,536 (10.1)	1,203 (6.0)		
≥66	3,179 (1.7)	143 (0.7)		
Marital status			368.10	<0.001
Married	40,653 (22.1)	3,553 (17.7)		
Unmarried	118,629 (64.4)	14,296 (71.1)		
Divorced	24,636 (13.4)	2,215 (11.0)		
Unknown	359 (0.2)	53 (0.3)		
Ethnic group			13.63	<0.001
Han	172,746 (93.7)	18,724 (93.1)		
Others	11,531 (6.3)	1,393 (6.9)		
Education background			217.19	<0.001
Primary school and below	10,818 (5.9)	1,280 (6.4)		
Junior high school	46,254 (25.1)	5,851 (29.1)		
Senior high school	46,062 (25.0)	5,094 (25.3)		
College and above	81,143 (44.0)	7,892 (39.2)		
Occupation			383.77	<0.001
Farming, factory worker & off-farm worker	44,199 (24.0)	4,448 (22.1)		
Domestic service &unemployed*	48,676 (26.4)	4,914 (24.4)		
Commercial staff†	42,231 (22.9)	5,477 (27.2)		
Student	14,614 (7.9)	1,988 (9.9)		
Government employee	9,224 (5.0)	693 (3.4)		
Others	25,333 (13.7)	2,597 (12.9)		
STD history			46.88	<0.001
Yes	25,378 (13.8)	3,101 (15.4)		
No	138,559 (75.2)	14,724 (73.2)		
Unknown	20,340 (11.0)	2,292 (11.4)		
Source of detection			242.38	<0.001
PITC	74,741 (40.6)	7,673 (38.1)		
Testing among key populations§	19,033 (10.3)	2,573(12.8)		
Others	7,366 (4.0)	964 (4.8)		
VCT	83,137 (45.1)	8,907 (44.3)		
Reporting years			1,961.53	<0.001
2016–2019	114,954 (62.4)	15,726 (78.2)		
2020–2022	69,323 (37.6)	4,391 (21.8)		

Abbreviation: HIV=human immunodeficiency virus; PITC=provider-initiated testing and counselling; VCT=voluntary counseling and testing; STD=sexually transmitted disease; MSM=men who have sex with men.

* Domestic service included housekeepers and caregivers, etc., and "Unemployed" contained job seekers, temporarily unemployed, stay-at-home parents and laid-off workers, etc.

† Commercial staff included individuals employed in various commercial sectors such as retail, sales, marketing, business services, and other non-sex work related commercial activities.

§ Testing among key populations included premarital examination, screening of spouses or sexual partners of individuals living with HIV, testing of children born to HIV-positive women, screening of blood donors, and health examinations for individuals in entertainment venues, those entering or leaving the country, and new recruits, etc.

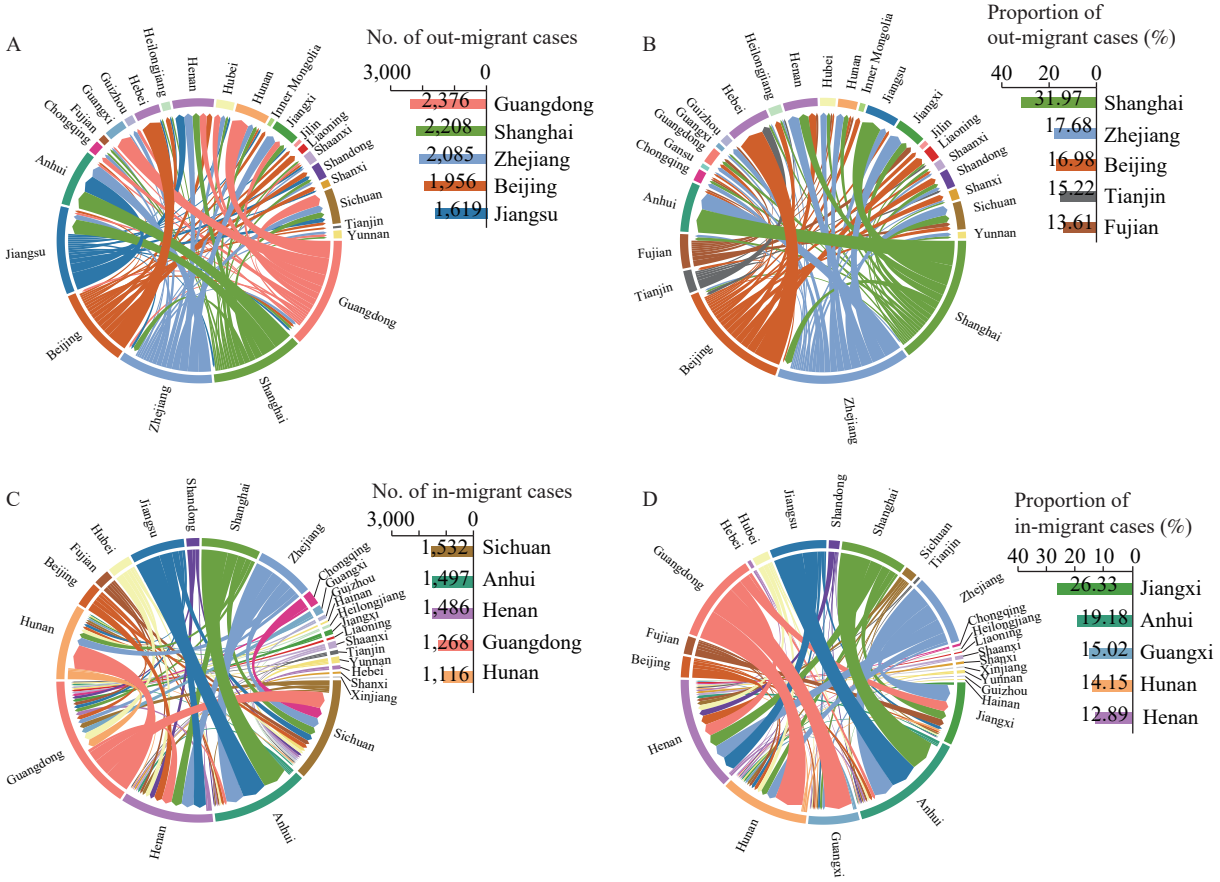

FIGURE 1. The out-migration and in-migration of HIV+ MSM among key PLADs regarding numbers and proportion, 2016–2022. (A) Top five PLADs with highest out-migrant numbers; (B) Top five PLADs with the highest proportion of out-migrants; (C) Top five PLADs with highest in-migrant numbers; (D) Top five PLADs with the highest proportion of in-migrants.

Note: This figure showed the top five PLADs in terms of out-migrant and in-migrant numbers/proportions in PLADs. Abbreviation: HIV=human immunodeficiency virus; MSM=men who have sex with men; PLAD=provincial-level administrative division.

HIV-positive population (7.8%). This elevated mobility among MSM reflects complex intersections of cultural, economic, and health-related factors. Young, single individuals with lower educational attainment and STD history demonstrated higher mobility patterns. These younger, single individuals typically exhibit greater sexual activity, and their engagement in high-risk behaviors during migration may facilitate HIV transmission to the general population, making them crucial targets for intervention strategies. Limited educational attainment often restricts employment opportunities, necessitating increased geographical mobility in search of better prospects. This mobility, combined with potentially limited HIV awareness, increases vulnerability to high-risk sexual behaviors during migration, contributing to HIV transmission patterns (*4*). Commercial staff, characterized by complex social networks, present particular challenges for AIDS response due to their inherent mobility. Additionally, the marked decrease in migration during 2020–2022 likely reflects the impact of coronavirus disease 2019 (COVID-19) pandemic restrictions, including travel limitations, lockdowns, and economic uncertainty.

Economically developed regions, particularly Guangdong, Beijing, and the Yangtze River Delta (Shanghai-Zhejiang-Jiangsu), attract MSM due to their superior employment opportunities, enhanced anonymity, and greater social acceptance. However, the findings reveal that many MSM subsequently return to their home PLADs, including Anhui, Henan, Sichuan, Hunan, and Hebei, for follow-up care. This pattern aligns with the "coming home" phenomenon described in previous research, which identified proximity to family as the primary motivator for relocation among HIV-infected individuals (*5*). HIV-positive MSM may face heightened privacy concerns and social stigma in metropolitan areas, making smaller

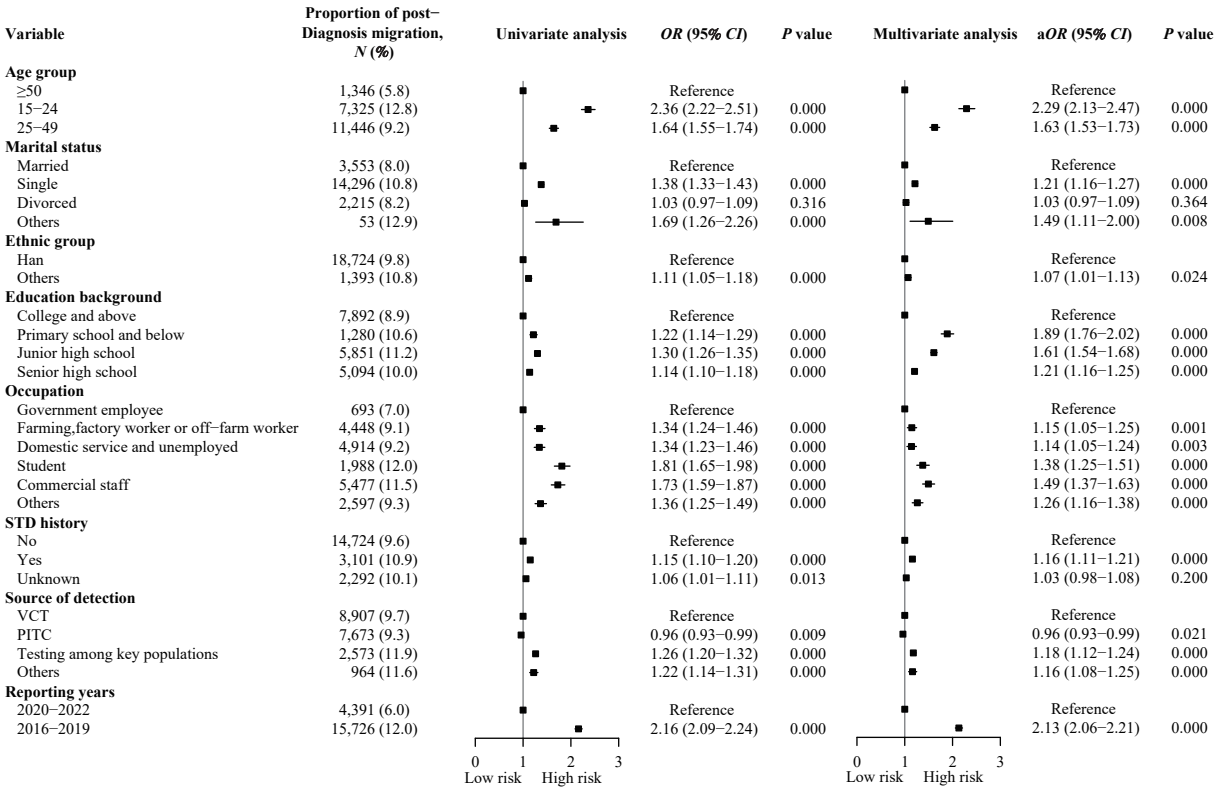

FIGURE 2. Univariate and multivariable analysis for the association between related factors and migration among HIV-positive MSM in China, 2016–2022.
Abbreviation: *OR*=odds ratio; a*OR*=adjusted odds ratio; *CI*=confidence interval; HIV=human immunodeficiency virus; MSM=men who have sex with men.

cities or their places of household registration more appealing (*6*). These familiar environments often provide greater acceptance and understanding (*7*). This contrasts with findings from the United States, where HIV-positive individuals typically migrate to larger urban centers post-diagnosis, attracted by more favorable healthcare policies, particularly liberal Medicaid coverage (*8*).

Local insurance policies emerge as crucial determinants of migration patterns. Despite China's provision of free HIV treatment, non-local MSM encounters significant barriers, including variable testing fees and reduced reimbursement rates, which often compel them to return to their home PLADs. This migration can delay treatment initiation, potentially increasing the risk of drug resistance. Pre-treatment testing fees in major cities vary considerably, ranging from full reimbursement to complete self-payment, imposing substantial economic burdens on migrant patients (*9*). Furthermore, out-of-province treatment restrictions, including lower reimbursement rates, complex administrative procedures, and extended reimbursement cycles, contribute to patient outflow. It is recommended establishing a streamlined, cross-provincial reimbursement system with a centralized digital platform for efficient claim processing and tracking is recommended. Notably, the findings indicate that a significant proportion of patients-initiated treatment post-migration, increasing their risk of drug resistance. This observation parallels U.S. research showing that 11.3% of HIV-positive individuals discontinued treatment during travel periods (*10*).

These findings underscore the necessity for targeted services to promote timely treatment among the nearly one-third of migrant MSM who delay treatment initiation. It is recommended that economically developed PLADs consider relaxing household registration requirements, streamlining administrative processes, and reducing policy barriers for non-local residents. Additionally, major cities should enhance transparency in medical insurance policies and ensure timely communication of policy changes to maximize accessibility for non-local patients.

Beyond the major economic centers, PLADs such as Tianjin and Fujian demonstrate notable post-diagnosis out-migration patterns, highlighting the need for comprehensive management protocols for non-local

patients. These protocols should encompass strengthened treatment referral mechanisms and enhanced HIV prevention and control measures. The significant inflow to PLADs like Anhui, Henan, and Hunan necessitates effective case management strategies in both origin and destination regions to prevent HIV transmission. To facilitate this, it is recommended that incentive structures be implemented for local governments, such as the allocation of additional funding and resources based on migrant case management metrics. Furthermore, establishing robust partnerships between local health departments, NGOs, and community-based organizations would enable comprehensive care delivery for this mobile population. It is suggested that proactive information-sharing systems and coordinated healthcare provider networks among affected PLADs be implemented to ensure continuity of care and follow-up services. This integrated approach represents an effective long-term strategy for HIV/AIDS management from both public health and individual care perspectives.

This study has several limitations. First, this study only analyzed migration patterns between initial diagnosis and follow-up visits, leaving the precise timing and location of HIV acquisition unknown. Second, detailed data on the time interval between diagnosis and initial follow-up were lacking, highlighting the need for more comprehensive temporal data collection in future research. Despite these limitations, the large sample size and broad geographic coverage of the study provide valuable insights into post-diagnosis migration patterns and significant implications for HIV prevention among mobile HIV-positive MSM populations. Additionally, information on economic status and behavioral characteristics were not examined. Future studies should address these factors to better understand how mobility influences and enhances AIDS response strategies.

The evidence of substantial post-diagnosis migration among HIV-positive MSM in China underscores the critical need for policymakers to address the unique HIV prevention and care requirements of this mobile population. Specifically, tailored behavioral interventions and continuous treatment support must be readily accessible at both origin and destination locations to effectively control HIV transmission and ensure treatment adherence. Implementing comprehensive care strategies throughout the migration process can better protect the health of HIV-positive MSM, reduce transmission rates, and improve treatment outcomes in China.

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Preplanned Studies

Associations of First-Year Low-Level Viremia with Subsequent Viral Non-Suppression in People Living with HIV on Antiretroviral Therapy — Dehong Dai and Jingpo Autonomous Prefecture, Yunnan Province, China, 2008–2021

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Summary

What is already known about this topic?

Human immunodeficiency virus (HIV) low-level viremia (LLV) during antiretroviral therapy (ART) occurs frequently in Dehong Dai and Jingpo Autonomous Prefecture, Yunnan Province.

What is added by this report?

Among people living with HIV who achieved virological success [viral load (VL) <1,000 copies/mL] after initiating ART in Dehong Prefecture, Southwest China, 17.6% experienced first-year LLV of 50–999 copies/mL First-year LLV emerged as an independent risk factor for subsequent viral non-suppression compared with participants maintaining first-year VL <50 copies/mL.

What are the implications for public health practice?

Enhanced monitoring and interventions for early LLV occurrence during the first year of ART are essential, including adherence education and timely VL testing.

Antiretroviral therapy (ART) can dramatically reduce the human immunodeficiency virus (HIV) viral load (VL) in people living with HIV (PLHIV). However, a subset of PLHIV experience detectable VL between 50 and 999 copies/ml during long-term ART, a phenomenon referred to as low-level viremia (LLV) (*1*). Multiple studies have demonstrated that LLV is associated with adverse clinical outcomes, including virological failure (*1–5*). Despite these findings, the relationship between first-year LLV and subsequent VL trajectories remains understudied in China. This study investigated the association between first-year LLV and subsequent viral non-suppression during five-year follow-ups in Dehong Dai and Jingpo Autonomous Prefecture, Yunnan Province, China. We analyzed data from 4,087 PLHIV on ART who achieved first-year VL <1,000 copies/mL in Dehong Prefecture from 2008 to 2021, employing nominal logistic regression analyses to examine these associations. Among the study population, 12.8% experienced first-year LLV of 50–199 copies/mL, while 4.8% had LLV of 200–999 copies/mL. The adjusted odds ratios (a*OR*s) [95% confidence interval (*CI*)] of first-year LLV for five-year LLV 50–999 and VL ≥1,000 copies/mL were 18.99 (95% *CI*: 14.55, 24.79) and 4.90 (95% *CI*: 3.55, 6.76), respectively. Our findings demonstrate that first-year LLV of 50–999 copies/mL significantly increases the risk of poor virological outcomes, highlighting the critical need for enhanced monitoring and intervention strategies for early LLV occurrence in patients on ART.

We conducted a retrospective cohort study analyzing treatment-naive PLHIV enrolled in China's National Free Antiretroviral Treatment Program in Dehong Prefecture, Yunnan Province, Southwest China. Dehong Prefecture is a highly endemic area for HIV transmission and holds historical significance as the location of China's first reported HIV infection through injection drug use (IDU) in 1989. Well-trained local healthcare providers collected comprehensive data through participant interviews, including demographic characteristics, HIV infection details, VL measurements, CD4 cell counts, hemoglobin levels, hepatitis B surface antigen (HBsAg), anti-hepatitis C virus (HCV) antibody status, ART regimens, initiation dates, and adherence (*6–7*). Bad ART adherence was defined as ≥2 missed ART doses during first-year or two-year follow-ups, or ≥3 missed doses during five-year follow-ups. Follow-up duration was segmented into one-year intervals after six months of ART: 1±0.5, 2±0.5, 3±0.5, 4±0.5, and 5±0.5 years. For multiple VL tests within an interval,

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the last value was used. Study inclusion criteria were: 1) ART initiation in Dehong Prefecture between 2008 and 2016 with follow-up through 5 years or until December 2021; 2) age ≥18 years at ART initiation; 3) minimum of three VL tests after 6 months of ART initiation; and 4) first-year VL <1,000 copies/mL (achieving virological success) with documented second-year VL. Participants were excluded if their transmission route was neither sexual contact nor IDU, or if ethnicity, education level, or baseline CD4 data were missing.

We analyzed participants' baseline characteristics stratified by first-year VL groups and described VL distribution (VL <50, LLV 50–199, LLV 200–999, and ≥1,000 copies/mL) across follow-up years. Univariate and multivariate nominal logistic regression models using stepwise selection investigated associations between first-year VL and subsequent viral outcomes. Second-year VL outcomes were categorized as <50, LLV 50–999, and ≥1,000 copies/mL. Five-year VL profiles were classified as: VL ≥1,000 (≥2 instances of VL ≥1,000 copies/mL or one VL ≥1,000 copies/mL plus one LLV 50–999), LLV 50–999 (one or no VL ≥ 1,000 copies/mL and ≥2 instances of LLV 50–999), and VL <50 (maximum one instance of VL ≥ 50 copies/mL, otherwise <50 copies/mL). Statistical significance was set at $P<0.05$ (two-tailed), and analyses were performed using SAS (version 9.4; SAS Institute Inc., Cary, NC, USA). The study received approval from the institutional review board of the National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention.

Among 4,087 participants enrolled in Dehong Prefecture, Yunnan Province during 2008–2021, 93.8% (4,087/4,356) achieved first-year virological success. The cohort's median age was 36 years (interquartile range, *IQR*: 30–44), with 56.0% being male and 79.2% acquiring HIV through sexual transmission. The ethnic composition comprised Han (44.6%), Dai (29.6%), and Jingpo (20.2%) populations. Educational attainment was predominantly at or below primary school level (58.4%). Baseline median CD4 count was 256 cells/μL (*IQR*: 145–369 cells/μL), with 36.4% of participants having counts below 200 cells/μL. ART initiation was distributed across three periods: 2008–2010 (30.5%), 2011–2013 (46.9%), and 2014–2016 (22.6%). The standard first-line regimen — [tenofovir (TDF) or zidovudine (AZT)] + lamivudine (3TC) + [efavirenz (EFV) or nevirapine (NVP)] — was initiated in 79.8% of participants. During the first year of ART, 12.8% and 4.8% of participants experienced LLV 50–199 and LLV 200–999 copies/mL, respectively (Table 1). At the five-year follow-up conclusion, treatment retention was 94.36% (3,856 participants), with 2.4% (99) lost to follow-up and 3.2% (132) deceased.

The proportion of participants experiencing LLV decreased progressively over the five-year follow-up period: 17.6% (719/4,087) in year 1, 12.4% (505/4,087) in year 2, 8.1% (291/3,590) in year 3, 6.6% (228/3,436) in year 4, and 5.6% (185/3,329) in year 5 (Figure 1). Second-year viral load distribution showed 83.5% with VL <50 copies/mL, 12.3% with LLV 50–999 copies/mL and 4.2% with VL ≥1,000 copies/mL. The five-year viral load profile revealed 84.6% maintained VL <50 copies/mL, 10.1% experienced LLV, and 5.3% had VL ≥1,000 copies/mL.

Using multivariate logistic regression with VL < 50 copies/mL as the reference event, participants with first-year LLV showed significantly higher risks of subsequent viral non-suppression. The a*OR*s for second-year outcomes were 2.58 (95% *CI*: 2.06, 3.24) for LLV 50–999 copies/mL and 3.42 (95% *CI*: 2.37, 4.93) for VL ≥1,000 copies/mL. For five-year outcomes, the a*OR*s were even more pronounced: 18.99 (95% *CI*: 14.55, 24.79) for LLV 50–999 copies/mL and 4.90 (95% *CI*: 3.55, 6.76) for VL ≥ 1,000 copies/mL (Table 2). The association between first-year LLV and subsequent detectable VL remained robust across multiple sensitivity analyses, accounting for baseline CD4 count, ART initiation year, adherence, and regimen changes.

DISCUSSION

This cohort study, comprising 4,087 participants on ART from 2008–2021 in Dehong Prefecture, demonstrated that 17.6% of participants experienced LLV of 50–999 copies/mL during their first year of ART follow-up. Furthermore, the presence of first-year LLV significantly increased the risk of sustained LLV or VL ≥1,000 copies/mL during early ART follow-up.

The observed 17.6% prevalence of first-year LLV among participants achieving virological success in Dehong Prefecture (2008–2021), along with the

TABLE 1. Baseline characteristics of 4,087 people living with HIV who achieved virological success in first-year ART in Dehong Prefecture, Yunnan Province, China, 2008–2021.

Characteristics	Total (%) (*N*=4,087)	VL <50 copies/mL (*n*=3,368, 82.4%)	LLV 50–199 copies/mL (*n*=523, 12.8%)	LLV 200–999 copies/mL (*n*=196, 4.8%)
Age at ART				
18–30 years	1,172 (28.7)	976 (83.3)	140 (11.9)	56 (4.8)
31–50 years	2,458 (60.1)	2,004 (81.5)	329 (13.4)	125 (5.1)
>50 years	457 (11.2)	388 (84.9)	54 (11.8)	15 (3.3)
Gender				
Female	1,799 (44.0)	1,510 (83.9)	201 (11.2)	88 (4.9)
Male	2,288 (56.0)	1,858 (81.2)	322 (14.1)	108 (4.7)
Ethnicity				
Han	1,823 (44.6)	1,476 (81.0)	267 (14.6)	80 (4.4)
Dai	1,208 (29.5)	1,010 (83.6)	145 (12.0)	53 (4.4)
Jingpo	824 (20.2)	682 (82.8)	93 (11.3)	49 (5.9)
Other	232 (5.7)	200 (86.2)	18 (7.8)	14 (6.0)
Education				
Illiteracy	591 (14.5)	508 (86.0)	64 (10.8)	19 (3.2)
Primary school	1,795 (43.9)	1,446 (80.6)	230 (12.8)	119 (6.6)
Middle school and above	1,701 (41.6)	1,414 (83.1)	229 (13.5)	58 (3.4)
Transmission route				
Sexual contact	3,235 (79.2)	2,699 (83.4)	392 (12.1)	144 (4.5)
IDU	852 (20.8)	669 (78.5)	131 (15.4)	52 (6.1)
Duration from HIV diagnosis to ART				
<1 years	2,134 (52.2)	1,740 (81.5)	298 (14)	96 (4.5)
≥1 years	1,953 (47.8)	1,628 (83.4)	225 (11.5)	100 (5.1)
WHO clinical stage				
1–2	2,283 (55.9)	1,950 (85.4)	242 (10.6)	91 (4.0)
3–4	1,804 (44.1)	1,418 (78.6)	281 (15.6)	105 (5.8)
Baseline CD4 cells, cells/μL				
<200	1,490 (36.4)	1,161 (77.9)	238 (16.0)	91 (6.1)
200–349	1,453 (35.6)	1,158 (79.7)	214 (14.7)	81 (5.6)
≥350	1,144 (28.0)	1,049 (91.7)	71 (6.2)	24 (2.1)
Baseline hemoglobin, g/L				
≥90	3,847 (94.1)	3,179 (82.6)	490 (12.8)	178 (4.6)
<90	192 (4.7)	147 (76.6)	28 (14.6)	17 (8.9)
Not tested	48 (1.2)	42 (87.5)	5 (10.4)	1 (2.1)
Baseline HBsAg				
Negative	2,847 (69.6)	2,521 (88.6)	249 (8.7)	77 (2.7)
Positive	215 (5.3)	190 (88.4)	22 (10.2)	3 (1.4)
Not tested	1,025 (25.1)	657 (64.1)	252 (24.6)	116 (11.3)
Baseline Anti-HCV				
Negative	2,306 (56.4)	2,050 (88.9)	195 (8.5)	61 (2.6)
Positive	544 (13.3)	465 (85.5)	64 (11.8)	15 (2.7)
Not tested	1,237 (30.3)	853 (69.0)	264 (21.3)	120 (9.7)

Continued

Characteristics	Total (%) (*N*=4,087)	VL <50 copies/mL (*n*=3,368, 82.4%)	LLV 50–199 copies/mL (*n*=523, 12.8%)	LLV 200–999 copies/mL (*n*=196, 4.8%)
Baseline regimen				
TDF+3TC+EFV/NVP	1,427 (34.9)	1,323 (92.7)	77 (5.4)	27 (1.9)
AZT+3TC+EFV/NVP	1,833 (44.9)	1,466 (80.0)	274 (14.9)	93 (5.1)
LPV/r+3TC+AZT/TDF	316 (7.7)	292 (92.4)	16 (5.1)	8 (2.5)
Other*	511 (12.5)	287 (56.2)	156 (30.5)	68 (13.3)
ART initiation year				
2008–2010	1,246 (30.5)	775 (62.2)	342 (27.4)	129 (10.4)
2011–2013	1,916 (46.9)	1,732 (90.4)	137 (7.1)	47 (2.5)
2014–2016	925 (22.6)	861 (93.1)	44 (4.7)	20 (2.2)

Abbreviation: 3TC=lamivudine; ART=antiretroviral therapy; AZT=zidovudine; CD4=CD4+ T lymphocytes; *CI*=confidence interval; D4T=stavudine; EFV=efavirenz; HBsAg=hepatitis B surface antigen; HCV=hepatitis C virus; HIV=human immunodeficiency virus; IDU=injection drug use; LLV=low-level viremia; LPV/r=lopinavir/ritonavir; NVP=nevirapine; *OR*=odds ratio; TDF=tenofovir; VL=viral load; VS=viral suppression.
* Primarily D4T+3TC+EFV/NVP regimen (491, 12.0%).

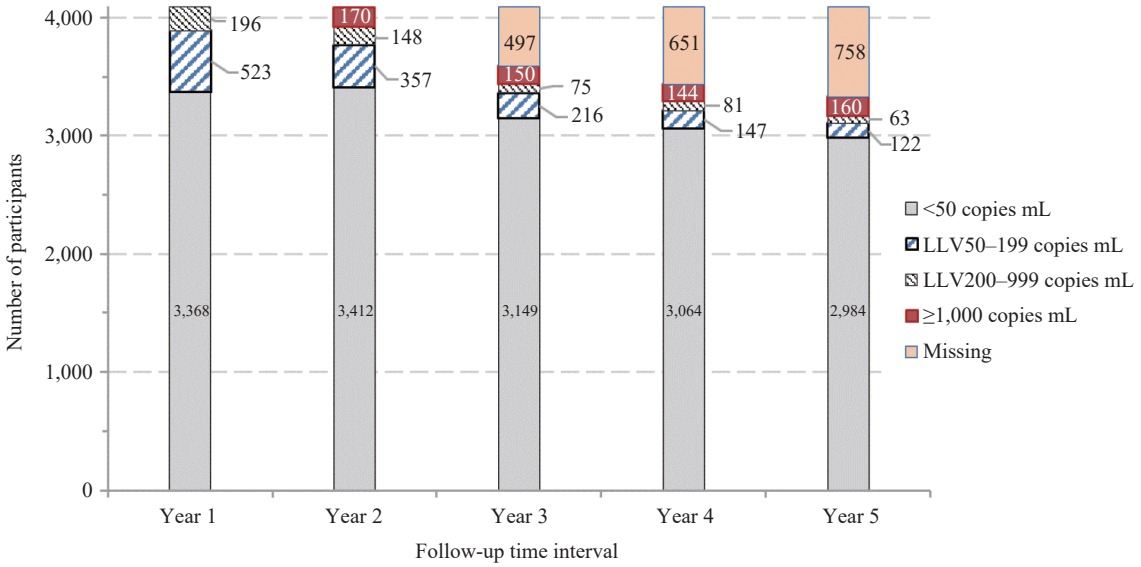

FIGURE 1. Temporal distribution of viral load levels during 5 years of antiretroviral therapy among 4,087 people living with HIV who achieved initial virological success in Dehong Prefecture, Yunnan Province, China, 2008–2021.
Note: Missing data indicates the proportion of individuals for whom viral load measurements were insufficient to determine viral load categorization.

10.1% five-year LLV rate, aligns with findings reported by Hermans, et al. (*1*), An, et al. (*8*), Ding, et al. (*9*), and Bai, et al. (*2*). These consistent findings across studies indicate that LLV represents a common challenge in ART management among PLHIV in Dehong Prefecture, warranting careful consideration in treatment protocols.

The multivariate logistic model demonstrated that first-year LLV of 50–999 copies/mL was significantly associated with both second-year VL and five-year viral non-suppression, predicting subsequent sustained LLV or VL ≥1,000 copies/mL. These findings align with previous research (*1*,*8*). Various factors, including ART initiation year and baseline regimen (*3*,*10*), may contribute to the development of subsequent LLV or virological failure. Drug resistance rates among PLHIV with LLV vary considerably, ranging from 10% to 40%. Current protocols in China mandate adherence assessment and drug-resistance testing when PLHIV experience persistent VL ≥1,000 copies/mL during ART. Since 2022, Dehong Prefecture has implemented a case-management program targeting PLHIV with LLV 200–999 copies/mL. Given the significance for sustained virological success, monitoring and

TABLE 2. Associations of first-year low-level viremia with second-year and five-year viral load profiles among 4,087 adult people living with HIV on antiretroviral therapy with virological success in Dehong Prefecture, Yunnan Province, China, 2008–2021.

Covariate*	Second-year VL profile				Five-year VL profile			
	LLV 50–999 copies/mL		VL ≥1,000 copies/mL		LLV 50–999 copies/mL		VL ≥1,000 copies/mL	
	OR (95% *CI*)	a*OR* (95% *CI*)	*OR* (95% *CI*)	a*OR* (95% *CI*)	*OR* (95% *CI*)	a*OR* (95% *CI*)	*OR* (95% *CI*)	a*OR* (95% *CI*)
First-year VL (copies/mL)								
VL<50	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
LLV 50–999	4.22 (3.44, 5.17)†	2.58 (2.06, 3.24)†	3.51 (2.52, 4.88)†	3.42 (2.37, 4.93)†	28.16 (21.94, 36.14)†	18.99 (14.55, 24.79)†	5.58 (4.14, 7.52)†	4.90 (3.55, 6.76)†
Transmission route								
Sexual contact	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
IDU	1.11 (0.89, 1.40)	0.92 (0.72, 1.19)	2.12 (1.53, 2.94)†	1.55 (1.09, 2.22)§	1.44 (1.14, 1.82)†	1.04 (0.75, 1.44)	2.31 (1.73, 3.09)†	1.74 (1.23, 2.47)†
Duration from HIV diagnosis to ART		–		–		–		–
<1 years	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)		1.0 (Ref)	
≥1 years	0.97 (0.80, 1.17)	1.05 (0.85, 1.29)	1.67 (1.22, 2.28)†	1.57 (1.10, 2.22)§	0.94 (0.76, 1.15)		1.52 (1.15, 2.01)†	
WHO clinical stage		–		–				
1–2	1.0 (Ref)		1.0 (Ref)		1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
3–4	0.72 (0.53, 0.96)		1.02 (0.68, 1.52)		2.02 (1.64, 2.49)†	1.44 (1.10, 1.88)†	0.99 (0.75, 1.30)	1.05 (0.77, 1.43)
Baseline CD4 cells, cells/μL						–		–
<200	2.73 (2.06, 3.61)†	1.65 (1.21, 2.24)†	1.41 (0.95, 2.09)	1.41 (0.92, 2.17)	3.59 (2.58, 5.01)†		1.72 (1.19, 2.48)†	
200–349	2.57 (1.94, 3.41)†	1.56 (1.15, 2.12)†	1.32 (0.88, 1.98)	1.28 (0.83, 1.97)	3.39 (2.43, 4.74)†		1.61 (1.11, 2.33)§	
≥350	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)		1.0 (Ref)	
Baseline HBsAg								
Negative	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Positive	1.39 (0.89, 2.17)	1.36 (0.86, 2.14)	0.54 (0.20, 1.48)	0.60 (0.22, 1.65)	1.26 (0.71, 2.21)	1.35 (0.72, 2.52)	1.66 (0.95, 2.89)	1.79 (1.01, 3.19)§
Not tested	3.80 (3.12, 4.63)†	2.37 (1.87, 3.00)†	2.34 (1.69, 3.23)†	2.42 (1.64, 3.58)†	5.80 (4.67, 7.22)†	2.57 (1.48, 4.46)†	2.22 (1.65, 2.99)†	0.91 (0.53, 1.56)
Baseline anti-HCV		–		–				
Negative	1.0 (Ref)		1.0 (Ref)		1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Positive	0.89 (0.63, 1.26)		1.75 (1.11, 2.78)§		1.59 (1.10, 2.30)§	1.43 (0.90, 2.27)	2.17 (1.47, 3.20)†	1.39 (0.87, 2.22)
Not tested	3.07 (2.51, 3.75)†		2.66 (1.90, 3.74)†		4.92 (3.90, 6.20)†	1.12 (0.64, 1.99)	2.58 (1.90, 3.50)†	2.24 (1.31, 3.83)†
ART initiation year						–		–
2008–2010	4.41 (3.28, 5.94)†	2.06 (1.47, 2.89)†	1.32 (0.86, 2.01)	0.58 (0.35, 0.98)§	6.14 (4.41, 8.55)†		1.90 (1.27, 2.84)†	
2011–2013	1.42 (1.04, 1.93)§	1.49 (1.08, 2.05)§	1.00 (0.67, 1.49)	1.00 (0.66, 1.51)	0.94 (0.65, 1.37)		1.31 (0.89, 1.92)	
2014–2016	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)		1.0 (Ref)	
Baseline regimen		–		–				
TDF+3TC+EFV/NVP	1.0 (Ref)		1.0 (Ref)		1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
AZT+3TC+EFV/NVP	1.77 (1.40, 2.25)†		1.04 (0.73, 1.49)		2.66 (1.97, 3.59)†	1.23 (0.87, 1.75)	1.32 (0.96, 1.82)	1.14 (0.80, 1.62)
LPV/r+3TC+AZT/TDF	0.71 (0.42, 1.19)		0.77 (0.39, 1.52)		1.13 (0.63, 2.01)	1.23 (0.66, 2.28)	0.85 (0.45, 1.59)	0.96 (0.50, 1.83)
Other	4.58 (3.47, 6.04)†		2.00 (1.27, 3.15)†		10.05 (7.27, 13.89)†	2.10 (1.37, 3.22)†	2.53 (1.67, 3.82)†	1.46 (0.90, 2.38)

Continued

Covariate*	Second-year VL profile				Five-year VL profile			
	LLV 50–999 copies/mL		VL ≥1,000 copies/mL		LLV 50–999 copies/mL		VL ≥1,000 copies/mL	
	OR (95% *CI*)	a*OR* (95% *CI*)	*OR* (95% *CI*)	a*OR* (95% *CI*)	*OR* (95% *CI*)	a*OR* (95% *CI*)	*OR* (95% *CI*)	a*OR* (95% *CI*)
Adherence to ART								
Good	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Bad	0.91 (0.68, 1.22)	1.39 (1.02, 1.90)§	2.31 (1.61, 3.34)†	2.62 (1.78, 3.85)†	1.00 (0.75, 1.34)	1.61 (1.13, 2.29)†	2.83 (2.10, 3.82)†	3.22 (2.32, 4.48)†

Abbreviation: a*OR*=adjusted odds ratio; AIDS=acquired immune deficiency syndrome; ART=antiretroviral therapy; CD4=CD4+ T lymphocytes; *CI*=confidence interval; HIV=human immunodeficiency virus; LLV=low-level viremia; Ref=reference group; VL=viral load.
* Univariate and multivariate multinomial logistic regression analyses were conducted separately for second-year VL and five-year VL profile models, with VL <50 copies/mL serving as the reference outcome. Sex, ethnicity, and education were statistically significant in univariate analyses (P<0.10) but not in multivariate analyses (P≥0.05) and are therefore not shown. Age and hemoglobin were not significant in univariate analyses (P≥0.10).
† P<0.01;
§ P<0.05.

interventions for early-stage LLV 50–999 copies/mL should be piloted and expanded.

This study has several limitations. First, as the data are derived from a single city in Yunnan Province, China, generalizability to other regions require caution. Second, the use of routine clinical data, with only one VL measurement per follow-up year, may introduce selection and information bias through data entry processes.

In conclusion, analysis of this PLHIV cohort on ART from Dehong Prefecture, Southwest China (2008–2021) revealed that first-year LLV of 50–999 copies/mL significantly increased the risk of poor virological outcomes. These findings underscore the importance of early LLV monitoring in ART patients and the need for timely interventions when detected.

Conflicts of interest: No conflicts of interest.

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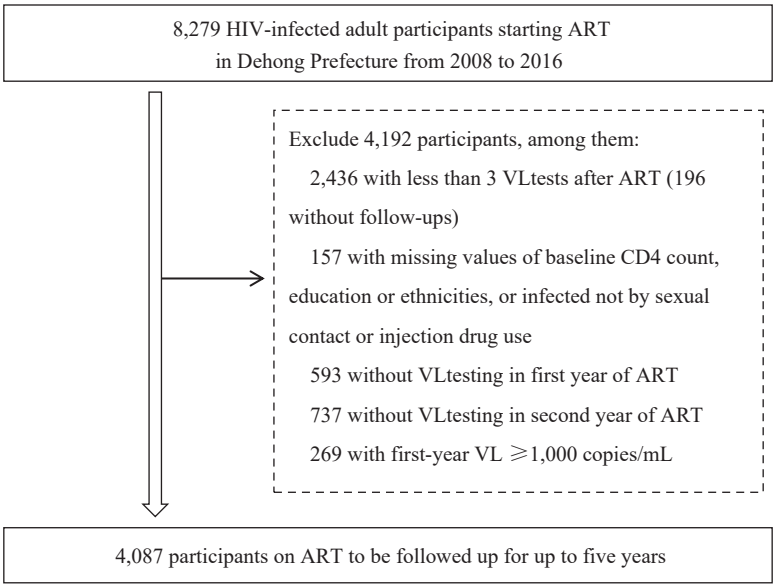
SUPPLEMENTARY MATERIALS



SUPPLEMENTARY FIGURE S1. Flow diagram of participant enrollment and selection.
Abbreviation: ART=antiretroviral therapy; CD4=CD4+ T lymphocytes; HIV=human immunodeficiency virus; VL=viral load.

Preplanned Studies

Accuracy of the Self-Administered Rapid HIV Urine Test in a Real-World Setting and Individual Preferences for HIV Self-Testing — Guangzhou City, Guangdong Province, China, July 2020–February 2021

Chunli Zhang[1,&]; Mengdie Li[2,&]; Yuzhou Gu[3]; Yongheng Lu[4,5]; Sha Chen[6]; Zhongqi Liu[7]; Yuantao Hao[8,9,10,#]; Chun Hao[1,2,#]

Summary

What is already known about this topic?

Human immunodeficiency virus (HIV) self-testing serves as a crucial strategy for overcoming testing barriers, with urine-based self-testing emerging as a potential novel approach.

What is added by this report?

In a real-world setting, this study demonstrated that the urine rapid test exhibited lower diagnostic accuracy compared to the blood rapid test. Study participants expressed stronger preferences for HIV self-testing methods utilizing finger prick samples, accompanied by standard written instructions and lower costs.

What are the implications for public health practice?

Our findings indicate that rapid urine testing requires additional validation before widespread implementation. Future development efforts should prioritize user-friendly HIV self-testing approaches to enhance testing accessibility.

Achieving 95% human immunodeficiency virus (HIV) testing coverage represents the crucial first step in meeting the 95-95-95 targets for eliminating HIV transmission (*1*). HIV self-testing has emerged as a promising strategy to overcome testing barriers (*2*). In 2019, China introduced a self-administered rapid HIV urine antibody test that demonstrated high sensitivity (99.17%) and specificity (100.00%) under trial and laboratory conditions (*3*). However, its real-world diagnostic performance in clinical practice and self-administered scenarios requires further empirical validation, and preferences regarding HIV self-testing methods remain unexplored. This study evaluated the accuracy of the self-administered rapid HIV urine test compared to the blood rapid test in a real-world setting. Additionally, a discrete choice experiment (DCE) survey was conducted to identify key attributes and preferences for HIV self-testing (*4*). Our findings revealed that the urine rapid test exhibited lower accuracy than the blood rapid test, particularly when self-administered by participants. The results indicated preferences for HIV self-testing using finger prick samples, standard instruction text, and lower-cost options. These findings suggest that urine-based self-testing requires additional validation before integration into routine screening protocols, and future HIV self-testing development should prioritize user-friendliness to enhance testing accessibility.

This study was conducted in Guangzhou City, Guangdong Province, China, from July 2020 to February 2021. Men who have sex with men (MSM) participants were recruited through convenience sampling at a peer-friendly HIV test clinic (*5*). Each participant independently collected their urine sample, performed the urine rapid test, and interpreted the results. Subsequently, staff members conducted a second urine rapid test and interpretation using the same sample. Participants then underwent the standard blood rapid test, with positive results confirmed through western blot testing. For the DCE design (*6*), attributes and their corresponding levels are presented in Supplementary Table S1 (available at https://weekly.chinacdc.cn/), with eight DCE choice sets detailed in Supplementary Table S2 (available at https://weekly.chinacdc.cn/). MSM testers who were permanent residents of Guangzhou and aged 18 years or older were invited to complete the DCE survey. The study was approved by the Ethics Committee of Sun Yat-sen University (Institutional Review Board number 054/19; February 28, 2019) and written informed consent was obtained from the participants.

Differences in sensitivity and specificity among the three rapid tests (blood rapid test, staff-conducted

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urine rapid test, and participant-conducted urine rapid test) were evaluated using Cochran's Q test. The Delong method was employed to assess differences in the area under the curve (AUC). For the DCE analysis, we utilized the conditional logit model, willingness to pay (WTP), and choice probability to identify participants' preferences for HIV self-testing attributes and levels. Statistical significance was set at $P<0.05$. Multiple comparisons between the three rapid tests were adjusted using the Bonferroni method, with significance level α set at 0.017 (0.05/3). All analyses were performed using R software (version 4.0.2, R Core Team, Vienna, Austria).

Among the 1,094 participants who underwent rapid urine test accuracy assessment (Table 1), 46 (4.20%) were confirmed HIV-positive by western blot.

The blood rapid test demonstrated optimal performance with 100.00% sensitivity [95% confidence interval (*CI*): 92.29, 100.00] and 99.81% specificity (95% *CI*: 99.31, 99.95). The staff-conducted urine rapid test showed 89.13% sensitivity (95% *CI*: 76.96, 95.27) and 99.90% specificity (95% *CI*: 99.46, 100.00), while the participant-conducted urine rapid test exhibited 82.61% sensitivity (95% *CI*: 69.28, 90.91) and 99.81% specificity (95% *CI*: 99.16, 99.90). Sensitivity differed significantly among the three rapid tests (P=0.002), whereas specificity did not (P=0.549). Multiple comparisons revealed significantly lower sensitivity in the participant-conducted urine rapid test compared to the blood rapid test (P=0.013). No significant differences were found between the staff-conducted urine rapid test and either the blood rapid test (P=0.074) or the participant-conducted urine rapid test (P=0.249). The AUC analysis showed significant differences (P=0.008) among the blood rapid test (0.9990) (Figure 1A), staff-conducted urine rapid test (0.9452), and participant-conducted urine rapid test (0.9116). Further pairwise comparisons revealed significantly lower AUC for the participant-conducted urine rapid test compared to the blood rapid test (P=0.002) (Figure 1B), marginally significant differences between the staff-conducted urine rapid test and blood rapid test (P=0.020) (Figure 1C), and no significant difference between staff-conducted and participant-conducted urine rapid tests (P=0.317) (Figure 1D).

Of the 1,094 participants, 846 completed the DCE questionnaire. Compared to reference conditions (Table 2), participants showed significant preferences for finger prick sampling [odds ratio (*OR*)=1.470, 95% *CI*: 1.338, 1.616, $P<0.001$], regular instruction text (*OR*=1.169, 95% *CI*: 1.044, 1.308, P=0.007), and lower cost (*OR*=0.980, 95% *CI*: 0.977, 0.981, $P<0.001$). No significant preferences emerged regarding test result interpretation (*OR*=1.063, 95% *CI*: 0.928, 1.218, P=0.466). Willingness-to-pay analysis revealed participants would pay an additional $2.823 for finger prick sampling over urine sampling, and $1.141 more for regular instruction text compared to instructional video. Detailed hierarchical DCE analyses are presented in Supplementary Tables S3–S4 (available at https://weekly.chinacdc.cn/), with choice probabilities for test type and instruction method shown for the total sample and subgroups in Supplementary Figure S1 (available at https://weekly.chinacdc.cn/).

TABLE 1. The accuracy of the blood rapid test, staff-conducted urine rapid test, and participant-conducted urine rapid test (*N*=1,094).

Types of HIV rapid self-tests		Western blot result		Total	Sensitivity (%) (95% *CI*)	Specificity (%) (95% *CI*)
		Positive	Negative			
Blood rapid test	Positive	46	2	48	100.00 (92.29, 100.00)	99.81 (99.31, 99.95)
	Negative	0	1,046	1,046		
	Total	46	1,048	1,094		
Staff-conducted urine rapid test	Positive	41	1	42	89.13 (76.96, 95.27)	99.90 (99.46, 100.00)
	Negative	5	1,047	1,052		
	Total	46	1,048	1,094		
Participant-conducted urine rapid test	Positive	38	3	41	82.61 (69.28, 90.91)	99.71 (99.16, 99.90)
	Negative	8	1,045	1,053		
	Total	46	1,048	1,094		

Abbreviation: HIV=human immunodeficiency virus; *CI*=confidence interval.

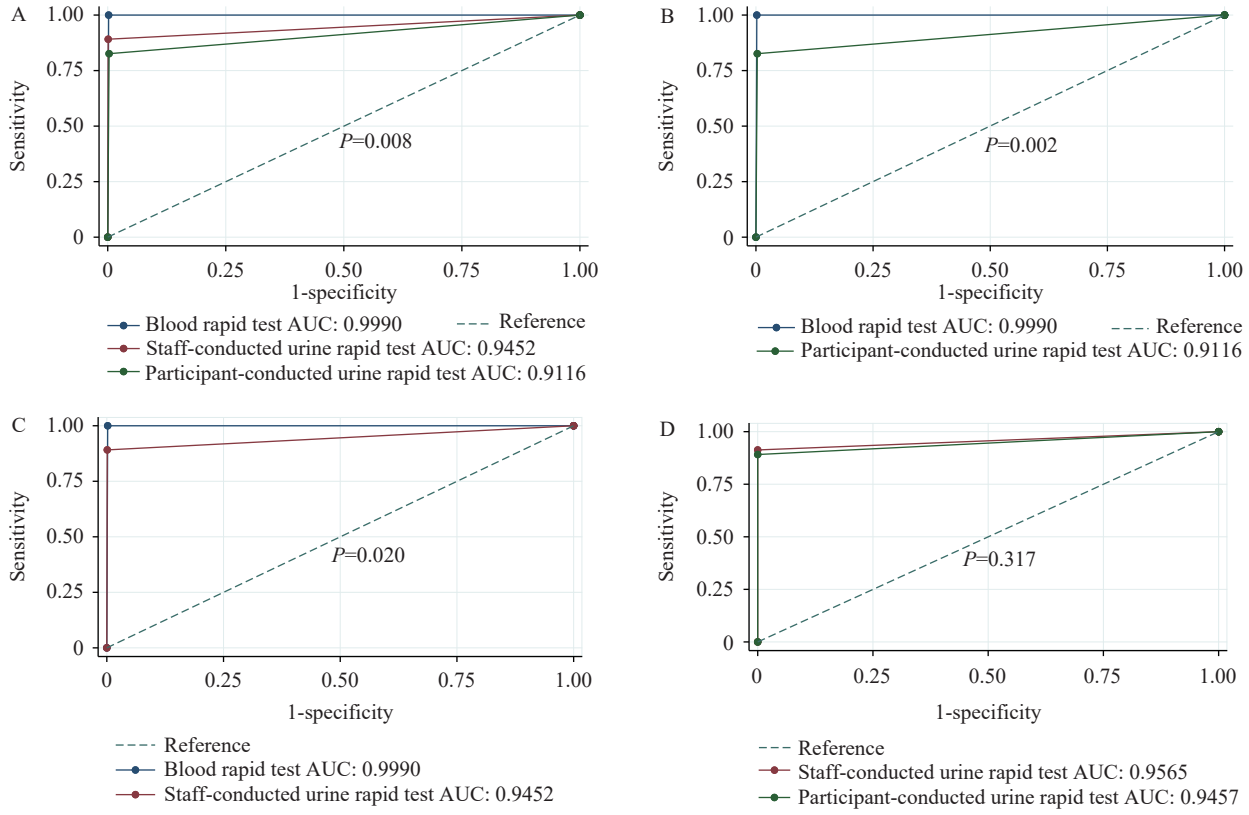

FIGURE 1. Comparison of AUC among blood rapid test, staff-conducted urine rapid test, and participant-conducted urine rapid test. (A) Overall AUC comparison among the three test methods; (B) AUC comparison between blood rapid test and staff-conducted urine rapid test; (C) AUC comparison between blood rapid test and participant-conducted urine rapid test; (D) AUC comparison between staff-conducted and participant-conducted urine rapid tests.
Note: Panels B, C, and D represent post-hoc analyses following the overall comparison in panel A. Results were adjusted using the Bonferroni method (P<0.017 was considered statistically significant).
Abbreviation: AUC=area under the curve.

TABLE 2. Estimation of DCE in the total population (N=846).

Attributes and levels	*OR*	95% *CI*	*P*	WTP (USD)[†]
Type of test				
Finger prick	1.470	(1.338, 1.616)	<0.001*	2.823
Urine sample (reference)	–	–	–	–
Instructions on how to conduct the test				
Regular instruction text	1.169	(1.044, 1.308)	0.007*	1.141
Instructional video (reference)	–	–	–	–
The interpretation of test result				
By themselves	1.063	(0.928, 1.218)	0.381	0.446
By clinic staff (reference)	–	–	–	–
Cost of the test[§]	0.980	(0.977, 0.981)	<0.001*	–

Note: "–" means this level is the reference level and there are no corresponding parameter values. This indicates the baseline category for comparison in the regression model.
Abbreviation: WTP=willingness to pay; *OR*=odds ratio; *CI*=confidence interval; USD=United States dollar; DCE=discrete choice experiment.
* P<0.05.
[†] $WTP_{fingerprick} = -\beta_{fingerprick} / \beta_{price}$.
[§] The cost attribute was treated as a continuous variable in the DCE analysis to calculate willingness to pay, although it was constrained to four discrete values: 0 USD, 3 USD, 7.5 USD, and 12 USD.

DISCUSSION

Our study revealed that the urine rapid test demonstrated lower accuracy compared to the blood rapid test in real-world settings, particularly when self-administered by participants. The findings also indicated that participants expressed preferences for HIV self-testing using finger prick samples, conventional instruction text, and lower-cost options.

Previous evaluations of urine rapid tests have predominantly been conducted in controlled laboratory settings (*7*–*8*), with limited evidence of their diagnostic performance in real-world conditions. The underlying mechanism of urine rapid tests relies on detecting HIV antigens or nucleic acids through antibody-antigen binding or nucleic acid amplification. However, urine samples inherently contain lower concentrations of HIV antigens and nucleic acids compared to blood samples. Our study population likely included individuals in various stages of infection, including the incubation period with fluctuating viral loads, contrasting with laboratory studies that typically focus on confirmed positive cases. The reduced accuracy in real-world settings may be attributed to lower and more variable HIV antibody levels in non-blood samples, compounded by environmental variables absent in laboratory conditions. Furthermore, the visual interpretation of the urine rapid test strip bands presented additional challenges. Due to insufficient professional training and experience, coupled with the relatively weaker band intensity in some positive results, participants were more prone to misclassifying positive results as negative compared to trained staff. Staff surveys also revealed that positive results consistently showed weaker band intensity on urine rapid test strips compared to blood rapid test strips.

While extensive research exists on oral HIV self-testing (*9*), studies examining urine-based tests remain limited. Our DCE results demonstrated that high-risk populations in China preferred traditional blood-based testing methods with standard instruction text and affordable pricing. This aligns with previous research on oral tests, where participants similarly favored blood-based testing (*1*). These preferences may reflect limited awareness and uncertainty regarding novel testing methodologies. Nevertheless, some individuals preferred non-blood self-testing methods, citing advantages such as rapid results and painless administration (*9*). The preference for traditional instructional text over video formats may be attributed to its efficiency, accessibility, and independence from electronic devices. Future development efforts should prioritize creating user-friendly HIV test kits with clear instructions and streamlined procedures.

This study has several limitations. First, its geographical scope was restricted to a single city in Guangdong Province, China, potentially limiting the generalizability of our findings. Additionally, the DCE methodology did not include an opt-out option, consistent with similar DCE studies (*10*).

In conclusion, test accuracy is significantly influenced by detection methodology and test brand characteristics, highlighting the necessity for further validation of rapid urine testing. Furthermore, the development of user-friendly, cost-effective test kits with clear instructions is essential for enhancing HIV testing uptake among high-risk populations.

Conflicts of interest: The authors declare no competing interests.

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SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. List of four attributes with levels relevant to self-administered HIV tests.

Attributes	Levels
Type of test	Finger prick
	Urine sample
Instruction on how to conduct the test	Regular instruction text
	Instructional video
The interpretation of test result	By themselves
	By clinic staff
Cost of the test	Free
	3 USD
	7.5 USD
	12 USD

Abbreviation: USD=United States dollar.

SUPPLEMENTARY TABLE S2A. DCE choice 1.

Attributes	Test A	Test B
Type of test	Finger prick	Finger prick
Instructions on how to conduct the test	Regular instruction text	Instructional video
The interpretation of test result	By yourself	By yourself
Cost of the test	Free	3 USD
Which test would you prefer?	☐	☐

SUPPLEMENTARY TABLE S2B. DCE choice 2.

Attributes	Test A	Test C
Type of test	Finger prick	Finger prick
Instructions on how to conduct the test	Regular instruction text	Regular instruction text
The interpretation of test result	By yourself	By clinic staff
Cost of the test	Free	7.5 USD
Which test would you prefer?	☐	☐

SUPPLEMENTARY TABLE S2C. DCE choice 3.

Attributes	Test A	Test D
Type of test	Finger prick	Finger prick
Instructions on how to conduct the test	Regular instruction text	Instructional video
The interpretation of test result	By yourself	By clinic staff
Cost of the test	Free	12 USD
Which test would you prefer?	☐	☐

SUPPLEMENTARY TABLE S2D. DCE choice 4.

Attributes	Test A	Test E
Type of test	Finger prick	Finger prick
Instructions on how to conduct the test	Regular instruction text	Regular instruction text
The interpretation of test result	By yourself	By yourself
Cost of the test	Free	12 USD
Which test would you prefer?	☐	☐

SUPPLEMENTARY TABLE S2E. DCE choice 5.

Attributes	Test A	Test F
Type of test	Finger prick	Urine sample
Instructions on how to conduct the test	Regular instruction text	Regular instruction text
The interpretation of test result	By yourself	By yourself
Cost of the test	Free	Free
Which test would you prefer?	☐	☐

SUPPLEMENTARY TABLE S2F. DCE choice 6.

Attributes	Test A	Test G
Type of test	Finger prick	Urine sample
Instructions on how to conduct the test	Regular instruction text	Instructional video
The interpretation of test result	By yourself	By yourself
Cost of the test	Free	3 USD
Which test would you prefer?	☐	☐

SUPPLEMENTARY TABLE S2G. DCE choice 7.

Attributes	Test A	Test H
Type of test	Finger prick	Urine sample
Instructions on how to conduct the test	Regular instruction text	Regular instruction text
The interpretation of test result	By yourself	By clinic staff
Cost of the test	Free	7.5 USD
Which test would you prefer?	☐	☐

SUPPLEMENTARY TABLE S2H. DCE choice 8.

Attributes	Test A	Test I
Type of test	Finger prick	Urine sample
Instructions on how to conduct the test	Regular instruction text	Instructional video
The interpretation of test result	By yourself	By clinic staff
Cost of the test	Free	12 USD
Which test would you prefer?	☐	☐

Abbreviation: DCE=discrete choice experiment; USD=United States dollar.

SUPPLEMENTARY TABLE S3. Estimation of DCE stratified by HIV testing history.

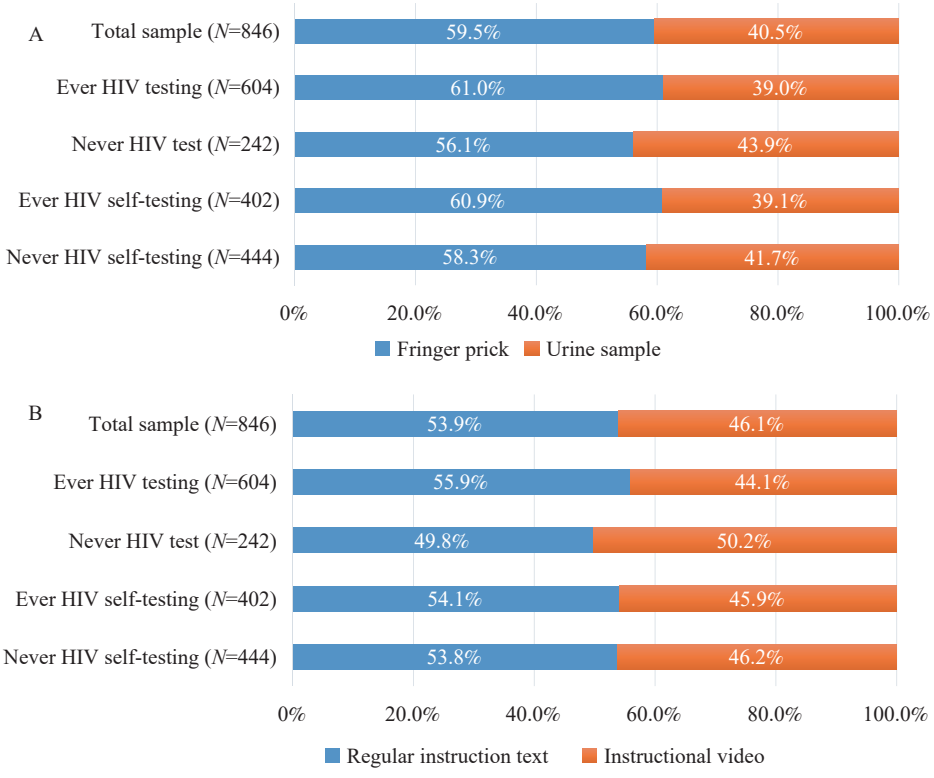
Attributes and levels	Ever HIV tested last year (*n*=604)				Never HIV tested last year (*n*=242)			
	OR	95% *CI*	*P*	WTP (USD)[†]	*OR*	95% *CI*	*P*	WTP (USD)[†]
Type of test								
Finger prick	1.562	(1.393, 1.752)	<0.001*	3.060	1.276	(1.080, 1.508)	0.004*	2.063
Urine sample (reference)	–	–	–	–	–	–	–	–
Instructions on how to conduct the test								
Regular instruction text	1.269	(1.106, 1.457)	0.001*	1.635	0.990	(0.811, 1.209)	0.924	−0.082
Instructional video (reference)	–	–	–	–	–	–	–	–
The interpretation of test result								
By themselves	1.131	(0.956, 1.337)	0.151	0.841	0.944	(0.744, 1.198)	0.635	−0.488
By clinic staff (reference)	–	–	–	–	–	–	–	–
Cost of the test[§]	0.978	(0.976, 0.981)	<0.001*	–	0.983	(0.979, 0.986)	<0.001*	–

Note: "−" means this level is the reference level and there are no corresponding parameter values. This indicates the baseline category for comparison in the regression model.
Abbreviation: WTP=willingness to pay; *OR*= odds ratio; *CI*=confidence interval; USD=united states dollar; DCE=discrete choice experiment; HIV=human immunodeficiency virus.
* *P*<0.050.
[†] For example, $WTP_{fingerprick} = -\beta_{fingerprick} / \beta_{price}$.
[§] The cost attribute is treated as a continuous variable in DCE analysis for willingness to pay calculations, although limited to four discrete values: 0 USD, 3 USD, 7.5 USD, and 12 USD.

SUPPLEMENTARY TABLE S4. Estimation of DCE stratified by HIV self-testing history.

Attributes and levels	Ever HIV self−testing (*n*=402)				Never HIV self−testing (*n*=444)			
	OR	95% *CI*	*P*	WTP (USD)[†]	*OR*	95% *CI*	*P*	WTP (USD)[†]
Type of test								
Finger prick	1.558	(1.355, 1.792)	<0.001*	2.942	1.398	(1.230, 1.589)	<0.001*	2.676
Urine sample (reference)	–	–	–	–	–	–	–	–
Instructions on how to conduct the test								
Regular instruction text	1.177	(0.994, 1.393)	0.059	1.079	1.162	(0.998, 1.353)	0.053	1.201
Instructional video (reference)	–	–	–	–	–	–	–	–
The interpretation of test result								
By themselves	1.082	(0.881, 1.330)	0.452	0.525	1.046	(0.872, 1.255)	0.626	0.362
By clinic staff (reference)	–	–	–	–	–	–	–	–
Cost of the test[§]	0.978	(0.975, 0.981)	<0.001*	–	0.981	(0.979, 0.984)	<0.001*	–

Note: "−" means this level is the reference level and there are no corresponding parameter values. This indicates the baseline category for comparison in the regression model.
Abbreviation: WTP=willingness to pay; *OR*=odds ratio; *CI*=confidence interval; USD=United States dollar; DCE=discrete choice experiment; HIV=human immunodeficiency virus.
* *P*<0.050.
[†] For example, $WTP_{fingerprick} = -\beta_{fingerprick} / \beta_{price}$.
[§] The cost attribute is treated as a continuous variable in DCE analysis for willingness to pay calculations, although limited to four discrete values: 0 USD, 3 USD, 7.5 USD, and 12 USD.



SUPPLEMENTARY FIGURE S1. Choice probability of different levels based on attributes. (A) Choice probability of two levels based on the type of test attribute in the total population and each subgroup; (B) Choice probability of two levels based on the instruction attribute for test conduct in the total population and each subgroup.

Note: For example, the choice probability for finger prick was estimated by: $P_{fingerprick} = e^{\beta_{fingerprick}} \Big/ \left(e^{\beta_{fingerprick}} + e^{\beta_{urinesample}}\right)$ $P_{urinesample}$=1-$P_{fingerprick}$ Only statistically significant attribute levels in Table 2 were included.

Recollection

Synergizing Digital and Physical Approaches: Experience Summary of the HIV PrEP Promotion Project

Shuyu Wang[1]; Wenting Kang[2]; Jingkun Hu[1]; Dapeng Zhang[1]; Jie Xu[1]; Houlin Tang[1]; Junjie Wang[1]; Fan Lyu[1]; Guang Zhang[1,#]

ABSTRACT

China's human immunodeficiency virus / acquired immune deficiency syndrome (HIV/AIDS) prevention and control efforts have entered a new stage, necessitating the exploration of more effective intervention strategies. HIV pre-exposure prophylaxis (PrEP) is a proven method to prevent HIV infection, but its promotion in China faces challenges such as low public acceptance and inadequate service capacity. To further promote PrEP, the "HIV PrEP Model Exploration Project" was launched, exploring three PrEP service models: PrEP clinics, Digital services and physical testing, and PrEP self-service vending machines. The project achieved certain results, establishing a PrEP service network, training professional staff, and promoting the use of PrEP. In the future, it is necessary to further expand publicity channels, enhance public awareness and acceptance, optimize follow-up management, and promote the popularization of PrEP and HIV/AIDS prevention and control efforts.

As of December 31, 2023, China reported approximately 1.29 million individuals living with human immunodeficiency virus (HIV)/ acquired immune deficiency syndrome (AIDS), including 719,000 HIV-positive individuals and 570,000 AIDS patients, with 458,000 reported deaths (*1*). While HIV/AIDS prevalence in China remains low, prevention and control efforts have entered a new phase. A cost-effectiveness analysis funded by the National Natural Science Foundation revealed that regions with substantial financial investment and high antiretroviral therapy coverage are experiencing diminishing marginal returns from existing interventions, suggesting current strategies may be approaching their effectiveness threshold (*2*–*3*). This necessitates the exploration of novel and more effective intervention strategies.

Pre-exposure prophylaxis (PrEP) has emerged as a proven HIV prevention method, demonstrating over 90% effectiveness when properly administered (*4*). PrEP has gained international recognition as a crucial HIV prevention tool, with World Health Organization (WHO) guidelines from 2016 recommending its use for high-risk populations, including men who have sex with men (MSM), female sex workers (FSW), seronegative partners among HIV serodiscordant couples (SNP), and transgender women (*5*). China's HIV/AIDS prevention and control frameworks have incorporated PrEP as a key preventive measure (*6*). Implementation of PrEP in China began in 2017 with Tianjin's pilot program, expanding to Beijing, Hunan, Yunnan, and Heilongjiang provinces from 2018 to 2019 (*7*). A significant milestone was reached in August 2020 when the China Food and Drug Administration approved Truvada as the country's first PrEP medication for HIV prevention in uninfected individuals. The subsequent publication of the *Chinese Expert Consensus on HIV Pre-Exposure Prophylaxis Medication* in November 2020 provided clinical guidance. However, PrEP implementation faces multiple challenges, including limited acceptance among target populations, incomplete policy frameworks and guidelines specific to the Chinese context, inadequate institutional capacity for PrEP service delivery, and high medication costs.

To address these challenges, the Chinese Association of STD & AIDS Prevention and Control and the National Center for AIDS/STD Control and Prevention jointly initiated the "HIV PrEP Mode Exploration Project" across 24 cities from February 2022 to February 2023. The project aimed to develop and evaluate PrEP implementation models, establish effective service systems, create successful models for PrEP implementation, and generate evidence for updating and enhancing PrEP guidelines.

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IMPLEMENTATION PROCESS

Launch Stage

In December 2021, nearly 400 participants from CDCs, non-government organizations (NGOs), and medical institutions across 24 cities attended a comprehensive project training conference. The conference focused on establishing proficiency in project mechanisms, technical guidelines, and data management procedures, while facilitating the development of locally tailored implementation strategies. By February 2022, three distinct PrEP implementation models were established and operational processes were finalized, allowing each city and municipality to select and adapt a model according to their specific circumstances.

Model Exploration Stage

PrEP Clinics: Dedicated PrEP clinics were established to provide comprehensive services, including consultation, risk assessment, testing, medication dispensing, and follow-up care. The service delivery process encompasses six key components: 1) Scientific outreach: disseminating PrEP knowledge through multiple channels to enhance awareness and demand among target populations; 2) Consultation and referral: providing consultation services through CDC staff, community organizations, or medical institutions, with appropriate referral pathways; 3) Risk assessment: professional medical evaluation of HIV infection risk to determine PrEP eligibility; 4) Medical evaluation: comprehensive screening including HIV, sexually transmitted infections (STI), and liver and kidney function tests to exclude contraindications; 5) Medication initiation: following informed consent, qualified individuals receive prescriptions and obtain PrEP medication from clinic pharmacies; 6) Follow-up care: implementation of routine HIV testing and clinical monitoring to assess medication efficacy and safety, with protocol adjustments as needed.

Digital services and physical testing: This model integrates internet-based medical platforms to deliver comprehensive assessment and medication services. The implementation process encompasses: 1) Health education: dissemination of PrEP information through internet platforms and social media channels; 2) online consultation and risk assessment: Users receive professional consultation through digital platforms; 3) Laboratory testing: based on online physician assessment, individuals either visit medical facilities for testing or utilize self-test kits; 4) digital prescription and delivery: Following prescription confirmation and payment through the online platform, medications are delivered directly to users; 5) telemedicine follow-up: Regular online monitoring with medication regimen adjustments as clinically indicated.

PrEP Self-service Vending Machine: This innovative approach utilizes automated dispensing systems for PrEP medication and HIV self-test kit distribution, primarily targeting experienced PrEP users. The service workflow consists of: 1) QR code-based user registration and information submission; 2) Integration with telemedicine platforms for consultation and risk assessment; 3) Online prescription services based on clinical evaluation results; 4) Automated dispensing of testing and medication packages with remote pharmacist support and follow-up care.

Evaluation and Promotion Stage

Project evaluation incorporated multiple methodologies including on-site assessments, quantitative data analysis, expert panel reviews, and experience-sharing forums. In March 2023, comprehensive project reports were compiled, documenting objectives, implementation phases, outcomes, and key insights to identify best practices. These findings were subsequently disseminated through peer learning sessions, professional meetings, formal reports, and digital platforms.

EXPERIENCE AND RESULTS

Establishment of PrEP Service Network

The project successfully established 59 PrEP clinics across 24 cities, primarily integrated into existing antiviral treatment facilities. Eighteen cities implemented collaborative partnerships with internet medical platforms, including BlueCity, JD Health, and DDMedicine. To ensure service quality, the project conducted over 64 capacity-building activities, including meetings, training sessions, and supervisory visits, reaching approximately 2,100 healthcare professionals with comprehensive PrEP-related training.

Growth in the Number of PrEP Users

Throughout the project period, HIV testing services were provided to 13,044 individuals. The total number of PrEP users reached 5,505, showing consistent growth over time (Figure 1). The cumulative

	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Total
Beijing	154	43	68	121	109	113	86	92	94	89	118	111	1,198
Nanchang	0	0	3	2	3	4	6	14	136	74	16	175	433
Kunming	104	13	28	17	39	25	18	21	20	17	16	26	344
Chongqing	13	1	3	1	6	8	2	6	29	76	81	63	289
Guizhou	16	12	30	20	21	8	0	21	39	46	15	30	258
Hangzhou	0	0	28	10	7	2	19	0	5	1	126	49	247
Chengdu	27	17	13	7	18	4	6	25	38	6	13	59	233
Zhengzhou	0	3	4	9	30	22	17	14	7	34	46	35	221
Changsha	5	2	7	7	14	16	12	17	13	50	41	36	220
Hefei	9	6	5	8	5	7	8	27	11	40	46	43	215
Tianjin	0	0	25	9	13	8	10	11	13	46	56	23	214
Changchun	0	0	0	11	16	10	13	39	18	5	7	91	210
Qingdao	4	6	5	6	15	10	32	33	29	25	18	25	208
Nanjing	32	5	5	2	30	28	8	17	13	16	12	38	206
Shenzhen	0	33	30	13	20	7	9	5	20	5	0	60	202
Guangzhou	4	0	2	26	54	32	15	24	2	5	14	23	201
Fuzhou	18	8	12	16	16	12	9	18	11	11	17	20	168
Nanning	0	1	24	21	12	12	11	13	6	5	8	14	127
Shanghai	0	0	0	0	0	66	8	8	8	6	6	20	122
Shijiazhuang	2	3	2	3	5	6	9	11	2	26	27	24	120
Xi'an	2	0	5	0	0	7	4	9	2	7	1	1	38
Wuhan	0	3	1	0	1	6	4	1	1	0	1	2	20
Harbin	0	0	0	0	0	0	0	0	0	0	6	4	10
Taiyuan	0	0	0	0	0	0	1	0	0	0	0	0	1
Total	390	156	300	309	434	413	307	426	517	590	691	972	5,505
	15	29	44	85	73	88	102	117	131	146	160	175	

FIGURE 1. Temporal and geographical distribution of PrEP users across 24 project cities and municipalities, 2022–2023.
Abbreviation: PrEP=pre-exposure prophylaxis.

distribution analysis revealed sustained user growth particularly in Beijing Municipality and Kunming City, Yunnan Province, China (Figure 2). The demographic analysis showed that MSM comprised 97.7% (5,381/5,505) of users, followed by 78 SNP and 46 individuals reporting multiple sexual partnerships.

Comparison of Three PrEP Implementation Models

Analysis of advantages and disadvantages: The PrEP clinic model offers distinct advantages in service delivery. First, specialized medical practitioners ensure high-quality care through direct clinical assessments, comprehensive testing, and supervised medication provision. Second, the outpatient service structure maintains complete medical records, facilitating systematic follow-up visits and robust data collection. However, this model presents certain limitations, including potential privacy concerns among clients visiting clinics and a relatively complex service process involving multiple steps such as registration, payment, and waiting times.

The digital services with physical testing model has successfully mitigated concerns regarding discrimination and privacy exposure. This approach offers flexible service timing that aligns with contemporary consumption patterns and enables broad geographical coverage with minimal professional staffing requirements. However, this model faces significant challenges in maintaining consistent follow-up care and comprehensive data collection.

The PrEP self-service vending machine model similarly addresses discrimination and privacy concerns while specifically catering to experienced PrEP users. The primary challenges include developing sophisticated hardware and software systems for automated dispensing machines and ensuring seamless integration with online medical platforms. This model shows potential for widespread adoption once PrEP becomes established as a routine HIV prevention method, similar to the current ubiquity of condom vending machines.

Data Comparison

Based on their PrEP access patterns for initial and

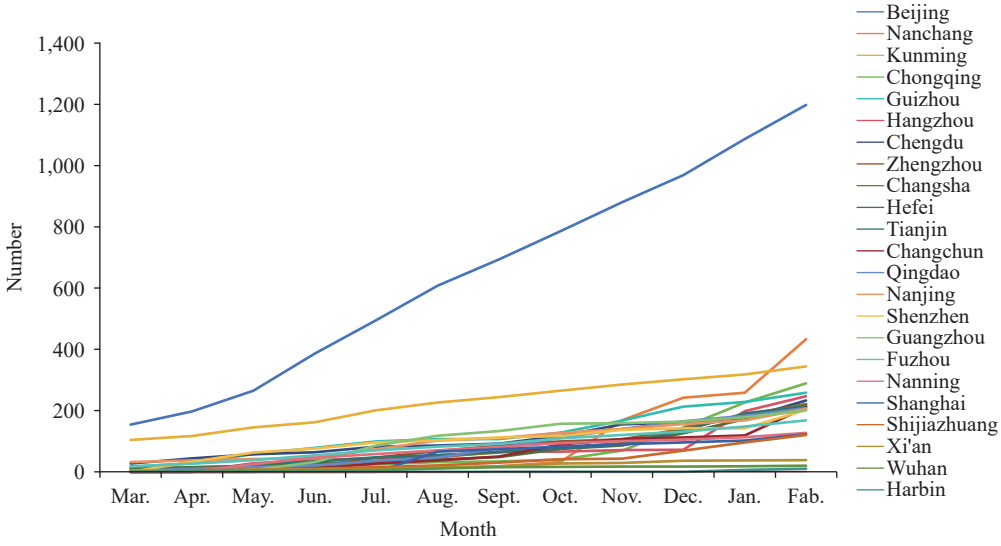

FIGURE 2. Cumulative PrEP initiation by city or municipality.
Abbreviation: PrEP=pre-exposure prophylaxis.

subsequent visits, users were categorized into three distinct groups: those receiving services entirely offline, those transitioning from initial offline to subsequent online services, and those utilizing fully remote consultation and medication delivery. The offline-only group comprised 2,195 individuals, averaging 56 patients per clinic. The hybrid offline-to-online group included 1,754 users, while the fully remote service group consisted of 1,556 users.

Due to requirements for medical assessment and testing, most users (70.73%) initially accessed PrEP through clinics to ensure comprehensive medical evaluation. Subsequently, 60.13% of users transitioned to online services, potentially driven by privacy considerations or coronavirus disease 2019 (COVID-19)-related constraints.

The Refinement of Best Practices

Cooperation and expansion: Through strategic partnerships with government agencies, NGOs, healthcare providers, and online medical platforms, we established a comprehensive service network that enhanced PrEP accessibility. This collaborative approach optimized resource allocation through clear role delineation: CDCs coordinated operations, provided technical guidance, and managed data collection; medical institutions conducted promotion activities, medical assessments, medication management, and follow-up care; and NGOs facilitated outreach, counseling, referrals, and retention services, effectively bridging the gap between clients and healthcare providers. This integrated approach not only advanced organizational knowledge and strategy implementation but also fostered the development of innovative PrEP service delivery models.

Optimization of the service process: The service delivery framework encompasses six essential stages: promotion, consultation, assessment, testing, medication dispensing, and follow-up monitoring. While most stages can be conducted either online or offline, renal function testing remains exclusively hospital-based. Cities implemented locally adapted service processes while maintaining standardized training protocols to ensure consistent service quality. The online platform features a streamlined, user-friendly navigation process that prioritizes privacy protection. The offline clinic model, operating in partnership with social organizations, has achieved higher user trust levels through its community-based approach.

PROBLEMS AND CHALLENGES

Cognition and Acceptance Remained Low

The awareness and acceptance of PrEP among high-risk populations beyond MSM remains significantly limited. Survey results from participating project cities revealed that among individuals involved in sex work and drug use, only 37.0% had heard of PrEP, and merely 27.3% expressed willingness to use it — markedly lower than the corresponding rates of 86.3% and 96.4% among MSM populations.

Through user interviews regarding PrEP hesitancy,

two primary concerns emerged. First, participants expressed apprehension about medication efficacy and adverse effects, as illustrated by one respondent: "My only concern is the side effects, and for me, the side effects are noticeable, such as dizziness." Second, users feared potential stigmatization associated with PrEP use, exemplified by another participant's statement: "From what I understand, only those who frequently go to bars need such things. If I take this medication, others might think I'm 'promiscuous' and that scares me." These barriers to PrEP adoption align with previous research findings, which have identified concerns about personal privacy disclosure, medication side effects, and social discrimination as key deterrents (*8*).

Drug Accessibility and Prices

The consistent increase in PrEP users throughout the project demonstrates growing recognition of PrEP's vital role in HIV prevention and heightened adoption willingness. This trend necessitates ensuring stable and accessible drug supply channels. Surveys across project sites identified medication and testing costs as the primary barriers to PrEP adoption, aligning with ZHANG's findings (*9*). The limited availability of PrEP medications in China, with only Truvada currently approved, combined with regulatory constraints and pricing issues, has led some users to seek generic alternatives (*10*).

Qualitative data from MSM participants highlighted these challenges: "Despite the current convenience of medication purchase through applications, many have discontinued their use. Some individuals, particularly those with lower educational levels, lack knowledge about medication access channels." "Regarding costs, the current pricing structure remains prohibitive. At present rates, I find it financially burdensome."

Follow-up Management

Initial follow-up evaluations are required within the first month of PrEP initiation to assess HIV status and monitor for adverse reactions. Subsequent follow-up visits are recommended quarterly for HIV and STI screening (*11*). Analysis of daily PrEP users in Beijing revealed that while initial follow-up achieved 100% coverage, adherence to follow-up visits declined significantly over time. The overall follow-up rate was notably low at 19.47% (Table 1).

OUTLOOK AND RECOMMENDATIONS

The implementation of PrEP in China remains in an exploratory phase, requiring strategic efforts to facilitate its integration into routine HIV prevention services. Three key areas demand immediate attention. First, awareness campaigns need to be expanded beyond MSM to reach other high-risk populations, particularly seronegative partners in HIV-discordant couples and female sex workers. Second, enhanced social support mechanisms and legal frameworks are

TABLE 1. Follow-up status of daily PrEP users in Beijing.

Months	Initiated PrEP count	Scheduled follow-ups	Actual follow-ups	Follow-up rate (%)*
March	59	–	–	–
April	16	59	59	100.00
May	19	16	16	100.00
June	98	19	19	100.00
July	75	157	32	20.38
August	88	91	45	49.45
September	124	107	49	45.79
October	138	281	42	14.95
November	146	229	36	15.72
December	245	253	31	12.25
January	164	526	30	5.70
February	144	393	56	14.25
Total	1,316	2,131	415	19.47

Note: "-" means the first month was not scheduled for follow-up.
Abbreviation: PrEP=pre-exposure prophylaxis.
* The numerator is the number of actual follow-ups, and the denominator is the number of scheduled follow-ups.

essential, with specific focus on reducing financial barriers through insurance coverage or government procurement programs to make PrEP accessible to a broader spectrum of high-risk individuals. Third, medical services must incorporate comprehensive psychosocial support to address users' emotional needs and build trust, thereby improving long-term engagement and follow-up adherence. As these conditions evolve and systems mature, PrEP is positioned to become a crucial component of China's HIV prevention strategy for key populations.

Conflicts of interest: No conflicts of interest.

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Notifiable Infectious Diseases Reports

Reported Cases and Deaths of National Notifiable Infectious Diseases — China, October 2024*

Diseases	Cases	Deaths
Plague	0	0
Cholera	0	0
SARS-CoV	0	0
Acquired immune deficiency syndrome†	4,403	1,598
Hepatitis	148,566	359
Hepatitis A	1041	0
Hepatitis B	128,731	24
Hepatitis C	16,035	335
Hepatitis D	9	0
Hepatitis E	2,312	0
Other hepatitis	438	0
Poliomyelitis	0	0
Human infection with H5N1 virus	0	0
Measles	107	0
Epidemic hemorrhagic fever	374	2
Rabies	20	14
Japanese encephalitis	21	2
Dengue	11,083	0
Anthrax	60	1
Dysentery	2,680	0
Tuberculosis	52,943	270
Typhoid fever and paratyphoid fever	456	0
Meningococcal meningitis	6	1
Pertussis	10,118	2
Diphtheria	0	0
Neonatal tetanus	0	0
Scarlet fever	3,040	0
Brucellosis	3,381	0
Gonorrhea	8,998	0
Syphilis	53,569	2
Leptospirosis	65	0
Schistosomiasis	2	0
Malaria	204	2
Human infection with H7N9 virus	0	0
Monkey pox§	38	0
Influenza	103,568	0
Mumps	8,424	0

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Continued

Diseases	Cases	Deaths
Rubella	72	0
Acute hemorrhagic conjunctivitis	1,927	0
Leprosy	12	0
Typhus	186	0
Kala azar	6	0
Echinococcosis	332	0
Filariasis	0	0
Infectious diarrhea[¶]	102,391	0
Hand, foot and mouth disease	46,520	0
Total	563,572	2,253

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