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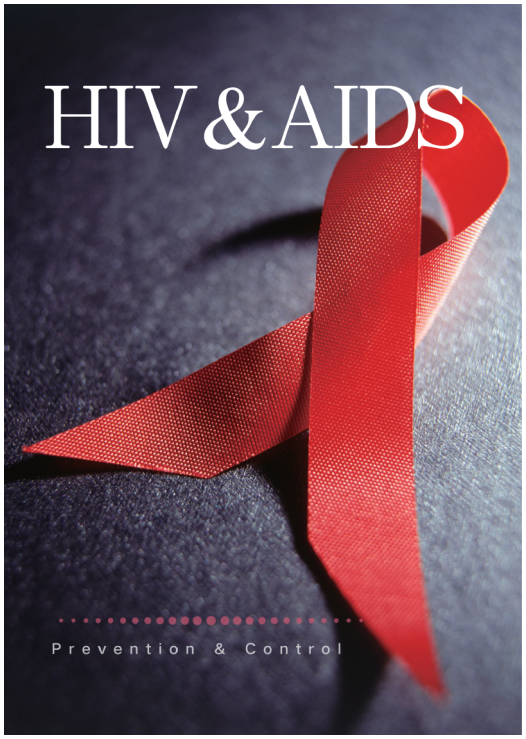

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Vital Surveillances

The Impact of ART on Stillbirth and Neonatal Death Among HIV-positive Pregnant Women — Yunnan Province, China, 2013–2022

Ailing Wang[1]; Shuiling Qu[2]; Jiarui Zheng[3]; Xiaoyan Wang[1]; Hongqiao Zheng[2]; Qian Wang[1]; Xiaolong Gui[3]; Pengbin Li[3]; Dongxu Huang[1]; Changhe Wang[1,#]; Leiyu Shi[4,#]

ABSTRACT

Introduction: This study assessed the impact of antiretroviral therapy (ART) on stillbirth and neonatal mortality and investigated associated risk factors among Human immunodeficiency virus-positive (HIV-positive) pregnant women in Yunnan, China during 2013–2022.

Methods: Data from the National Information System of Integrated Prevention of Mother-to-Child Transmission of HIV, Syphilis, and Hepatitis B Program (PMTCT) were analyzed to determine stillbirth and neonatal mortality rates. Multivariate Poisson regression was employed to identify risk factors associated with stillbirth and neonatal outcomes.

Results: Among 9,563 HIV-positive women with singleton pregnancies in Yunnan Province during 2013–2022, 9,404 (98.34%) received ART during pregnancy, while 159 (1.66%) did not. There were 9,421 live births, 76 stillbirths, and 66 neonatal deaths, yielding a stillbirth rate (SBR) of 8.07‰ and neonatal mortality rate (NMR) of 7.01 ‰. The SBR was significantly lower in pregnancies where ART was used (P=0.033). Univariate analysis revealed that ART (P=0.009), ethnicity (P=0.012), and antenatal care utilization (P<0.001) were associated with stillbirth and newborn survival. Multivariate Poisson regression identified that six or more antenatal care visits as an independent predictor of survival.

Conclusions: Stillbirth and neonatal mortality rates were elevated among mothers who did not receive ART during pregnancy compared to those who did. These findings emphasize the importance of ART during pregnancy, particularly since several mortality risk factors are amenable to intervention.

Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) is one of the most critical global public health challenges, particularly threatening the health of pregnant women living with HIV and their offspring. In 2022, among the 1.2 million pregnant women living with HIV globally, approximately 82% received antiretroviral drugs to prevent mother-to-child transmission (PMTCT) of HIV (*1*). Without intervention, mother-to-child transmission (MTCT) of HIV occurs at rates of 15%–45% (*2*), but antiretroviral therapy (ART) can reduce this to less than 2% (*3*). Yunnan Province, which first identified HIV infection among local drug users in China, has implemented the PMTCT for HIV Program since 2003, spanning more than two decades (*4*). In Yunnan, ART coverage increased substantially from 75.92% in 2006 to 99.72% in 2019, corresponding with a decrease in MTCT decreased from 8.78% to 1.93% during the same period (*5*).

Maternal HIV infection significantly elevates the risk of intrauterine death, with rates of 7.1% among HIV-positive pregnant women compared to 2.3% among HIV-negative pregnant women (*6*). Additionally, maternal HIV infection increases the risks of low birth weight and preterm birth (*6*–*7*), with 13.2% of live-born infants having low birth weight and 7.4% experiencing premature birth (*6*). Across seven African countries, HIV infection is associated with elevated preterm birth rates of 15%–20% of all pregnancies, varying notably by ART regimen (*8*). In China, preterm birth rates among women living with HIV were reported at 10.70% in Hubei province (*9*) and 14.70% in Guangxi province (*10*). However, research describing neonatal outcomes among HIV-positive pregnant women in Yunnan province, which has China's highest HIV/AIDS prevalence, remains limited, and the impact of maternal ART on stillbirth and neonatal death requires further investigation in this region.

This study utilized data from the National Information System of Integrated Prevention of Mother-to-Child Transmission of HIV, Syphilis and

Hepatitis B Program to evaluate the impact of maternal ART on stillbirth and neonatal death among HIV-positive pregnant women in Yunnan.

METHODS

This study conducted a descriptive study analyzing data from the PMTCT system to evaluate the impact of maternal ART use among HIV-positive pregnant women in Yunnan Province, with data extraction performed on December 16, 2024. The study included all HIV-positive pregnant women from 2013–2022 in Yunnan Province, excluding those with multifetal pregnancies, unknown ART status, or infant deaths occurring after 28 days postpartum. The PMTCT system, established in 2007, captures comprehensive data including maternal demographics, infant characteristics, HIV transmission routes, ART regimens, and antenatal care utilization.

Our primary outcomes were stillbirth and neonatal mortality. The stillbirth rate (SBR) was defined as the number of babies born with or without signs of life at or after 28 weeks gestation per 1,000 total births. The neonatal mortality rate (NMR) was defined as deaths occurring within the first 28 days after birth per 1,000 total births.

ART during pregnancy was administered to reduce perinatal transmission. Two standardized regimens were used: the first comprised Zidovudine (AZT)–lamivudine (3TC)–lopinavir/ritonavir (LPV/r), and the second comprised of Tenofovir (TDF)–3TC–efavirenz (EFV).

Statistical analysis included descriptive statistics to characterize the study population and outcomes, stratified by maternal ART use. Chi-square tests were employed to assess differences in outcomes across education levels, marital status, ethnicity, and maternal ART use. Multivariate Poisson regression analysis was conducted to identify risk factors for stillbirth and newborn outcomes. All statistical analyses were performed using R packages stats and MASS, with statistical significance set at $P<0.05$.

The study was exempt from ethical review by the Ethics Review Committee of the National Center for Women and Children's Health Chinese Center for Disease Control and Prevention, as the National Information System of Integrated Prevention of Mother-to-Child Transmission of HIV, Syphilis and Hepatitis B Program is a mandatory, legally supported public health surveillance system.

RESULTS

During 2013–2022, a total of 9,563 HIV-positive women pregnant with singleton pregnancies were identified in Yunnan province. The mean maternal age was 29.71 (±5.91) years, and 7,480 (78.22%) were less than 35 years old. Educational attainment varied: 1,347 (14.09%) were illiterate, and 3,048 (31.87%) had primary education. 4,696 (49.11%) had secondary education, and 472 (4.94%) had tertiary education. ART coverage was high, with 9,404 (98.34%) women receiving treatment. Of these, 8,220 (87.41%) initiated ART before pregnancy, 599 (6.40%) during pregnancy, 78 (0.83%) during delivery, and 507 (5.39%) after delivery. Only 159 (1.66%) women did not receive ART.

Table 1 presents the demographic and clinical characteristics of the study population stratified by ART use. Marital status ($P=0.047$), educational level, parity number of children, and antenatal care visits were significantly associated with ART utilization ($P<0.001$).

Survival of HIV-exposed Newborns

Among the study population, there were 9,421 live births, 76 stillbirths, and 66 neonatal deaths (Table 2), yielding an SBR of 8.07‰ and an NMR of 7.01‰. Poisson test analysis revealed a statistically significant difference in SBR between pregnant women who used ART and those who did not ($P=0.033$). However, no statistically significant difference was observed in NMR between these groups ($P=0.088$).

Impact on Stillbirth and Newborn Outcomes

Maternal age, marital status, education level, parity, and number of children were independently associated with newborn survival. Additionally, ART use ($P=0.009$), ethnicity ($P=0.012$), and antenatal care utilization ($P<0.001$) had demonstrated significant associations with stillbirth and newborn survival outcomes (Table 3).

Multivariate Poisson regression analysis revealed that ART use, ethnicity, and parity were independent risk factors for stillbirth and neonatal mortality. Notably, compared to women who received no antenatal care, those who attended six or more antenatal care visits showed significantly reduced risk of stillbirth and neonatal mortality [odds ratio (OR)=0.13] (Table 4).

TABLE 1. Basic characteristics of HIV-positive pregnant women.

Characteristics	Overall, *n* (%)	No ART, *n* (%)	ART, *n* (%)	χ^2, *P*
Age (years)				0.00, 0.979
<35	7,480 (78.22)	125 (78.62)	7,355 (78.21)	
≥35	2,083 (21.78)	34 (21.38)	2,049 (21.79)	
Ethnicity				0.02, 0.891
Han	4,670 (48.83)	79 (49.69)	4,591 (48.82)	
Other	4,893 (51.17)	80 (50.31)	4,813 (51.18)	
Marital status				0.047*
Single	591 (6.18)	13 (8.18)	578 (6.15)	
Married	8,817 (92.20)	140 (88.05)	8,677 (92.27)	
Divorced/widowed	155 (1.62)	6 (3.77)	149 (1.58)	
Level of education				20.42, <0.001
Illiterate	1,347 (14.09)	32 (20.13)	1,315 (13.98)	
Primary	3,048 (31.87)	68 (42.77)	2,980 (31.69)	
Secondary	4,696 (49.11)	57 (35.85)	4,639 (49.33)	
Tertiary	472 (4.94)	2 (1.26)	470 (5.00)	
Parity				14.39, <0.001
Primiparity	3,178 (33.23)	30 (18.87)	3,148 (33.48)	
≥1	6,385 (66.77)	129 (81.13)	6,256 (66.52)	
No. of child				19.98, <0.001
0	3,486 (36.45)	36 (22.64)	3,450 (36.69)	
1	3,965 (41.46)	68 (42.77)	3,897 (41.44)	
≥2	2,112 (22.09)	55 (34.59)	2,057 (21.87)	
Antenatal care visits				828.89, <0.001
0	516 (5.42)	89 (55.97)	427 (4.54)	
1–5	4,151 (43.41)	57 (35.85)	4,094 (43.53)	
≥6	4,896 (51.20)	13 (8.18)	4,883 (51.92)	
Total	9,563 (100.00)	159 (100.00)	9,404 (100.00)	

Abbreviation: ART=antiretroviral therapy.
* Fisher's exact test.

TABLE 2. Impact of ART on stillbirth and newborn outcomes.

Characteristics	Overall	No Maternal ART	Maternal ART	*P*
Live births	9,421	152	9,269	
SBR (‰)	76 (8.07)	4 (26.32)	72 (7.77)	0.033
NMR (‰)	66 (7.01)	3 (19.74)	63 (6.80)	0.088

Abbreviation: ART=antiretroviral therapy; SBR=stillbirth rate; NMR=neonatal mortality rate.

DISCUSSION

The health outcomes of infants born to HIV-infected mothers are crucial for promoting newborn health and evaluating mother-to-child transmission prevention efforts. Our analysis of surveillance data examined the impact of maternal ART use during pregnancy on adverse pregnancy and newborn outcomes among women living with HIV. In accordance with China's technical guidelines for PMTCT of HIV, Syphilis, and Hepatitis B, newborns have not yet received an HIV diagnosis. Our study primarily evaluated two major health conditions: stillbirth as an adverse pregnancy outcome and neonatal death (within 28 days of birth) as an adverse newborn outcome. This study found significantly

TABLE 3. Independent associations with stillbirth and newborn outcomes and relevant factors.

Characteristics	Live births, *n* (%)	Death, *n* (%)	χ^2, *P*
ART			0.009
No	152 (1.61)	7 (4.93)	
Yes	9,269 (98.39)	135 (95.07)	
Age (years)			0.82, 0.364
<35	7,364 (78.17)	116 (81.69)	
≥35	2,057 (21.83)	26 (18.31)	
Ethnicity			6.30, 0.012
Han	4,616 (49.00)	54 (38.03)	
Other	4,805 (51.00)	88 (61.97)	
Marital status			0.133*
Single	586 (6.22)	5 (3.52)	
Married	8,680 (92.13)	137 (96.48)	
Divorced/widowed	155 (1.65)	0 (0.00)	
Level of education			7.10, 0.069
Illiterate	1,319 (14.00)	28 (19.72)	
Primary	3,002 (31.86)	46 (32.39)	
Secondary	4,630 (49.15)	66 (46.48)	
Tertiary	470 (4.99)	2 (1.41)	
Parity			0.71, 0.400
Primiparity	3,136 (33.29)	42 (29.58)	
≥1	6,285 (66.71)	100 (70.42)	
No. of child			3.97, 0.137
0	3,437 (36.48)	49 (34.51)	
1	3,913 (41.53)	52 (36.62)	
≥2	2,071 (21.98)	41 (28.87)	
Antenatal care visits			84.05, <0.001
0	497 (5.28)	19 (13.38)	
1–5	4,048 (42.97)	103 (72.54)	
≥6	4,876 (51.76)	20 (14.08)	
Total	9,421 (100.00)	142 (100.00)	

Abbreviation: ART=antiretroviral therapy.
* Fisher's exact test.

higher stillbirth rates among mothers who did not use ART during pregnancy compared to those who did, highlighting the critical importance of ART adherence in this vulnerable population.

Neonatal mortality serves as a crucial indicator of maternal and child health. Yunnan province has a substantial population of HIV-positive pregnant women, with both crude HIV-positivity rates and the proportion of subsequent pregnancies among HIV-positive women showing consistent annual increases between 2006 and 2019 (*11*). Consequently, the number of infants born to mothers living with HIV is projected to rise. Previous research has demonstrated that HIV-exposed but uninfected infants, compared to HIV-unexposed infants, experience poorer health outcomes and may face impaired physical and neurological development (*12*–*13*). These findings underscore the need for enhanced neonatal healthcare and the development of targeted interventions to improve child health outcomes.

Our findings suggest that HIV exposure may increase the probability of stillbirth in pregnancies of women living with HIV. Comparative data from India showed a significantly higher SBR among HIV-

TABLE 4. Risk factors of stillbirth and the outcomes of newborn by multivariate Poisson regression.

Characteristics	Estimate (95% *CI*)	*OR* (95% *CI*)	SE	Z value	*P*
Intercept	−3.11 (−3.99, −2.40)	0.04 (0.02,0.09)	0.40	−7.74	<0.001
ART					
No	Reference		Reference	Reference	
Yes	−0.48 (−1.30, 0.42)	0.62 (0.29, 1.52)	0.42	−1.16	0.247
Ethnicity					
Han	Reference		Reference	Reference	
Others	0.30 (−0.03, 0.65)	1.35 (0.97, 1.91)	0.17	1.75	0.081
Antenatal care visits					
0	Reference		Reference	Reference	
1−5	−0.29 (−0.79, 0.27)	0.75 (0.45, 1.30)	0.27	−1.09	0.274
≥6	−2.06 (−2.72, −1.39)	0.13 (0.07, 0.25)	0.34	−6.13	<0.001

Abbreviation: *CI*=confidence intervals; *OR*=odds ratio; SE=standard error; ART=antiretroviral therapy.

infected women (26.7‰, 93/3,478) compared to the national average (5‰) (*14*). Similarly, in Zambia, a stillbirth rate of 26 per 1,000 live births was reported among 1,229 HIV-infected pregnant women (*15*). While our study revealed lower stillbirth rates among HIV-infected women (8.07 ‰) compared to these international studies, the statistically significant difference in stillbirth rates between ART users (26.32‰) and non-users (7.77‰) remained.

Notably, multivariable Poisson regression analysis did not identify ART use as independently associated with adverse pregnancy outcomes. The discrepancy between chi-square testing and multivariable regression results may be attributed to several factors. First, the single stillbirth case among pregnant women who did not use ART could represent a random occurrence. Second, when controlling for ethnicity, parity, and antenatal care visits in the multivariable Poisson regression, the differences in SBR and NMR between ART users and non-users became non-significant at certain variable levels. The regression results demonstrated that women with six or more antenatal care visits had a lower risk of adverse pregnancy outcomes compared to those without any visits, emphasizing the importance of regular antenatal care.

Our study has limitations. As a descriptive analysis focusing solely on mortality, we did not examine other health aspects of infants born to HIV-positive women. There is an urgent need for in-depth analysis of specific causes of death and comprehensive evaluation of health conditions beyond survival. Future research should prioritize both psychological and physiological studies in this population.

The stillbirth and neonatal mortality rates were significantly higher among HIV-positive mothers who did not receive ART during pregnancy compared to those who received ART. Healthcare interventions for HIV-positive pregnant women warrant increased attention to ensure universal ART coverage and to address modifiable risk factors associated with stillbirth and neonatal mortality through targeted preventive measures.

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Conflict of interest: No conflicts of interest.

Ethical statement: The study was exempt from ethical review by the Ethics Review Committee of National Center for Women and Children's Health Chinese Center for Disease Control and Prevention.

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[#] Corresponding authors: Changhe Wang, wangchanghe@chinawch.org.cn; Leiyu Shi, lshi2@jhu.edu.

[1] National Center for Women and Children's Health, National Health Commission of the People's Republic of China, Beijing, China; [2] Chinese Center for Disease Control and Prevention, Beijing, China; [3] Yunnan Maternal and Child Health Care Hospital, Kunming City, Yunnan Province, China; [4] Johns Hopkins University, Baltimore, Maryland, United States.

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Preplanned Studies

Risk Assessment of Cardiovascular Disease in HIV Infected Individuals Receiving Antiretroviral Therapy — Shanghai Municipality, China, 2023

Xiaomeng Li[1,2,&]; Lin Wang[2,&]; Li Liu[2]; Zihui Zhao[1,2]; Ye Li[2]; Jiawei Huang[2]; Huiqin Yan[2]; Yiping Jin[2]; Meiyan Sun[2]; Jun Chen[2]; Yingying Ding[3]; Renfang Zhang[2]; Yinzhong Shen[2,#]

Summary

What is already known about this topic?

Antiretroviral therapy (ART) is transforming human immunodeficiency virus (HIV) infection into a chronic condition, leading to an altered disease spectrum in patients. The risk of cardiovascular disease (CVD) in HIV-infected individuals are twice that of the general population.

What is added by this report?

This study demonstrates elevated cardiovascular risk among the HIV population. The findings reveal that traditional CVD risk factors are prevalent among people living with HIV but remain inadequately addressed in clinical practice.

What are the implications for public health practice?

These findings underscore both the necessity and urgency of implementing systematic CVD risk screening and intervention programs for HIV population. Furthermore, the study emphasizes the critical need to develop CVD screening tools specifically calibrated for the HIV population in China.

ABSTRACT

Introduction: Cardiovascular disease (CVD) has emerged as a critical determinant of prognosis and quality of life among individuals living with human immunodeficiency virus (HIV). The primary objective of this study is to assess the CVD risk among HIV-infected individuals and determine the proportion of high-risk individuals using multiple evaluation methods.

Methods: A cross-sectional study was conducted among HIV-infected individuals aged 18 years and older who were receiving antiretroviral therapy between April 26, 2023, and December 16, 2023. Participants were categorized into low-risk, intermediate-risk, and high-risk groups for CVD based on six risk assessment tools.

Results: Our analysis revealed that the 5-year overall CVD risk estimates ranged from 2.37% to 2.50%, while the 10-year overall risk estimates spanned from 3.42% to 18.35%, with significant variations observed between subgroups. The proportion of high-risk individuals in the 10-year risk assessment, identified using five different tools, ranged from 7.85% to 31.94%, demonstrating moderate consistency across tools.

Conclusions: The findings underscore the importance of closely monitoring and managing CVD risk in HIV-infected individuals. Given the variability in risk stratification methods, it is imperative to develop an assessment model tailored to the specific characteristics of the Chinese population.

Cardiovascular disease (CVD) has emerged as a critical determinant of prognosis and quality of life among individuals living with human immunodeficiency virus (HIV). Consequently, the screening, prevention, and treatment of CVD have become integral components of comprehensive HIV care (*1*). While risk prediction models and assessment criteria serve as essential tools for CVD primary prevention, their application to HIV-infected individuals presents challenges due to inconsistent results and incomplete consideration of HIV-specific risk factors. We conducted a cross-sectional study of HIV-infected individuals aged 18 years and older who were receiving antiretroviral therapy (ART) at Department of Infection and Immunity of Shanghai Public Health Clinical Center between April 26, 2023, and December 16, 2023. Our analysis revealed 5-year CVD risk estimates ranging from 2.37% to 2.50%, and 10-year risk estimates spanning 3.42% to 18.35%,

with significant variations observed between subgroups. This study aims to heighten clinician awareness regarding CVD risk in HIV-infected individuals and advocates for the development of tailored assessment tools for this population.

Study participants were screened according to the eligibility criteria of different prediction models, with cases of incomplete data being excluded (Supplementary Figure S1, available at https://weekly.chinacdc.cn/). Demographic and clinical data were collected through questionnaires, including gender, age, region, ethnicity, smoking status, marital status, family history of CVD, antihypertensive medication use, and diabetes mellitus history. Anthropometric measurements were performed on site, including height, weight, waist circumference (measured horizontally at an umbilical level), body mass index (BMI), systolic blood pressure (SBP), and diastolic blood pressure (DBP). Laboratory parameters including total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglyceride (TG), and estimated glomerular filtration rate (eGFR) were obtained through standardized testing. Treatment-related data, including regimen details, initial and most recent CD4 counts, ART initiation date, duration of follow-up, and clinical outcomes, were extracted from the treatment database using patient age and treatment identification numbers.

Baseline characteristics were summarized using percentages for categorical variables and medians with interquartile ranges (IQRs) for continuous variables. We applied multiple validated atherosclerotic cardiovascular disease (ASCVD) risk assessment tools: The American College of Cardiology/American Heart Association 2013 ASCVD risk score (ACC/AHA-ASCVD) (*2*), the Framingham 2008 ASCVD risk score (FHS-CVD) (*3*), European AIDS Clinical Society (EACS) guidelines (*4*), the Predicting the 10-Year risks of Atherosclerotic Cardiovascular Disease in Chinese Population (China-PAR) (*5*), Data-collection on Adverse Effects of Anti-HIV Drugs (D:A:D) study (*6*), and the Chinese guidelines for lipid management (2023 edition) (*7*). Detailed comparisons of cohort populations, endpoint definitions, and risk stratification criteria across models are provided inSupplementary Table S1 (available at https://weekly.chinacdc.cn/). To ensure standardized comparison, we focused on 10-year risk assessment, excluding lifetime risk calculations. For EACS guidelines, we utilized Version 11.0 recommendations based on the Framingham equation or national guidance, rather than Version 12.0's SCORE-2 model, given our focus on Shanghai's HIV-infected population. Statistical analyses were performed using R (version 4.4.1; R Foundation for Statistical Computing, Vienna, Austria) and the R package 'CVrisk' version 1.1.1 (*8*). For D:A:D risk assessment, we implemented the reduced model and sex-specific adjusted Framingham model to calculate 5-year incidence risk. We conducted subgroup analysis by gender, age group, and diabetes status, computing mean values and 95% confidence intervals (*CI*) for each subgroup, with pairwise t-tests for between-group comparisons. Inter-rater reliability was assessed using Fleiss' kappa, with values interpreted as: 0.00–0.20 (slight), 0.21–0.40 (fair), 0.41–0.60 (moderate), 0.61–0.80 (substantial), and 0.81–1.00 (almost perfect) agreement.

The study comprised 3,815 individuals, with males constituting 93.69% of the cohort and a median age of 44 years (interquartile range: 33–55 years). Among participants, 27.79% (1,060/3,815) were smokers, with a median BMI of 23.04 (interquartile range: 20.83–24.77), and 33.94% (1,295/3,815) were overweight (BMI>24). Dyslipidemia was present in 61.57% (2,349/3,815) of participants, with 22.2% (848/3,815) exhibiting elevated low cholesterol levels. Hypertension affected 27.02% (1,031/3,815) of the cohort, with 42.78% (441/1,031) receiving antihypertensive medication. Treatment records indicated that 96.75% of individuals maintained stable and continuous treatment, while approximately 3% were lost to follow-up, transferred out, or deceased. The majority of participants (85.95%) presented with baseline viral loads below 100,000 copies/mL, and 63.94% maintained baseline CD4 levels exceeding 200 cells/μL, indicating the absence of severe immunosuppression. The most frequently prescribed antiretroviral medications were efavirenz (EFV), lamivudine (3TC), and tenofovir (TDF), with over half of the cohort receiving each of these agents (Table 1).

In the baseline population, 2,893 individuals aged 40-74 years met the age range requirements for all risk assessment tools. The five-year risk assessment revealed an overall population risk of 2.37% (95% *CI*: 2.26%, 2.48%) with the reduced D:A:D model, while the adjusted Framingham model estimated a risk of 2.50% (95% *CI*: 2.38%, 2.62%). The proportion of high-risk

TABLE 1. Demographic,cardiovascular, and HIV-related risk factors and clinical characteristics of the study population (*n*=3,815).

Variable	Individuals Included in This Analysis
Demographic characteristics	
Age in years [median (IQR)]	44.07 (33–55)
Male sex (%)	3,536 (93.69)
Southern/Northern region	3,814/1
Urban/Rural address	3,814/1
CVD-related risk factors	
BMI in kg/m^2 [median (IQR)]	23.04 (20.83–24.77)
≥24 (%)	1,295 (33.94)
SBP in mmHg [median (IQR)]	125.64 (116–134)
DBP in mmHg [median (IQR)]	76.51 (70–83)
Hypertension (%)	1,031 (27.02)
Waist circumference in cm [median (IQR)]	81.32 (75–86)
TC in mmol/L [median (IQR)]	4.56 (3.97–5.15)
≥5.2 (%)	909 (23.08)
HDL-C in mmol/L [median (IQR)]	1.21 (0.99–1.37)
<1 (%)	985 (25.82)
LDL-C in mmol/L [median (IQR)]	2.82 (2.27–3.29)
≥3.4 (%)	848 (22.20)
TG in mmol/L [median (IQR)]	2.58 (1.05–2.69)
≥1.7 (%)	1,880 (49.28)
GFR in ml/(min·1.73m^2) [median (IQR)]	94.96 (81–108)
<60 (%)	123 (3.22)
Dyslipidemia (%)	2,349 (61.57)
Smoking (%)	1,060 (27.79)
Family history of CVD (%)	396 (10.38)
Diabetes status (%)	
Not diabetic	3,597 (94.29)
Less than 10 years	132 (3.46)
More than 10 years	86 (2.25)
Use of antihypertensive drugs (%)	441 (11.56)
HIV-related risk Factors	
Current status (%)	
Undergoing treatment	3,691 (96.75)
Lost to follow-up	112 (2.94)
Transferred out	4 (0.01)
Death	8 (0.21)
Baseline viral load in copies/mL (%)	
<100, 000	3,279 (85.95)
100,000–500,000	388 (10.17)
>500,000	148 (3.88)
Baseline CD4+T-Cell count in cells/μL (%)	
<200	1,376 (36.07)
200–350	1,360 (35.65)
351–800	1,036 (27.16)
≥801	43 (1.13)
EFV-based ART	2,129 (55.81)
TAF-based ART	912 (23.91)
TDF-based ART	2,071 (54.29)
INSTI-based ART	1,383 (36.25)
PI-based ART	221 (5.80)
ART duration in weeks	62 (22–105)

Note: Hypertension is defined as blood pressure ≥140/90 mmHg, or in patients with hypertension taking antihypertensive medications.
Abbreviation: CVD=cardiovascular disease; BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure; TC=total cholesterol; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein; TG=triglyceride; GFR=glomerular filtration rate; EFV=efavirenz; TDF=tenofovir disoproxil fumarate; TAF=tenofovir alafenamide; INSTI=integrase strand transfer inhibitor; PI=protease inhibitor.

individuals for 5-year risk ranged from 2.45% (95% *CI*: 1.93%, 3.10%) to 3.39% (95% *CI*: 2.78%, 4.13%). 10-year risk assessment using five different tools demonstrated substantial variation in both mean risk values and high-risk population proportions. The China-PAR identified the smallest proportion of high-risk individuals at 7.85% (95% *CI*: 6.91%, 8.90%), while the FHS-CVD identified the highest at 31.94%. The Chinese guidelines for lipid management, ACC/AHA-ASCVD, and EACS criteria identified high-risk groups comprising 14.86% (95% *CI*: 13.60%, 16.22%), 20.26% (95% *CI*: 18.81%, 21.78%), and 26.58% (95% *CI*: 24.99%, 28.24%) of the population, respectively. The 10-year overall risk estimates spanned from 3.42% (95% *CI*: 3.28%, 3.56%) to 18.35% (95% *CI*: 17.70%, 19.00%). Subgroup analysis revealed statistically significant mean differences within each subgroup across all models (P<0.05). Risk assessment results are summarized in Table 2. Inter-rater reliability assessment of the grading outcomes yielded a Fleiss' kappa coefficient of 0.51. A Wayne diagram (Figure 1A) revealed that 137 (4.7%) individuals were classified as high risk across all 10-year tools. Comprehensive grading analysis and mosaic visualization were performed using 10-year tools (Figure 1B).

TABLE 2. Risk estimates and high-risk population proportions across assessment models (*n*=2,893) [mean (95% *CI*)].

Subgroup	D:A:D study, mean (95% *CI*)		FHS-CVD, mean (95% *CI*)	China-PAR, mean (95% *CI*)	ACC/AHA-ASCVD, mean (95% *CI*)	EACS, mean (95% *CI*)	Chinese guidelines for lipid management, mean (95% *CI*)
	D:A:D reduced model	5-years Framingham model					
Overall	2.37 (2.26, 2.48)	2.50 (2.38, 2.62)	18.35 (17.70, 19.00)	3.42 (3.28, 3.56)	11.17 (10.67, 11.68)		
Gender							
Female	1.75 (1.54, 1.96)	1.65 (1.42, 1.88)	13.07 (11.58, 14.56)	2.08 (1.83, 2.33)	7.88 (6.65, 9.11)		
Male	2.42 (2.30, 2.54)	2.58 (2.45, 2.70)	18.82 (18.13, 19.52)	3.54 (3.39, 3.70)	11.47 (10.94, 12.00)		
Age, years							
≤40	0.62 (0.59, 0.65)	0.68 (0.65, 0.71)	6.08 (5.85, 6.32)	1.06 (0.96, 1.16)	2.35 (2.20, 2.50)		
41–50	1.48 (1.40, 1.56)	1.56 (1.48, 1.64)	13.27 (12.69, 13.85)	2.20 (2.05, 2.35)	6.07 (5.68, 6.45)		
51–60	3.58 (3.35, 3.81)	3.78 (3.53, 4.04)	28.10 (26.72, 29.48)	5.21 (4.91, 5.51)	16.39 (15.46, 17.31)		
61–70	5.96 (5.56, 6.36)	6.18 (5.77, 6.59)	40.75 (39, 42.51)	8.04 (7.68, 8.40)	30.04 (28.77, 31.31)		
≥71	7.03 (6.12, 7.95)	7.84 (6.76, 8.92)	49.88 (45.58, 54.17)	10.71 (9.67, 11.76)	43.67 (40.51, 46.83)		
Diabetes							
Yes	8.08 (7.17, 9.00)	8.29 (7.38, 9.20)	48.09 (44.54, 51.63)	9.28 (8.45, 10.11)	35.02 (31.87, 38.17)		
No	1.98 (1.90, 2.06)	2.11 (2.01, 2.20)	16.33 (15.75, 16.91)	3.03 (2.90, 3.15)	9.55 (9.13, 9.98)		
High risk Proportion	2.94 (2.37, 3.64)	3.39 (2.78, 4.13)	31.94 (30.25, 33.68)	7.85 (6.91, 8.90)	20.26 (18.81, 21.78)	26.58 (24.99, 28.24)	14.86 (13.60, 16.22)

Abbreviation: CVD=cardiovascular disease; D:A:D=data-collection on adverse effects of anti-HIV drugs study; 5-years Framingham model=the Framingham model calibrated to the D:A:D data; ASCVD=atherosclerotic cardiovascular disease; FHS-CVD=the Framingham 2008 ASCVD risk score; ACC/AHA-ASCVD=the American College of Cardiology/American Heart Association 2013 ASCVD risk score; China-PAR=the predicting the 10-year risks of atherosclerotic cardiovascular disease in the Chinese population; EACS=European AIDS Clinical Society guidelines.

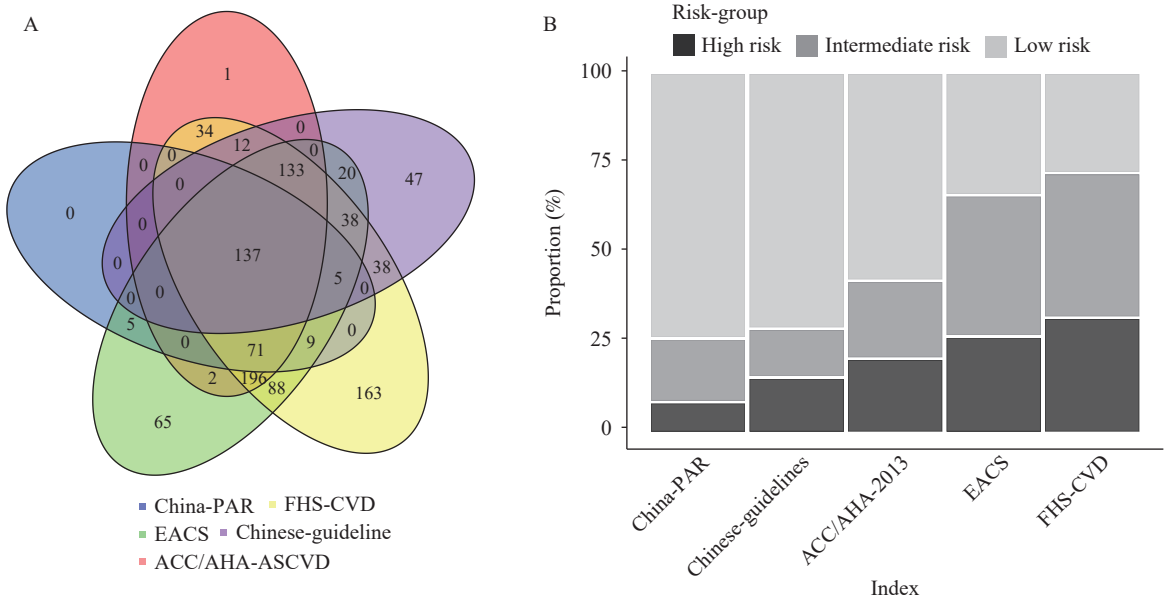

FIGURE 1. Overlap and Distribution of High-Risk Classifications Across Five Assessment Tools: A) Venn diagram showing overlap of high-risk classifications across five assessment criteria; B) Mosaic plot illustrating risk classification distribution under different criteria.
Abbreviation: China-PAR=the predicting the 10-year risks of atherosclerotic cardiovascular disease in Chinese population; EACS=European AIDS Clinical Society guidelines; FHS-CVD=the Framingham 2008 ASCVD risk score; ACC/AHA-ASCVD=the American College of Cardiology/American Heart Association 2013 ASCVD risk score.

DISCUSSION

Our 10-year risk assessment revealed that 7.85% to 31.94% of HIV-infected individuals are at high risk for CVD, highlighting a significant health concern that demands attention. While HIV-infected individuals typically exhibit more traditional risk factors, these alone cannot fully explain their elevated CVD risk (*9*). Therefore, systematic risk screening among the HIV population is crucial. The Chinese guidelines for diagnosis and treatment of HIV infection/AIDS (2024 edition) mandate regular CVD risk assessments, screenings, and preventive interventions for all HIV-infected individuals (*2*). For high-risk individuals, ART regimens should be modified accordingly, with active management of CVD risk factors, including smoking cessation, glycemic control, lipid management, obesity, and hypertension. Among antiviral medications, protease inhibitors and non-nucleoside reverse transcriptase inhibitors have a higher propensity to cause lipid metabolism disorders. Given the high usage rate of EFV observed in our study, individuals on these medications may require ART regimen modifications.

Based on our findings and current guideline recommendations, proactive CVD risk screening, and targeted interventions for the HIV population are imperative. However, our study revealed that fewer than half of hypertensive individuals received antihypertensive treatment, and effective interventions for risk factors such as smoking and dyslipidemia were inadequate. This underscores the need for enhanced primary prevention efforts, particularly in screening high-risk populations and implementing timely antihypertensive and lipid-lowering interventions to reduce CVD risk.

CVD risk screening should be integrated into routine clinical management of HIV, necessitating appropriate screening tools. However, current risk screening tools have significant limitations. General population prediction models show reduced accuracy in HIV-infected individuals due to factors such as drug toxicity and immune reconstitution (*9*). Our study demonstrated poor consistency among the five tools used for 10-year CVD risk assessment in the general population. This inconsistency partly stems from differences in outcome indicators. Most predictive model cohorts were established in the last century, and temporal changes in lifestyle and environmental factors may compromise their current accuracy. In clinical practice, this poor consistency results in different models identifying distinct patient groups for intervention, leading to varied preventive care decisions. Treating HIV-infected individuals as part of the general population for cardiovascular prevention fails to account for the increased CVD risk associated with HIV infection itself. While the D:A:D model was specifically designed for HIV-infected populations, it lacks external validation and excludes the Asian population data. In the absence of an accurate and reliable model, priority should be given to determining the most suitable predictive model for Asian HIV-infected populations and developing a new CVD risk assessment model for HIV-infected individuals. Previous studies have suggested that FHS-CVD is most useful for determining statin eligibility in primary prevention; however, its significant differences in outcome indicators make it generally incomparable with other models (*10*).

Our study has several limitations. First, reliance on voluntary participation in daily follow-up surveys may introduce volunteer bias. Second, identifying valid cases through patient-reported treatment numbers is susceptible to input errors and duplications. Despite manual screening and comparison of treatment records for baseline population data, some missing data persist. Finally, the cross-sectional nature of this baseline survey in an HIV-infected population without a control group precludes comparisons with the general population. Continued follow-up of the study population is necessary to validate these findings, particularly regarding observed outcome events.

In conclusion, our comprehensive evaluation using six risk assessment tools reveals a substantial CVD risk burden among Shanghai's HIV population. The high prevalence of traditional CVD risk factors in this population, coupled with inadequate management, emphasizes the urgent need for systematic screening and intervention programs. Furthermore, our findings underscore the critical importance of developing HIV-specific CVD screening tools tailored to the Chinese population.

Conflicts of interest: No conflicts of interest.

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[#] Corresponding author: Yinzhong Shen, shenyinzhong@shphc.org.cn.

[1] Shanghai Institute of Infectious Disease and Biosecurity, Fudan University, Shanghai, China; [2] Shanghai Public Health Clinical Center, Fudan University, Shanghai, China; [3] School of Public Health, Fudan University, Shanghai, China.
[&] Joint first authors.

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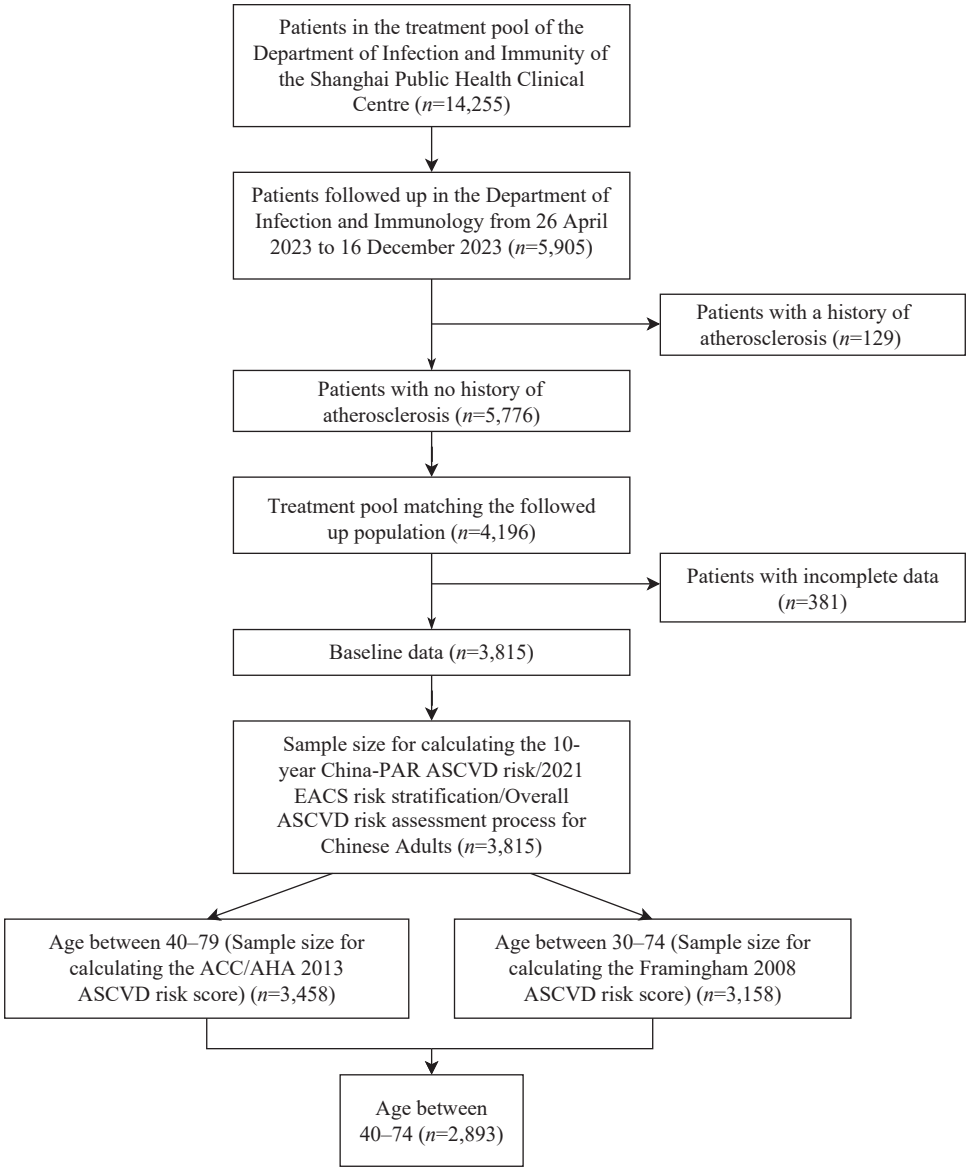
SUPPLEMENTARY MATERIAL



SUPPLEMENTARY FIGURE S1. Flowchart for baseline population selection.
Abbreviation: ACC/AHA=the American College of Cardiology/American Heart Association; ASCVD=atherosclerotic cardiovascular disease.

SUPPLEMENTARY TABLE S1. Basic information about cardiovascular risk assessment models and grading criteria used in this study.

Evaluation criteria	Endpoint definition	Cohort	Follow-up	Assessment results	Criteria for classification
Prediction for ASCVD RISK in China (the China-Par Project)	ASCVD was defined as nonfatal acute MI or CHD death or fatal or nonfatal stroke. Acute MI was identified as a change in biochemical markers of myocardial necrosis accompanied by ischemic symptoms, pathological Q waves, ST-segment elevation or depression, or coronary intervention.18 CHD death included all fatal events resulting from MI or other coronary deaths. Stroke included clinical signs and symptoms of subarachnoid or intracerebral hemorrhage or cerebral infarction, which were rapidly developing signs of focal (or global) disturbances in cerebral function lasting >24 hours without an apparent nonvascular cause.	The China-PAR project used InterASIA (International Collaborative Study of Cardiovascular Disease in Asia) and China MUCA (1998) (China Multi-Center Collaborative Study of Cardiovascular Epidemiology) to develop the Chinese ASCVD risk equations as the derivation cohort. 21,320 participants are included in the project to derive the China-PAR equations	An average follow-up duration of 12.3 years.	Estimation of 10-year and lifetime risk of CVD	Based on the China-PAR equations for risk assessment of ASCVD, those with predicted risks of <5%, 5%–10%, and ≥10% could be classified into categories of low-, moderate-, and high-risk for ASCVD, respectively.
The European AIDS Clinical Society (EACS)					In accordance with the requirements of Version 11.0 of the EACS guidelines, the China-PAR was adopted as the scoring tool, and grading was then conducted based on the EACS grading criteria. Classification criteria include total cholesterol level, LDL cholesterol level, the number of risk factors, and the presence of hypertension.
Chinese guidelines for lipid management (2023)	All fatal and non-fatal acute coronary events and acute stroke events. Acute coronary events included acute myocardial infarction, sudden coronary death, and other coronary deaths and acute stroke events including subarachnoid haemorrhage, intracerebral haemorrhage, or cerebral infarction.	The Chinese Multi-Provincial Cohort Study (CMCS). 21,953 participants aged 35 to 84 years without CVD at the baseline were included.	1992–2010	Estimation of 10-year and lifetime risk of CVD	Classification criteria depend on total cholesterol level, LDL cholesterol level and number of risk factors, and the presence of hypertension.
Framingham 2008 ASCVD risk score	The Framingham Heart Study defines CVD as a composite of CHD (coronary death, myocardial infarction, coronary insufficiency, and angina), cerebrovascular events (including ischemic stroke, hemorrhagic stoke, and transient ischemic attack), peripheral artery disease (intermittent claudication), and heart failure.	In 8,491 Framingham study participants (mean age, 49 years; 4,522 women) who attended a routine examination between 30 and 74 years of age and were free of CVD.	12 years	10-year risk of CVD (We have also adopted the recalibrated 5-year risk of Framingham CVD prediction model in the D:A:D study)	Based on *General Cardiovascular Risk Profile for Use in Primary Care: The Framingham Heart Study*, this project categorized risk levels as 0% to 6%, 6% to 20%, and over 20%

Continued

Evaluation criteria	Endpoint definition	Cohort	Follow-up	Assessment results	Criteria for classification
ACC/AHA 2013 ASCVD risk score	First hard ASCVD events (defined as first occurrence of nonfatal myocardial infarction, CHD death, or fatal or nonfatal stroke)	Provide sex- and race-specific estimates of the 10-year risk of ASCVD for African-American and white men and women 40 to 79 years of age. The final pooled cohorts included participants from several large, racially and geographically diverse, modern NHLBI-sponsored cohort studies, including the ARIC (Atherosclerosis Risk in Communities) study, the Cardiovascular Health Study, and the CARDIA (Coronary Artery Risk Development in Young Adults) study, combined with applicable data from the Framingham Original and Offspring Study cohorts.	>12 years	Estimation of 10-year and lifetime risk of CVD	Predicted risks of <7.5%, 7.5%–20%, and ≥20% could be classified into categories of low-, moderate-, and high-risk for ASCVD, respectively.
The Data-collection on Adverse Effects of Anti-HIV Drugs (D:A:D) study	The study endpoints include all incident cases of MI, stroke, invasive cardiovascular procedures and deaths which were reported to the study co-ordinating office for central validation and coding as detailed previously. Non-fatal MIs not associated with clinical symptoms (silent MIs) were not included.	They conducted a collaborative, observational study of 11 previously established cohorts comprising 23,468 HIV-1–infected patients followed at 188 clinics in 21 countries in Europe, the United States, and Australia.	The median follow-up time was 5.7 (IQR, 2.9–8.8) years	Estimation of 5-year risk of CVD	For each model, they categorized each individua's five-year predicted CVD risk into one of the following categories: <1%, 1%–5%, 5%–10% and >10% five-year CVD predicted risk.

Abbreviation: CHD=congenital heart disease; ASCVD=atherosclerotic cardiovascular disease; MI=myocardial infarction; LDL=low-density lipoprotein; AIDS=acquired immunodeficiency syndrome; CVD=cardiovascular disease.

Preplanned Studies

Association Between Incorrect Use of Pre- and Post-Exposure Prophylaxis and HIV infection Among Men Who Have Sex with Men — Shenzhen City, Guangdong Province, China, 2021–2023

Zijie Yang[1,2]; Jiachun Chen[1,3]; Lan Wei[1]; Delei Dai[1,3]; Hu Tang[1,4]; Yan Zhang[1]; Wei Xie[1]; Shaochu Liu[1]; Wei Tan[1]; Xiangdong Shi[1]; Chenli Zheng[1]; Xiaohong Yuan[1,5]; Zhongliang Xu[6]; Wei Ye[6]; Jin Zhao[1,#]

Summary

What is already known about this topic?

Preexposure prophylaxis (PrEP) and postexposure prophylaxis (PEP) have been proven effective in preventing human immunodeficiency virus (HIV) transmission.

What is added by this report?

Men who have sex with men (MSM) who incorrectly used PrEP/PEP demonstrated higher HIV positivity rates compared to both correct users and non-users. Since PrEP/PEP users are more likely to engage in unprotected anal intercourse (UAI), incorrect use of these prophylactic measures may constitute a significant risk factor for HIV transmission among MSM.

What are the implications for public health practice?

It is crucial to implement strategies that guide MSM toward correct PrEP/PEP utilization while emphasizing that these prophylactic measures should not be considered substitutes for condom use.

ABSTRACT

Introduction: Pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) are promising interventions to curb HIV transmission among men who have sex with men (MSM). However, incorrect use may elevate HIV risk. This study investigated the impact of improper PrEP/PEP use on HIV infection among MSM.

Methods: A cross-sectional survey was conducted in Shenzhen (2021–2023) using time-location sampling and respondent-driven sampling. χ^2 tests and Poisson regression with robust error variance were employed for univariate and multivariate analyses.

Results: Compared to PrEP/PEP non-users, MSM who incorrectly used PrEP [adjusted odds ratio (a*OR*)=2.17, 95% confidence interval (*CI*): 1.05, 4.49] and PEP (a*OR*=3.76, 95% *CI*: 1.40, 10.15) were more likely to be HIV-positive. No HIV-positive cases were reported among MSM who correctly used PrEP. Correct PEP users showed no significant difference in HIV prevalence compared to non-users.

Conclusions: Correct PrEP/PEP use is an effective HIV prevention strategy for MSM, but incorrect use may increase infection risk. Public health efforts must prioritize interventions promoting adherence to PrEP/PEP guidelines, emphasizing that PrEP/PEP should complement — not replace — consistent condom use.

Men who have sex with men (MSM) constitute one of the populations at highest risk for human immunodeficiency virus (HIV) infection. In 2022, MSM accounted for approximately 25% of newly diagnosed HIV cases in China, with this proportion exceeding 60% in developed urban areas (*1*). A significant disconnect exists between knowledge and behavioral practices among MSM, creating substantial challenges for HIV risk reduction interventions. Post-exposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP) have emerged as the most promising strategies for preventing HIV transmission in the MSM population. However, incorrect implementation of PrEP/PEP may increase HIV infection risk among MSM and potentially contribute to HIV drug resistance (*2*), thereby accelerating viral transmission. Our findings indicate that MSM who incorrectly used PrEP/PEP were more likely to test HIV-positive compared to both correct users and non-users. This observation highlights the critical importance of proper PrEP/PEP utilization, particularly given that PrEP/PEP users demonstrate

higher rates of unprotected anal intercourse (UAI), which may explain why incorrect PrEP/PEP usage represents a significant risk factor for HIV infection among MSM.

This cross-sectional study investigated PEP and PrEP utilization and HIV infection status among MSM in Shenzhen City, Guangdong Province, China, from 2021–2023. Participants were recruited through time-location sampling (TLS) and respondent-driven sampling (RDS), following previously described methodologies (*3*). The inclusion criteria for study participation were as follows: Biologically male, aged 16 years or older and had engaged in sexual activity with men within the past 12 months. Data collection was conducted via tablet-based self-administered questionnaires, capturing demographic information and HIV risk behaviors. Blood samples were collected for laboratory HIV testing to determine infection status. Correct PEP use was defined as medication obtained from healthcare facilities with proper medical prescription, accompanied by HIV testing both before initiation and after completion of the treatment course. Correct PrEP use was defined as medication obtained from healthcare facilities and taken according to medical professionals' prescriptions. Incorrect PrEP/PEP use encompassed any medications obtained through non-healthcare facilities or those obtained from healthcare facilities but not taken as prescribed.

Statistical analyses were performed using SPSS (version 20.0, IBM Corp, State of New York, America). Univariate analyses employed chi-square tests, with factors showing $P<0.1$ included in multivariate analyses. Multivariate regression analyses utilized Poisson regression with robust error variance through generalized linear models. Results are presented as number (%), means ± standard deviations, adjusted odds ratios (a*OR*s), and 95% confidence intervals (*CI*s). Statistical significance was set at 0.05.

This study surveyed 3,723 MSM with a mean age of 33.65±8.81 years, yielding an HIV prevalence of 2.67% (99/3,723). Significant differences in HIV infection status were observed across ethnicity, educational level, sexual role, syphilis infection status, engagement in UAI, PEP use, and PrEP use ($P<0.05$, Table 1). Poisson regression analysis revealed that, compared to HIV-negative MSM, HIV-positive individuals were more likely to be of other ethnicities (a*OR*=2.94, 95% *CI*: 1.49, 5.81), have receptive sexual roles (a*OR*=3.11, 95% *CI*: 1.64, 5.87) or versatile roles (a*OR*=2.34, 95% *CI*: 1.33, 4.10), be infected with syphilis (a*OR*=2.59, 95% *CI*: 1.12, 5.97), and engage in UAI (a*OR*=3.03, 95% *CI*: 1.93, 4.76). Notably, compared to PrEP/PEP non-users, MSM who incorrectly used PrEP (a*OR*=2.17, 95% *CI*: 1.05, 4.49) and PEP (a*OR*=3.76, 95% *CI*: 1.40, 10.15) were more likely to report HIV-positive status. Furthermore, no HIV-positive cases were reported among MSM who correctly used PrEP, and no significant difference in HIV prevalence was observed between correct PEP users and non-users (Table 1).

Among the study participants, 8.5% (316/3,723) reported PrEP/PEP usage. Significant differences were observed in the distribution of PrEP/PEP users across education level, duration of residence, monthly income, sexual role, HIV testing history, and UAI engagement ($P<0.05$, Table 2). Poisson regression analysis revealed that MSM who used PrEP/PEP were more likely to have college or higher education (a*OR*=1.49, 95% *CI*: 1.03, 2.15), recent HIV testing within 6 months (a*OR*=1.49, 95% *CI*: 1.03, 2.15), and engagement in UAI (a*OR*=1.95, 95% *CI*: 1.54, 2.47). These individuals were also more likely to report both insertive and receptive sexual roles (a*OR*=0.74, 95% *CI*: 0.57, 0.97) but were less likely to have resided in Shenzhen for more than 6 months (a*OR*=0.60, 95% *CI*: 0.44, 0.82) (Table 2).

DISCUSSION

The adoption rate of PrEP/PEP among MSM in Shenzhen remains relatively low at 8.5%, considerably below the approximately 20% utilization rate reported in a recent multicenter study across China from 2019–2022 (*4*). This disparity highlights an urgent need for enhanced implementation strategies. Our analysis revealed that while 81.71% (143/175) of PEP users adhered to correct usage protocols, only 22.16% (37/167) of PrEP users demonstrated proper adherence. Notably, the study found complete protection against HIV transmission among MSM who correctly used PrEP, with zero HIV-positive cases in this group. Conversely, MSM who reported HIV-positive status were significantly more likely to have used PrEP/PEP incorrectly compared to HIV-negative individuals, suggesting a potential association between incorrect prophylaxis use and increased HIV acquisition risk, though causal relationships require further investigation. These findings emphasize the critical importance of ensuring proper PrEP/PEP utilization when recommending these interventions to MSM.

Our findings indicate that MSM utilizing PrEP/PEP

TABLE 1. Factors associated with HIV infection among MSM in Shenzhen city in 2021–2023 (*N*=3,718).

Variables	HIV-negative, no. (%)	HIV-positive, no. (%)	χ^2	*P*	a*OR*	95% *CI*
Year			3.63	0.06		
2021–2022	2,333 (96.96)	73 (3.03)				
2023	1,286 (98.01)	26 (1.98)			0.58	0.36, 0.93
Ethnicity			9.37	0.00		
Han	3,498 (97.46)	91 (2.54)				
Other	101 (92.66)	8 (7.34)			2.94	1.49, 5.81
Educational level			6.81	0.03		
Junior high school and below	517 (95.91)	22 (4.08)				
High middle school	893 (96.95)	28 (3.04)			0.78	0.44, 1.36
College and above	2,209 (97.82)	49 (2.17)			0.66	0.40, 1.11
Length of residence			1.43	0.23		
0–6 months	422 (96.56)	15 (3.43)				
≥7 months	3,008 (97.53)	76 (2.46)				
Income (CNY)			3.50	0.17		
≤3,000	350 (97.49)	9 (2.51)				
3,001–7,000	433 (96.00)	18 (3.99)				
≥7,001	2,836 (97.52)	72 (2.48)				
Marital status			0.53	0.77		
Unmarried	2,924 (97.30)	81 (2.70)				
Cohabiting/married	367 (97.86)	8 (2.13)				
Separated/divorced/widowed	328 (97.04)	10 (2.96)				
Sexual roles			14.42	0.00		
Inserters	1,282 (98.61)	18 (1.38)				
Receptive	583 (95.88)	25 (4.11)			3.11	1.64, 5.87
Both	1,754 (96.90)	56 (3.09)			2.34	1.33, 4.10
Sexual orientation			0.51	0.92		
Homosexual	2,596 (97.22)	74 (2.77)				
Heterosexual	31 (96.87)	1 (3.13)				
Bisexual	711 (97.66)	17 (2.34)				
Unsure	281 (97.56)	7 (2.43)				
Syphilis infection			9.87	0.00		
No	3,556 (97.45)	93 (2.55)				
Yes	63 (91.30)	6 (8.70)			2.59	1.12, 5.97
HIV test			1.73	0.20		
No	2,026 (97.03)	62 (2.97)				
Yes	1,593 (97.73)	37 (2.27)				
UAI			30.34	<0.001		
Yes	1,320 (95.30)	65 (4.69)			3.03	1.93, 4.76
No	1,835 (98.54)	27 (1.45)				
PEP			12.18	0.00		
Unused	3,451 (97.40)	92 (2.60)				
Incorrect use	28 (87.50)	4 (12.50)			3.76	1.40, 10.15
Correct use	140 (97.90)	3 (2.10)			0.69	0.25, 1.93

Continued

Variables	HIV-negative, no. (%)	HIV-positive, no. (%)	χ^2	*P*	a*OR*	95% *CI*
PrEP			10.34	0.01		
Unused	3,461 (97.46)	90 (2.53)				
Incorrect use	121 (93.07)	9 (6.92)			2.17	1.05, 4.49
Correct use	37 (100.00)	0 (0)			0	0, 0

Abbreviation: a*OR*=adjusted odds ratio; *CI*=confidence intervals; HIV=human immunodeficiency virus; MSM=men who have sex with men; PEP=postexposure prophylaxis; PrEP=preexposure prophylaxis; UAI=unprotected anal intercourse; CNY=Chinese yuan.

were 1.9 times more likely to engage in UAI compared to non-users, suggesting that some individuals may view prophylaxis as a replacement for consistent condom use (*5*). The HIV yield was significantly higher among PrEP/PEP users compared to non-users (14.1% *vs*. 8.3%, *P*=0.041). This elevated infection rate likely stems from the combination of incorrect prophylaxis use and increased UAI, which collectively amplify HIV transmission risk among non-compliant MSM.

Previous research has indicated that Chinese MSM demonstrate a preference for event-driven PrEP over daily PrEP (*6*). Our findings reveal that more than 60% of MSM transitioned from daily to event-driven PrEP regimens. However, we observed that the HIV yield among MSM using event-driven PrEP was 6.1% (7/114), exceeding that of daily PrEP users (3.8%, 2/53). This disparity may be attributed to the inherent complexity of event-driven PrEP protocols, which increases the likelihood of incorrect usage among MSM, potentially leading to HIV infection. Therefore, while previous studies have demonstrated the effectiveness of event-driven PrEP in reducing HIV infection risk among MSM (*7*), additional real-world studies in China are essential to evaluate its efficacy and develop appropriate implementation guidelines.

Moreover, improper PrEP/PEP usage may contribute to HIV drug resistance (*2*,*8*), potentially catalyzing new epidemic waves. Our unpublished data indicates that the prevalence of nucleotide reverse transcriptase inhibitor resistance among HIV-infected individuals with PrEP/PEP exposure was significantly higher compared to those without exposure (12.5% versus 1.7%, *P*=0.025). Research has shown that PrEP/PEP-related HIV drug resistance can develop when these interventions are administered during undetected acute infection, emphasizing the critical importance of HIV testing prior to PrEP/PEP initiation (*9*). Furthermore, the increasing use of PrEP during acute HIV infection may result in false-negative HIV test results (*10*). Consequently, current HIV testing protocols may be insufficient for PrEP/PEP users, particularly regarding the recommended quarterly testing schedule for event-driven PrEP users. To prevent continued PrEP/PEP use among HIV-infected MSM, we recommend that individuals who use these interventions incorrectly or cannot ensure proper adherence undergo HIV testing before each subsequent use.

This study has two main limitations. First, this study was a cross-sectional study that could not establish the causality between incorrect PrEP/PEP use and HIV infection. In the future, we plan to undertake a longitudinal observational follow-up study to investigate the reasons for incorrect PrEP/PEP use among MSM and assess its causal association with HIV infection in this population. Second, as the study was conducted in a developed Chinese city characterized by a predominantly migratory population and where MSM constitute most newly diagnosed HIV-positive cases, the findings may have limited generalizability to other urban settings.

In conclusion, while correct PrEP/PEP usage among MSM represents a promising strategy for HIV prevention, incorrect usage may paradoxically increase HIV infection risk, particularly given that PrEP/PEP users demonstrate higher rates of UAI. The current priority lies in developing and implementing effective strategies to promote proper PrEP/PEP adherence while emphasizing that these preventive medications should complement, rather than replace, consistent condom use.

Conflicts of interest: No conflicts of interest.

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TABLE 2. Factors associated with PrEP/PEP use among MSM in Shenzhen city in 2021–2023 (*N*=3,723).

Variables	Unuse PrEP/PEP, no. (%)	Use PrEP/PEP, no. (%)	χ^2	*P*	a*OR*	95% *CI*
Year			1.13	0.29		
2021–2022	2,215 (91.87)	196 (8.13)				
2023	1,192 (90.85)	120 (9.15)				
Ethnicity			0.08	0.78		
Han	3,291 (91.56)	303 (8.43)				
Other	99 (90.82)	10 (9.17)				
Educational level			19.15	<0.001		
Junior high school and below	494 (91.48)	46 (8.52)				
High school	875 (94.90)	47 (5.10)			0.72	0.46, 1.14
College and above	2,038 (90.13)	223 (9.86)			1.49	1.03, 2.15
Length of residence			3.95	0.05		
0–6 months	391 (89.26)	47 (10.73)				
≥7 months	2,843 (92.06)	245 (7.93)			0.60	0.44, 0.82
Income (CNY)			9.32	0.01		
≤3,000	315 (87.50)	45 (12.50)				
3,001–7,000	409 (90.68)	42 (9.31)			0.94	0.59, 1.51
≥7,001	2,683 (92.13)	229 (7.86)			0.77	0.53, 1.14
Marital status			1.86	0.39		
Unmarried	2,744 (91.22)	264 (8.78)				
Cohabiting/married	348 (92.30)	29 (7.69)				
Separated/divorced/widowed	315 (93.19)	23 (6.80)				
Sexual roles			18.02	<0.001		
Inserter	1,176 (90.39)	125 (9.61)				
receptive	539 (88.36)	71 (11.63)			1.14	0.84, 1.56
Both	1,692 (93.37)	120 (6.62)			0.74	0.57, 0.97
Sexual orientation			1.10	0.78		
Homosexual	2,439 (91.24)	234 (8.75)				
Heterosexual	29 (90.62)	3 (9.38)				
Bisexual	671 (92.04)	58 (7.96)				
Unsure	268 (92.73)	21 (7.27)				
Syphilis infection			0.21	0.65		
No	3,344 (91.54)	309 (8.46)				
Yes	63 (90.00)	7 (10.00)				
HIV test			9.18	0.00		
No	1,940 (92.73)	152 (7.27)				
Yes	1,467 (89.94)	164 (10.05)			1.48	1.17, 1.88
UAI			34.07	<0.001		
Yes	1,224 (88.31)	162 (11.68)			1.95	1.54, 2.47
No	1,755 (94.05)	111 (5.95)				

Abbreviation: a*OR*=adjusted odds ratios; *CI*=confidence intervals; HIV=human immunodeficiency virus; MSM=men who have sex with men; PEP=postexposure prophylaxis; PrEP=preexposure prophylaxis; UAI=unprotected anal intercourse; CNY=Chinese yuan.

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[#] Corresponding author: Jin Zhao, szcdczj@163.com.

[1] STD & AIDS Control and Prevention Section, Shenzhen Center for Disease Control and Prevention, Shenzhen City, Guangdong Province, China; [2] School of Public Health, Peking University, Beijing, China; [3] School of Public Health, Shantou University, Shantou City, Guangdong Province, China; [4] School of Public Health, Shanxi Medical University, Taiyuan City, Shanxi Province, China; [5] School of Public Health Southern Medical University, Guangzhou City, Guangdong Province, China; [6] Shenzhen Nanshan Center for Disease Control and Prevention, Shenzhen City, Guangdong Province, China.

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Methods and Applications

Identification of Multiple Unique HIV-1 Recombinant Forms in Newly Reported HIV-1 Infected Individuals — Anhui Province, China, 2023

Huan Li[1]; Yi Feng[1]; Qi Li[1]; Jianjun Wu[2]; Hui Xing[1]; Lingjie Liao[1]; Zheng Wang[1,#]

ABSTRACT

Introduction: The genetic diversity of human immunodeficiency virus-1 (HIV-1) in China is characterized by multiple subtypes, circulating recombinant forms (CRFs) and unique recombinant forms (URFs) across the country. Through timely molecular surveillance, over 65 distinct CRFs have been identified in China to date. In this study, we identified five novel URFs among newly reported HIV-1 infected individuals in Anhui Province, China.

Methods: Near-full length HIV genome sequences were obtained using two-half molecule amplification methods from five samples containing potential URFs. The sequences were subsequently subjected to phylogenetic and recombination analyses.

Results: Phylogenetic and recombination analyses of the five near-full length genome sequences confirmed their classification as novel URFs. Among these, three sequences were recombinants of CRF01_AE and CRF07_BC, one sequence was a recombinant of CRF01_AE, CRF07_BC and B, and one sequence resulted from CRF07_BC and CRF08_BC recombination.

Conclusions: The identification of URFs in newly infected individuals indicates ongoing transmission of multiple HIV-1 clades in Anhui Province, with superinfection occurring at notable frequencies. These findings emphasize the importance of enhancing long-term surveillance of circulating HIV-1 clades using near-full length sequence analysis in Anhui, China.

The first acquired immune deficiency syndrome (AIDS) case in China was reported in 1985 (*1*), marking the beginning of HIV-1 spread throughout the country. According to the National Statutory Infectious Disease Epidemic Profile published by the National Bureau of Disease Control and Prevention (NBDCP) in 2023, China documented 59,533 AIDS cases and 22,393 related deaths (https://www.ndcpa.gov.cn/). Although the implementation of immediate identification and treatment strategies has significantly reduced HIV incidence, HIV-1 remains a substantial threat to public health in China.

In Anhui Province, the identification of the first human immunodeficiency virus-positive (HIV-positive) case in 1994 was followed by a rapid increase in infections, particularly among commercial blood donors (*2*). Anhui has served as a crucial hub in the dissemination of HIV-1 across China (*3*). By 2018, the province had documented 17,183 HIV-infected individuals. The predominant HIV-1 subtypes circulating in Anhui include CRF01_AE, CRF07_BC, CRF08_BC, CRF55_01B, and subtype B. Previous studies have revealed a significant prevalence of unique recombinant forms (URFs), indicating frequent superinfections. The ongoing recombination between subtypes enhances HIV genetic diversity and facilitates the emergence of highly adaptive variants that could potentially trigger new pandemics (*4*). Given the substantial subtype diversity in Anhui, continuous monitoring of subtype distributions remains essential for effective HIV containment (*5*). Furthermore, surveillance of HIV genetic characteristics through near-full length genome (NFLG) analysis provides crucial insights into the HIV epidemic in Anhui and informs the development of innovative strategies for preventing and treating new HIV infections.

METHODS

Study Population

The sampling strategy in Anhui Province employed a risk-stratified approach, categorizing prefectural-level cities into high, medium, and low risk based on reported HIV cases over the preceding three years. The sampling framework mandated the inclusion of at least two cities from each risk category, with minimum

sampling proportions of 20%, 40%, and 60% for high-, medium-, and low-risk cities, respectively.

The study encompassed 238 newly confirmed HIV-1 positive samples collected from Anhui in 2023. Plasma samples were procured through the Anhui Provincial CDC.

Sequencing and Analysis of PR-RT, IN, and *env* Fragments

Viral RNA was extracted from plasma samples using the QIAamp Viral RNA Mini Kit (QIAGEN, Germany). HIV-1 cDNA synthesis and amplification were performed using the AccessQuick™ RT-PCR System (PROMEGA, China) in combination with 2× Taq PCR Mix (TIANGEN, China). The amplification and sequencing of HIV genome fragments were conducted according to previously established protocols (*6*–*7*).

Sequencing was performed on an ABI 3730XL sequencer (Applied Biosystems, USA). Sequence processing, including trimming, splicing, and mixed base interpretation, was conducted using Sequencher v5.4.6 (Gene Codes Corporation, Mississippi, USA). To ensure data quality and exclude experimental cross-contamination, sequences were validated using the WHO HIVDR QC Tool. Multiple sequence alignment was performed using MAFFT v7 (Research Institute for Microbial Diseases Osaka University, Osaka, Japan) (*8*). Reference sequences were obtained from relevant databases, and phylogenetic analysis was conducted using IQ-TREE (version 2.0, University of Vienna, Vienna, The Republic of Austria; The Australian National University, Canberra, Australia) (*9*) with the Maximum Likelihood (ML) method, implementing the General Time Reversible (GTR) + G nucleotide substitution model and 1,000 bootstrap replicates. The resulting phylogenetic trees were visualized using the interactive tree of life (iTOL) online platform (https://itol.embl.de/).

Sequencing and Analysis of Near Full-length Genome

Near full-length genome sequences were obtained using a two-amplicon strategy following previously established protocols. The methodologies for viral RNA extraction, PCR amplification, and sequencing procedures have been detailed in previous publications (*10*).

Sequence analysis was performed using Sequencher software (version 5.4.6, Gene Codes Corporation, USA) for sequence trimming, secondary peak detection, sequence assembly, and mixed base interpretation. Quality control of the assembled sequences was conducted using the online Gene Cutter tool (https://www.hiv.lanl.gov/content/sequence/GENE_CUTTER/cutter.html). To eliminate potential contamination, all sequences were compared against the comprehensive HIV sequence database using the Basic Local Alignment Search Tool (BLAST) (http://hiv-web.lanl.gov/content/index). Sequences meeting quality control criteria were analyzed for potential unique recombinant patterns using two complementary approaches: the Recombinant Identification Program (RIP) with default parameters (https://www.hiv.lanl.gov/content/sequence/RIP/RIP.html) and the jumping profile Hidden Markov Model (jpHMM) (http://jphmm.gobics.de/) within the HIV Database.

Based on the RIP and jpHMM analyses, we constructed a comprehensive reference sequence alignment incorporating predominant subtypes circulating in China (CRF01_AE, CRF07_BC, CRF08_BC, CRF55_01B, and subtype B), other Chinese CRFs, and relevant external sequences. Sequence alignment was performed using Aliview software (Uppsala University, Upsala, Sweden) (*11*). Phylogenetic analysis was conducted using IQ-TREE (version 2.0, University of Vienna, Vienna, The Republic of Austria; The Australian National University, Canberra, Australia) (*9*) with the GTR model and 1,000 bootstrap replicates. The resulting phylogenetic trees were visualized using the iTOL online platform. Recombination breakpoint analysis was performed using SimPlot (version 3.5.1, Biomatters, Auckland, New Zealand) (*12*) with parameters set to a 300 bp window size and 20 bp step size. The genetic structure of unique recombinant samples was mapped using the Recombinant Mapping Tool (https://www.hiv.lanl.gov/content/sequence/DRAW_CRF/recom_mapper.html) available in the HIV Database.

RESULTS

Demographic Information of the Study Population

From the total cohort of 238 newly reported cases in Anhui Province, 37 cases (15.5%) demonstrated subtype inconsistencies across at least two of the three analyzed genomic regions: PR-RT (nucleotides 2253-

3500, HXB2), IN (nucleotides 4230-5096, HXB2), and *env* (nucleotides 7016-7650, HXB2). Among these 37 samples exhibiting subtype discordance, seven contained sufficient plasma volume for NFLG amplification and sequencing, ultimately yielding 5 complete NFLG sequences. These 5 sequences were confirmed as URFs and designated as AHAQ230009, AHBZ230009, AHBZ230031, AHCUZ230011, and AHXC230017. The demographic characteristics of these 5 individuals are detailed in Supplementary Table S1 (available at https://weekly.chinacdc.cn/).

Phylogenetic Analysis of Genomic Regions

Comprehensive phylogenetic analysis was performed on three distinct genomic regions: PR-RT, IN, and *env*. Reference sequences were obtained from HIV databases, and maximum likelihood (ML) phylogenetic trees were constructed using IQ-TREE (version 2.0), implementing the GTR + G nucleotide substitution model with 1,000 bootstrap replicates. Tree visualization was accomplished using the iTOL online web tool. The subtype classifications for the three regions (PR-RT, IN, and *env*) corresponding to the five sequences are summarized in Figure 1 and Table 1.

Near Full-length Genome Analysis

The sequences obtained from the five potential URFs exceeded 8,000 base pairs in length, encompassing the complete coding regions for gag, pol, vif, vpr, vpu, rev, tat, *env*, and nef genes. Phylogenetic analysis conducted using IQ-TREE2 (Figure 2) demonstrates that these five samples represent distinct lineages independent of previously identified CRFs.

Detailed analysis revealed specific breakpoint locations within the HXB2 genome reference framework for all five sequences. As shown in Figure 3, the mosaic structures of these recombinants are characterized as follows: AHAQ230009 comprises three segments: Ⅰ$_{CRF07_BC}$ (634-4884); Ⅱ$_{CRF01_AE}$ (4885-8404); and Ⅲ$_{CRF07_BC}$ (8405-8960). AHBZ230009 consists of three regions: Ⅰ$_{CRF07_BC}$ (634-6323); Ⅱ$_{CRF01_AE}$ (6324-8327); and Ⅲ$_{CRF07_BC}$ (8328-9552). AHBZ230031 exhibits a

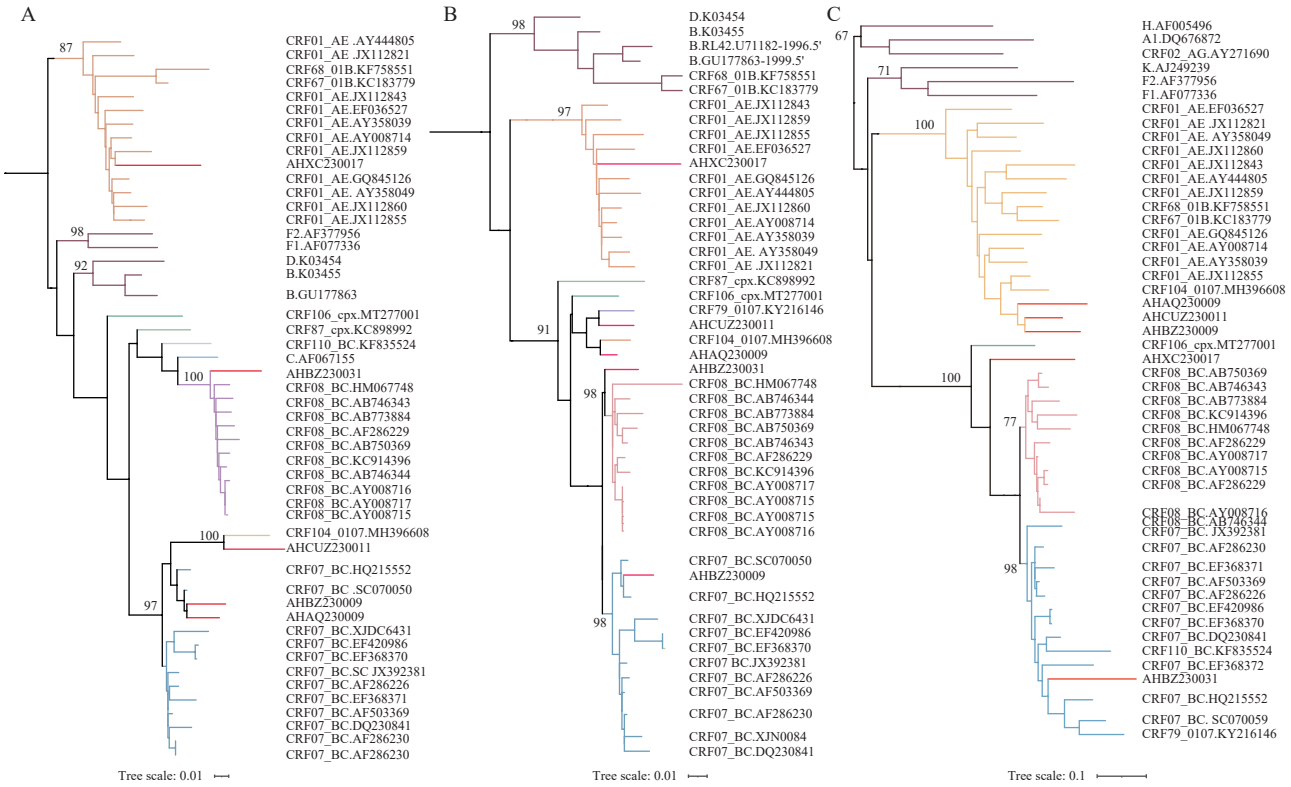

FIGURE 1. Phylogenetic tree of three fragments of five samples. (A) PR-RT; (B) IN; (C) *env*.
Note: Phylogenetic tree produced by IQ-TREE, the reliability of the tree branches was assessed by 1,000 bootstrap replicates, and trees were visualized by iTOL. The red line represents the five samples (AHAQ230009, AHBZ230009, AHBZ230031, AHCUZ230011 and AHXC230017).
Abbreviation: PR-RT=protease-reverse transcriptase; IN=integrase; *env*=envelope; iTOL=theinteractive tree of life.

TABLE 1. Subtypes of three fragments (PR-RT, IN, *env*) of five samples.

Sample ID	Subtype of PR-RT	Subtype of IN	Subtype of *env*
AHAQ230009	CRF07_BC	CRF104_0107	CRF01_AE
AHBZ230009	CRF07_BC	CRF07_BC	CRF01_AE
AHBZ230031	CRF08_BC	CRF08_BC	CRF07_BC
AHCUZ230011	CRF104_0107	CRF79_0107	CRF01_AE
AHXC230017	CRF01_AE	CRF01_AE	URF

Abbreviation: PR-RT=protease-reverse transcriptase; IN=integrase; *env*=envelope; URF=unique recombinant forms.

more complex structure with seven segments: $\mathrm{I}_{\mathrm{CRF07\_BC}}$ (620-1933); $\mathrm{II}_{\mathrm{CRF08\_BC}}$ (1934-3001); $\mathrm{III}_{\mathrm{CRF07\_BC}}$ (3002-3215); $\mathrm{IV}_{\mathrm{CRF08\_BC}}$ (3216-4628); $\mathrm{V}_{\mathrm{CRF07\_BC}}$ (4629-8518); $\mathrm{VI}_{\mathrm{CRF08\_BC}}$ (8519-9098); and $\mathrm{VII}_{\mathrm{CRF07\_BC}}$ (9099-9470). AHCUZ230011 displays six distinct regions: $\mathrm{I}_{\mathrm{CRF07\_BC}}$ (608-2959); $\mathrm{II}_{\mathrm{CRF01\_AE}}$ (2960-4244); $\mathrm{III}_{\mathrm{CRF07\_BC}}$ (4245-4885); $\mathrm{IV}_{\mathrm{CRF01\_AE}}$ (4886-8327); $\mathrm{V}_{\mathrm{CRF07\_BC}}$ (8328-8811); and $\mathrm{VI}_{\mathrm{CRF01\_AE}}$ (8812-9354). AHXC230017 shows six segments: $\mathrm{I}_{\mathrm{CRF01\_AE}}$ (621-4832); II_{B} (4833-4899); $\mathrm{III}_{\mathrm{CRF01\_AE}}$ (4900-6937); $\mathrm{IV}_{\mathrm{CRF07\_BC}}$ (6938-7679); V_{B} (7680-8240); and $\mathrm{VI}_{\mathrm{CRF01\_AE}}$ (8241-9552) (Supplementary Table S2, available at https://weekly.chinacdc.cn/). The phylogenetic analyses for all identified fragments are presented in Supplementary Figure S1 (available at https://weekly.chinacdc.cn/).

Bootscan analysis (Figure 3A) and similarity plot (Supplementary Figure S2, available at https://weekly.chinacdc.cn/) provide substantial evidence that these five isolates represent unique recombinants, distinct from previously identified CRFs or URFs. The recombinant structures of the five near-full-length sequences were delineated based on the breakpoint locations (Figure 3B), thereby confirming their classification as novel URFs.

Drug Resistance Analysis

Analysis of drug resistance mutations revealed that none of the five NFLGs exhibited resistance-associated mutations in either the protease or integrase regions. However, the AHXC230017 sequence contains the V179D mutation in the reverse transcriptase region, which is associated with non-nucleoside reverse transcriptase inhibitors. This mutation conferred intermediate-level resistance to Efavirenz (EFV) and Nevirapine (NVP), while demonstrating low-level resistance to Rilpivirine (RPV).

DISCUSSIONS

In this study, we identified five URFs in Anhui Province through comprehensive NFLG analysis. These URFs exhibited distinct recombination patterns, characterized by mosaic segments derived from multiple viral subtypes distributed throughout their genomes. While current CRF classification primarily relies on NFLG sequence analysis (*13*–*14*), this approach offers significant advantages over shorter gene fragment analysis (such as *PR-RT*, *IN*, and *env*), particularly in delineating recombination patterns and precise breakpoint locations. This methodology provides crucial insights for HIV-1 molecular epidemiological surveillance.

Recent years, the rapid dissemination of HIV-1 CRF07_BC strain among sexually transmitted populations in China leads to the emergence of numerous variants, including both URFs and novel CRFs (*15*). Our finding that CRF07_BC participated in all five URF recombination events suggests its enhanced transmission capability and infection prevalence (*1*).

Anhui Province, strategically located in central China and bordered by Jiangsu, Zhejiang, and Shanghai, serves as a major labor-exporting inland province and has emerged as a significant hub for HIV transmission and spread (*3*). The co-circulation of multiple subtypes in this region increases the probability of inter-subtype recombination (*16*), potentially challenging existing prevention and treatment strategies. Therefore, vigilant monitoring of novel URFs is essential for effectively evaluating and providing early warning of emergent strains with enhanced transmission potential.

However, the relatively small sample size of this study limits its contribution to monitoring the epidemic situation across the entire province. Furthermore, this study employed Sanger sequencing, which may not identify occurrences of superinfection or drug resistance mutations in certain samples. Future efforts should concentrate on increasing the sample size and utilizing more advanced sequencing techniques such as Nanopore technology to analyze the samples,

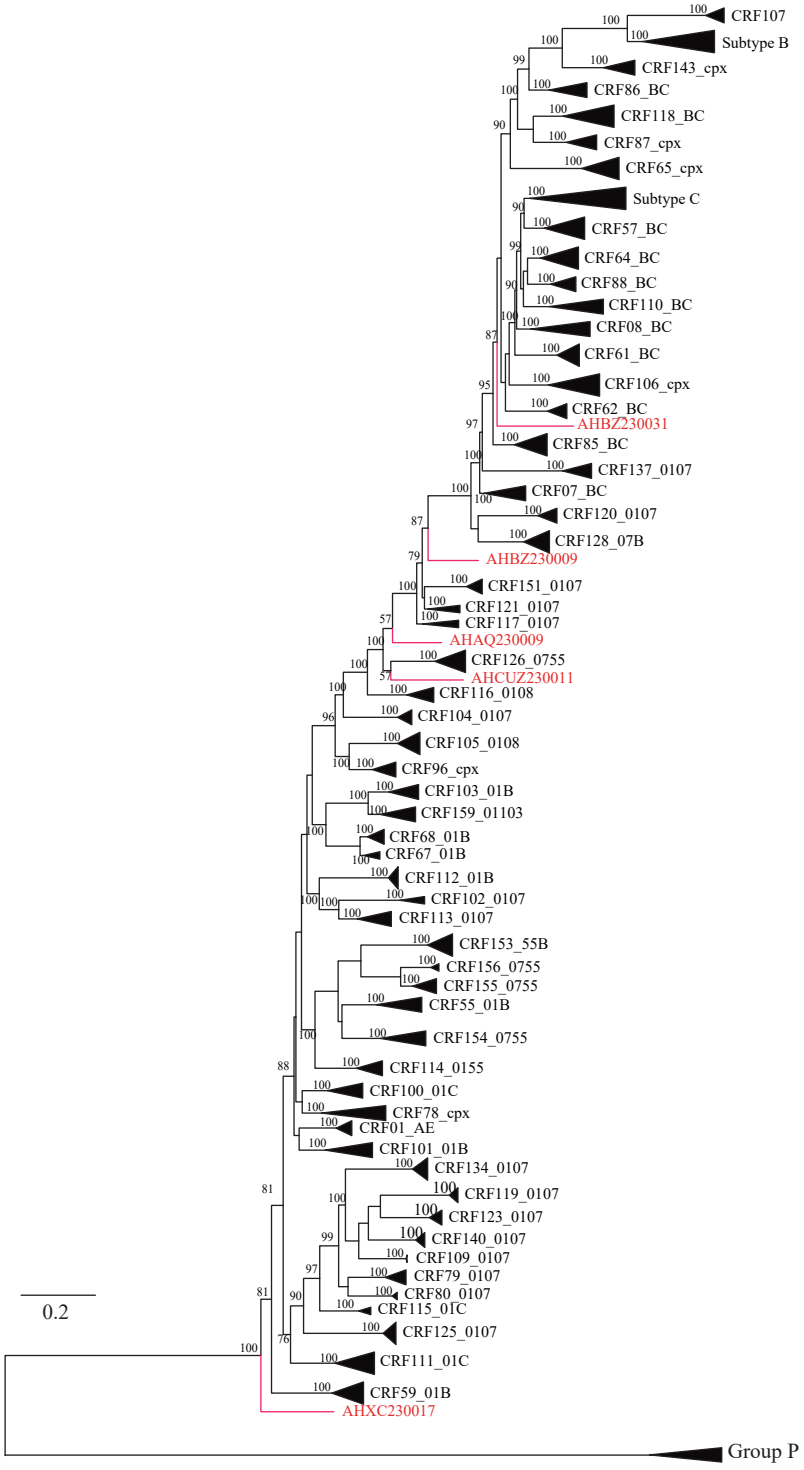

FIGURE 2. Phylogenetic tree of five NFLGs.
Note: The sequences of the potential URFs are marked in red. The neighbor joining tree of five NFLGs was constructed using IQ-TREE 2, and the reliability of the tree branches was assessed by 1,000 bootstrap replicates, and trees were visualized by iTOL.
Abbreviation: NFLGs=near-full length genome; URF=unique recombinant forms; iTOL=the interactive tree of life.

thereby obtaining more comprehensive information.

In conclusion, our identification of five URFs through near full-length HIV-1 genome analysis not only expands our understanding of HIV-1 genetic diversity but also underscores the critical importance of NFLG sequencing in molecular surveillance efforts.

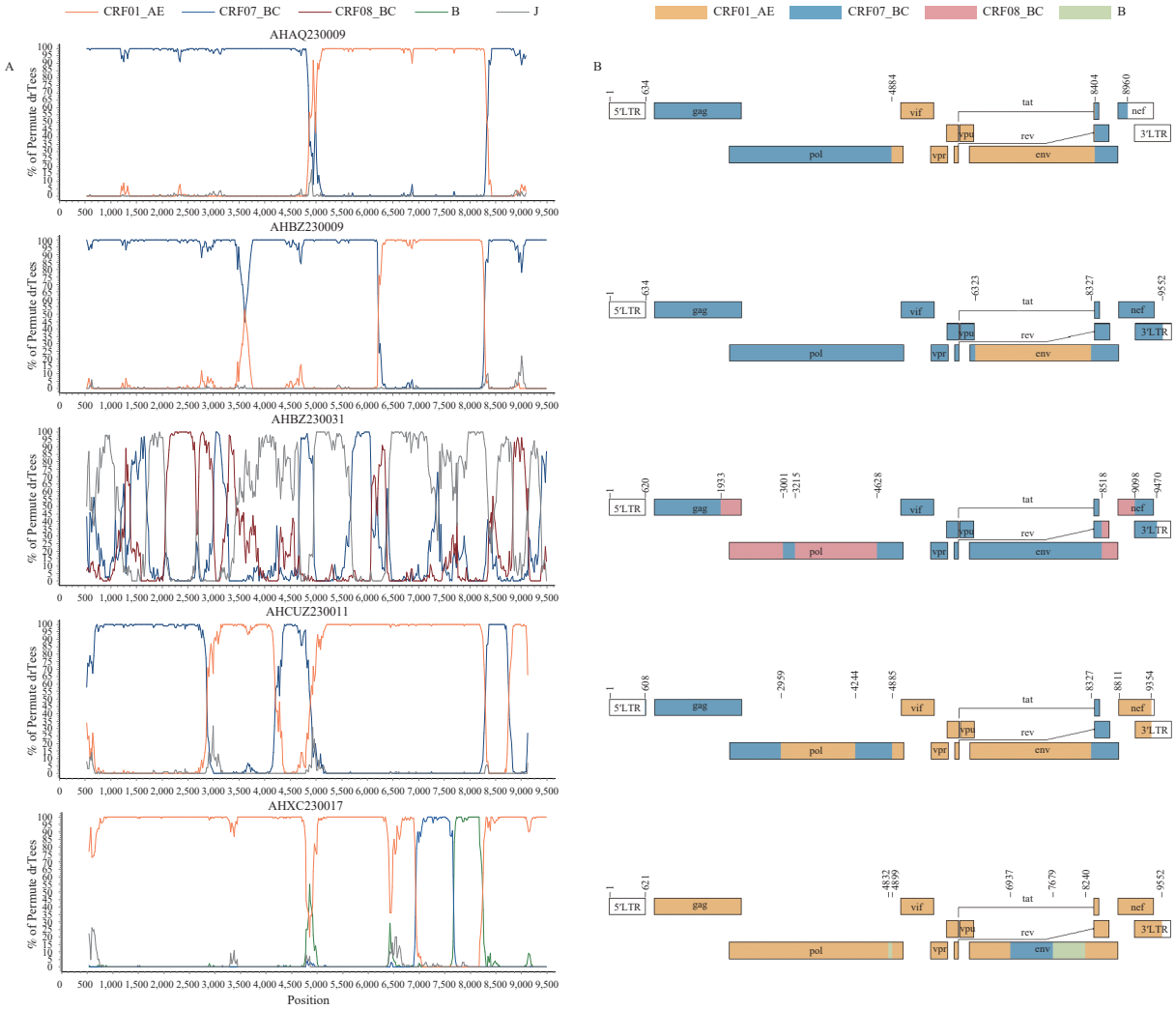

FIGURE 3. Recombinant analysis of the five identified URFs. (A) Bootscan analyses of the five URFs; (B) Genome map of the five URFs.

Note: (A) Bootscan analyses of the five URFs were performed using a window size of 300 bases and a step size of 20 bases, GapStrip: on, Kimura (2-parameter), T/t: 4.0. The CRF01_AE reference group includes JX112859, EF036527,and AY358049. The subtype CRF07_BC reference group includes SC070050, HQ215552 , AF286230. The subtype CRF08_BC reference group includes KC914396 and AY008715. The subtype B reference group includes GU177863 and U71182. The subtype J reference is SE9280. The x-axis represents the nucleotide positions, while the y-axis of the bootscan analysis shows the percentage bootstrap values of the permuted trees. (B) The analysis of recombination breakpoints in the five URFs. The mosaic fragments in the near-full-length genomes (NFLGs) recombinants are color-coded as follows: CRF01_AE (orange), CRF07_BC (blue), CRF08_BC (pink), and subtype B (green). The nucleotide positions of each fragment are numbered according to the HIV-1 reference sequence HXB2 (K03455).

Abbreviation: URF=unique recombinant forms.

Conflicts of interest: No conflicts of interest.

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[#] Corresponding author: Zheng Wang, wangzheng@chinaaids.cn.

[1] National Key Laboratory of Intelligent Tracking and Forecasting for Infectious Diseases, National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China; [2] Anhui Provincial Center for Disease Control and Prevention, Hefei City, Anhui Province, China.

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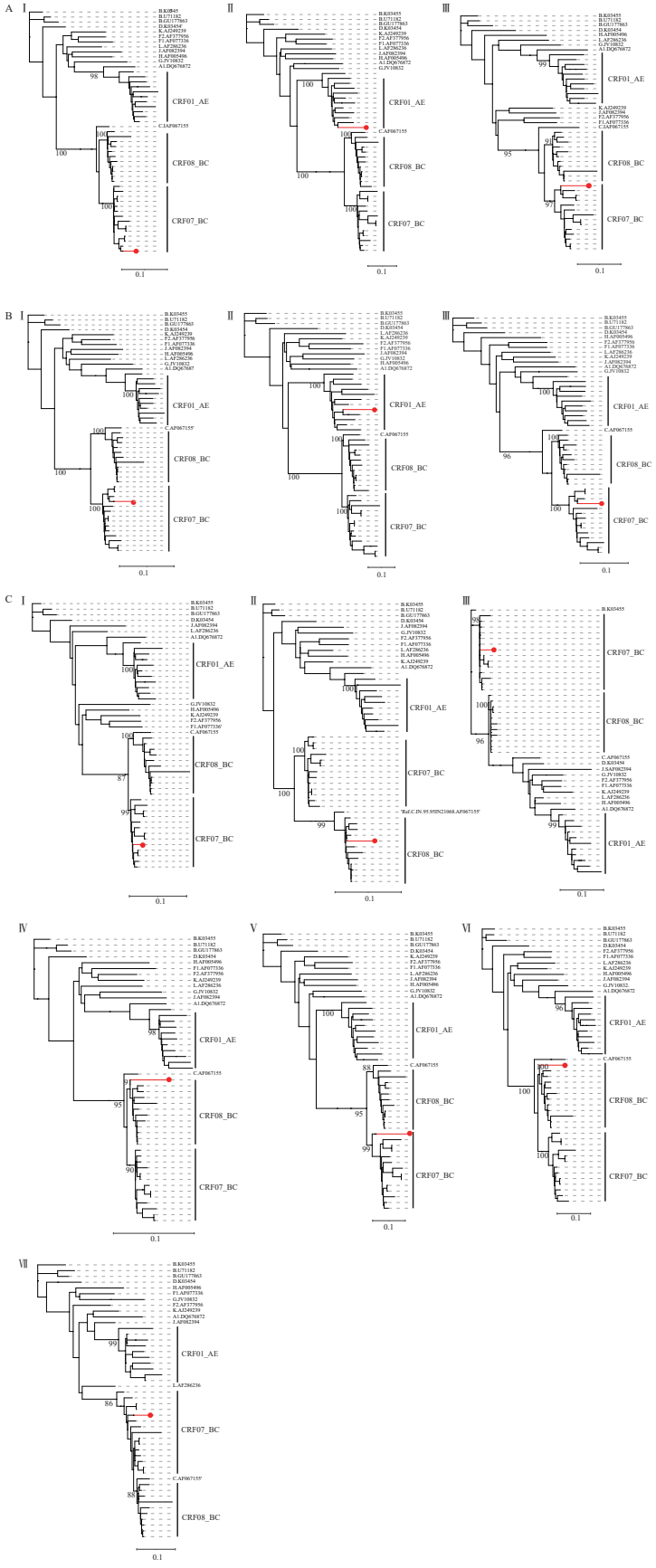
SUPPLEMENTARY MATERIALS

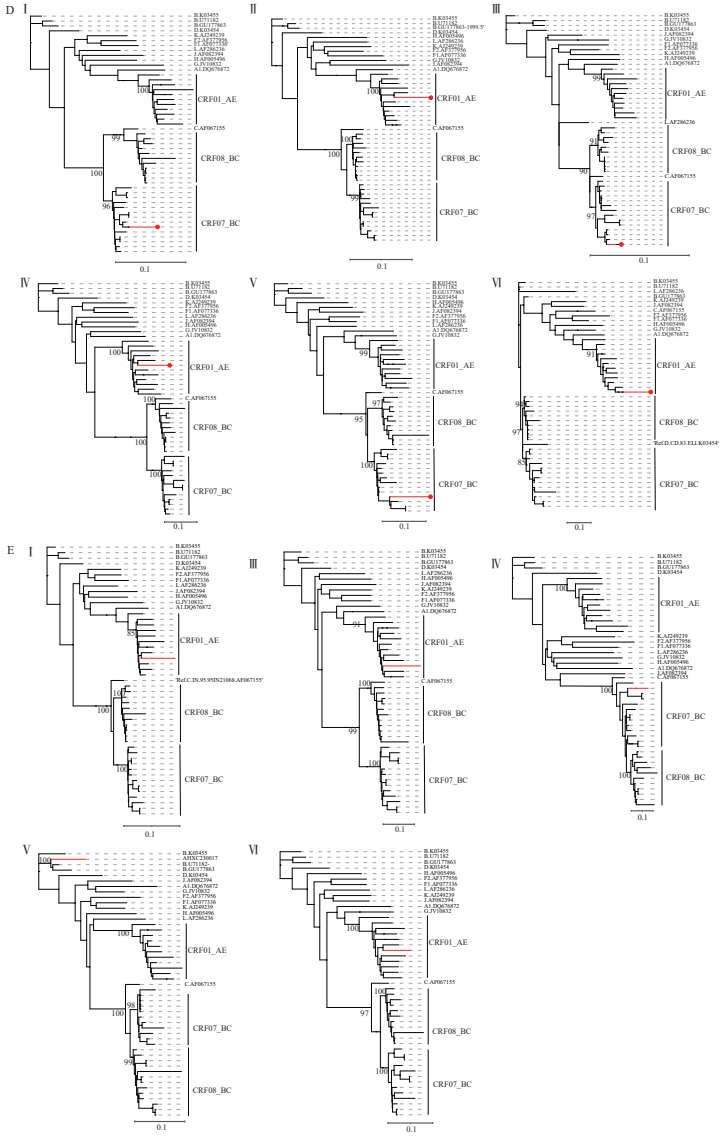
SUPPLEMENTARY TABLE S1. Demographic and clinical characteristics of newly reported cases.

Sample ID	Transmission	Age	Gender	Marriage	CD4+ (cells/mm^3)	Diagnose time	Sampling time
AHAQ230009	HET	31	Male	Unmarried	302	2023.5.8	2023.5.10
AHBZ230009	MSM	35	Male	Married	579	2023.4.20	2023.4.25
AHBZ230031	HET	29	Male	Unmarried	540	2023.5.25	2023.5.30
AHCUZ230011	HET	41	Male	Unmarried	227	2023.5.26	2023.6.13
AHXC230017	HET	56	Female	Married	228	2023.6.19	2023.6.27

SUPPLEMENTARY TABLE S2. Subtype classification of genomic subregions from five near full-length genomes.

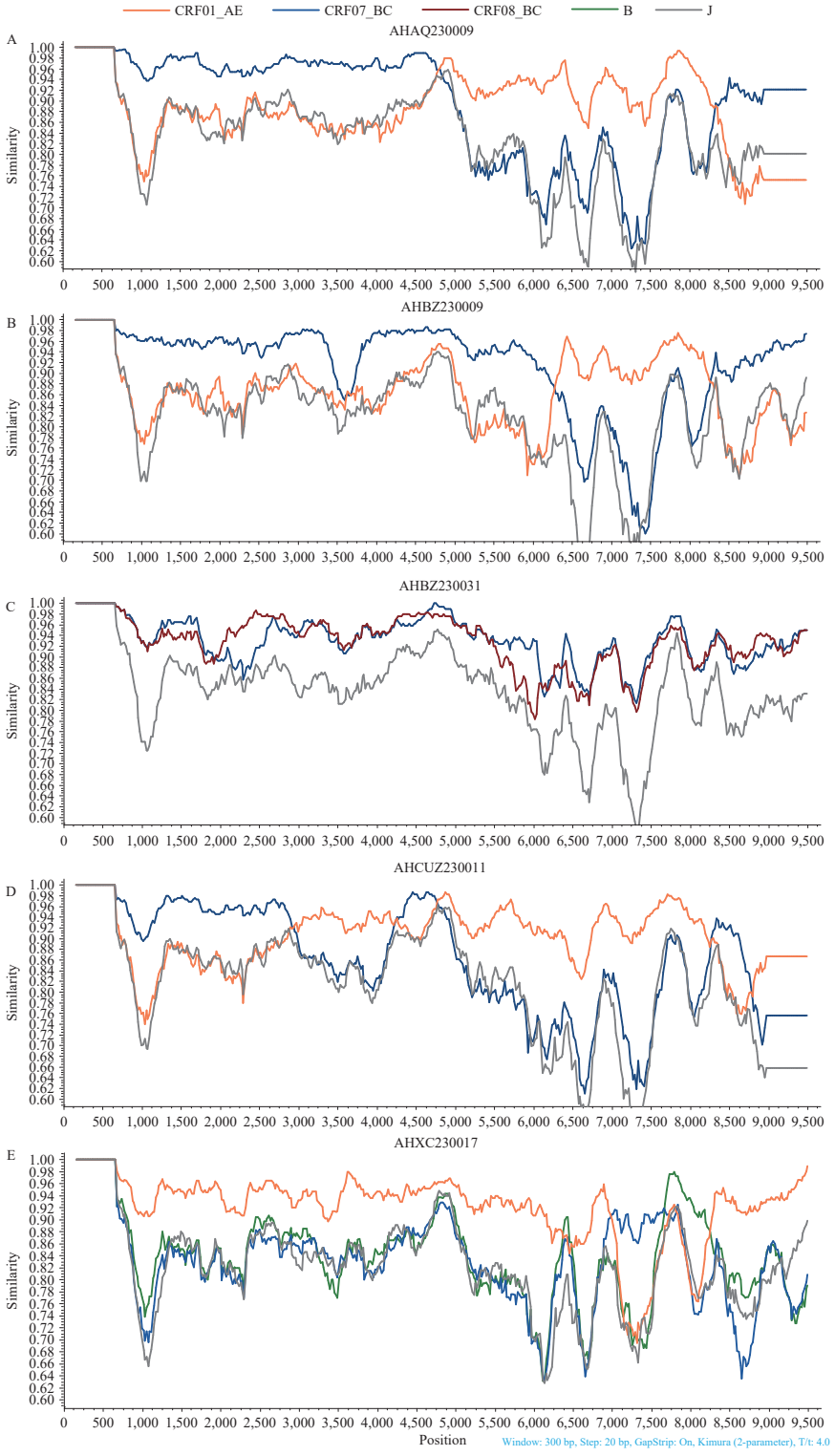
Fragments	AHAQ230009	AHBZ230009	AHBZ230031	AHCUZ230011	AHXC230017
Ⅰ	CRF07_BC (634-4884)	CRF07_BC (634-6323)	CRF07_BC (620-1933)	CRF07_BC (608-2959)	CRF01_AE (621-4832)
Ⅱ	CRF01_AE (4885-8404)	CRF01_AE (6324-8327)	CRF08_BC (1934-3001)	CRF01_AE (2960-4244)	B (4833-4899)
Ⅲ	CRF07_BC (8405-8960)	CRF07_BC (8328-9552)	CRF07_BC (3002-3215)	CRF07_BC (4245-4885)	CRF01_AE (4900-6937)
Ⅳ			CRF08_BC (3216-4628)	CRF01_AE (4886-8327)	CRF07_BC (6938-7679)
Ⅴ			CRF07_BC (4629-8518)	CRF07_BC (8328-8811)	B (7680-8240)
Ⅵ			CRF08_BC (8519-9098)	CRF01_AE (8812-9354)	CRF01_AE (8241-9552)
Ⅶ			CRF07_BC (9099-9470)		


A
I
II
III
CRF01_AE
CRF08_BC
CRF07_BC
B
C
IV
V
VI
VII
0.1



SUPPLEMENTARY FIGURE S1. Phylogenetic subregion analysis of (A) AHAQ230009; (B) AHBZ230009; (C) AHBZ230031; (D) AHCUZ230011; and (E) AHXC230017.

Note: Subregion phylogenetic trees were constructed using IQ-TREE 2 software implementing the neighbor-joining method with 1,000 bootstrap replications. Scale bars represent 10% genetic distance. Figure E(II) is absent due to insufficient sequence length of the second fragment of AHXC230017 for phylogenetic reconstruction.



SUPPLEMENTARY FIGURE S2. Similarity analysis of five near full-length genomes. (A) AHAQ230009; (B) AHBZ230009; (C) AHBZ230031; (D) AHCUZ230011; and (E) AHXC230017.

Note: Analyses were performed using a 300-base window size and 20-base step size, aligned against HIV-1 subtype references. The CRF01_AE reference group included JX112859, EF036527, and AY358049; the CRF07_BC reference group included SC070050, HQ215552, and AF286230; the CRF08_BC reference group included KC914396 and AY008715; and the subtype B reference group included GU177863 and U71182. The subtype J reference was SE9280. The x-axis represents nucleotide positions, while the y-axis shows similarity values.

Notifiable Infectious Diseases Reports

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

Diseases	Cases	Deaths
Plague	0	0
Cholera	0	0
SARS-CoV	0	0
Acquired immune deficiency syndrome†	2,832	1,375
Hepatitis	165,723	72
Hepatitis A	2,293	1
Hepatitis B	145,071	46
Hepatitis C	14,831	25
Hepatitis D	25	0
Hepatitis E	2,754	0
Other hepatitis	749	0
Poliomyelitis	0	0
Human infection with H5N1 virus	0	0
Measles	344	0
Epidemic hemorrhagic fever	301	1
Rabies	16	19
Japanese encephalitis	1	0
Dengue	49	0
Anthrax	21	0
Dysentery	1,659	0
Tuberculosis	49,311	209
Typhoid fever and paratyphoid fever	234	1
Meningococcal meningitis	26	2
Pertussis	5,611	1
Diphtheria	0	0
Neonatal tetanus	0	0
Scarlet fever	6,353	0
Brucellosis	3,365	1
Gonorrhea	8,037	0
Syphilis	48,495	6
Leptospirosis	6	0
Schistosomiasis	0	0
Malaria	295	0
Human infection with H7N9 virus	0	0
COVID-19	33,218	4
Monkey pox§	40	0
Influenza	2,870,849	9

Continued

Diseases	Cases	Deaths
Mumps	4,116	0
Rubella	53	0
Acute hemorrhagic conjunctivitis	1,340	0
Leprosy	33	0
Typhus	54	0
Kala azar	15	0
Echinococcosis	495	1
Filariasis	0	0
Infectious diarrhea[¶]	162,257	0
Hand, foot and mouth disease	16,962	0
Total	3,382,111	1,701

* According to the National Bureau of Disease Control and Prevention.
† 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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