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Vital Surveillances

Analysis of Service Utilization and Medication Adherence Among Attendees of HIV Nonoccupational Post-Exposure Prophylaxis Clinics — China, 2022–2024

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ABSTRACT

Introduction: Human Immunodeficiency Virus (HIV) nonoccupational post-exposure prophylaxis (nPEP) clinics are specialized healthcare facilities that provide urgent medical interventions to individuals with potential high-risk HIV exposures. This study analyzed utilization patterns of HIV nPEP services in China and examined factors associated with medication adherence among consultees, providing evidence to inform further implementation and optimization of HIV nPEP interventions.

Methods: We analyzed nPEP case data collected from the national nPEP data information system between November 1, 2022, and November 1, 2024, using SPSS 29.0 software. Chi-square tests were applied to analyze characteristics of nPEP consultees, and logistic regression models were used to identify factors influencing medication adherence and follow-up compliance among those who initiated treatment.

Results: As of November 1, 2024, 924 nPEP clinics nationwide received 54,108 consultees, with 53,405 (98.70%) initiating medication. Most individuals seeking services were male (88.63%), classified as high-risk (83.11%), and heterosexual with multiple partners (67.66%). The "BIC/FTC/TAF" regimen was selected by 63.07% of recipients. Nearly all users (99.03%) completed medication evaluation within 72 hours post-exposure. Among medication users, 60.34% (30,650) adhered to the full 28-day regimen, and 60.10% (30,509) completed either one-month or three-month follow-ups. Multivariate logistic regression analysis identified gender, exposure risk assessment results, exposure population classification, individual preferences, and medication regimen as significant factors influencing both 28-day medication adherence and follow-up compliance (P<0.05).

Conclusions: nPEP clinic consultees in China are predominantly young male heterosexual individuals with multiple sexual partners, with most selecting the Biktarvy regimen. However, both current 28-day medication adherence and follow-up compliance rates remain suboptimal. High-risk men and those receiving the Biktarvy regimen demonstrate superior medication adherence and follow-up compliance compared to other groups. Further research is needed to develop targeted interventions to improve medication adherence and follow-up rates among nPEP recipients. Enhancing adherence and follow-up should be prioritized in future interventions, supported by continuous monitoring to inform timely intervention strategy adjustments.

Non-occupational Post-Exposure Prophylaxis (nPEP) involves a 28-day course of antiretroviral drugs administered to Human Immunodeficiency Virus (HIV)-negative individuals following potential HIV exposure to prevent infection (*1*–*2*). PEP was first implemented in 1988 for occupational exposures before expanding to non-occupational contexts, including sexual contact and injection drug use (*3*). In 2007, the World Health Organization (WHO) recommended antiretroviral drugs for nPEP, initiating global implementation efforts (*4*).

China adopted nPEP later than many countries, but experienced rapid development in implementation. During 2018–2019, the National Center for Acquired Immunodeficiency Syndrome (AIDS)/Sexually Transmitted Diseases (STD) Control and Prevention (NCAIDS) conducted nPEP pilot studies among men who have sex with men across seven provincial-level administrative regions (PLADs) (*5*). In 2020, NCAIDS issued the "Technical Guidelines for Post-Exposure Prophylaxis of HIV (Trial)" (*6*). Subsequently, hospitals across the country established prevention clinics for HIV non-professional exposure. These outpatient services are primarily located in designated hospitals for treating HIV-infected

individuals and receiving HIV-negative individuals who have engaged in risky behaviors and experienced exposure within 72 hours, providing them with antiviral drugs to prevent possible infection. On November 1, 2022, an nPEP data information system was launched to collect nationwide outpatient data (*7*). This study evaluates utilization patterns among HIV nPEP clinic attendees in China, analyzes factors influencing medication adherence and follow-up compliance, and provides evidence to optimize HIV nPEP implementation strategies.

Methods

Introduction to the Outpatient Work Process of nPEP

As of November 1, 2024, China had established 924 clinics providing nPEP services across all 31 PLADs and the Xinjiang Production and Construction Corp (XPCC). These clinics operate within designated and non-designated antiretroviral treatment (ART) facilities, primary healthcare institutions such as community health centers, and private medical facilities. Each clinic is staffed by personnel from their respective host institutions. Upon presentation, attendees undergo a standardized eligibility assessment, including exposure history evaluation, time-since-exposure documentation, risk stratification, and relevant laboratory testing. Eligible individuals who provide informed consent receive a 28-day, three-drug antiretroviral regimen, typically consisting of (TDF or TAF)+(FTC or 3TC)+(DTG or RAL), with fixed-dose combinations preferred when available. Treatment must be initiated within 72 hours of exposure, and regimen selection is individualized based on the patient's clinical profile and local drug availability. Priority is given to formulations with fewer adverse effects or combination preparations to enhance medication adherence by reducing pill burden and minimizing side effects. Individuals at risk of HIV exposure can locate nPEP clinic addresses and contact information through the official website of the NCAIDS, WeChat official accounts of disease control agencies, or through referrals from local non-governmental organizations. They must seek consultation and assessment within 72 hours post-exposure. Clinics charge standard medical fees, including costs for HIV testing and hepatic and renal function assessments during medical evaluation. Patients pay for blocking medications according to hospital drug pricing.

Data Source

We analyzed surveillance data from the national HIV nPEP Information System, which captured comprehensive case information nationwide from November 2022 to November 2024. The dataset encompasses sociodemographic characteristics, exposure timing, risk assessment outcomes, exposed population classifications, HIV testing results, patient preferences, 28-day medication regimen completion data, and follow-up information at one and three months post-medication among nPEP clinic attendees.

We defined the standardized 28-day medication regimen — our primary measure for assessing medication adherence — as the initiation of PEP following medical evaluation, with consistent and timely drug intake at the prescribed dosage throughout a continuous 28-day period. The 28-day medication adherence rate was calculated as the number of individuals who completed the standardized 28-day regimen divided by the number of individuals who had taken medication for 31 days or more, multiplied by 100%. Follow-up adherence represents patient compliance with scheduled post-treatment medical visits at healthcare institutions, as directed by their healthcare providers.

Statistical Analysis and Data Availability

We conducted all analyses using SPSS 29.0 software [originally developed by SPSS Inc. (Chicago, United States) and is now owned and distributed by IBM Corporation (Armonk, United States)] Skewed measurement data were expressed as medians with interquartile ranges M (Q1, Q3), while categorical data were presented as case numbers and constituent ratios. We assessed group differences using χ^2 tests (α =0.05, two-sided) and employed logistic regression models to identify factors influencing medication adherence and follow-up compliance.

RESULTS

Characteristics of Attendees of HIV nPEP Clinics

As of November 1, 2024, a total of 54,108 evaluation records were reported by 924 PEP clinics across 31 PLADs and XPCC in China. The median

age of seekers was 31 (26, 37) years, with a median time from exposure to evaluation of 17 (10.2, 34.7) hours; 99.03% sought care within 72 hours. Most help seekers were male (88.63%), classified as high-risk (83.11%), and heterosexual with multiple partners (67.66%) (Table 1).

Among these individuals, 53,405 (98.70%) initiated PEP treatment. The Biktarvy regimen was selected by

TABLE 1. Characteristics of nPEP clinic attendees in China: initiators *vs.* non-initiators, 2022–2024.

Factors	Total (*N*=54,108)	Initiated medication (*N*=53,405)	Did not initiate medication (*N*=703)
Gender, *N* (%)			
Men	47,956 (88.63)	47,340 (98.72)	616 (1.28)
Female	6,152 (11.37)	6,065 (98.59)	87 (1.41)
Age (years), *N* (%)			
<18	438 (0.81)	431 (98.40)	7 (1.60)
18–23	7,310 (13.51)	7,216 (98.71)	94 (1.29)
24–49	43,831 (81.02)	43,266 (98.71)	565 (1.29)
≥50	2,529 (4.67)	2,492 (98.54)	37 (1.46)
Time from exposure to evaluation (hours), *N* (%)			
<12	15,885 (29.36)	15,603 (98.22)	282 (1.78)
12–23	18,506 (34.20)	18,340 (99.10)	166 (0.90)
24–71	19,192 (35.47)	19,002 (99.01)	190 (0.99)
≥72	525 (0.97)	460 (87.62)	65 (12.38)
Exposure risk assessment result, *N* (%)			
Low risk	9,139 (16.89)	8,639 (94.53)	500 (5.47)
High risk	44,969 (83.11)	44,766 (99.55)	203 (0.45)
Exposure population classification, *N* (%)			
MSM	10,837 (20.03)	10,562 (97.46)	275 (2.54)
Other people*	6,627 (12.25)	6,548 (98.81)	79 (1.19)
Heterosexual	36,611 (67.66)	36,264 (99.05)	347 (0.95)
Injection drug users	33 (0.06)	31 (93.94)	2 (6.06)
Results of Human Immunodeficiency Virus (HIV) testing[†] , *N* (%)			
Negative	54,042 (99.88)	53,405 (98.82)	637 (1.18)
Positive	66 (0.12)	0 (0)	66 (100.00)
Seeker's opinion, *N* (%)			
Refuse to take medicine	153 (0.28)	17 (11.11)	136 (88.89)
Request to take medicine	39,075 (72.22)	38,989 (99.78)	86 (0.22)
Follow the doctor's advice	14,880 (27.50)	14,399 (96.77)	481 (3.23)
Medication regimen[§] (*N*=53,405), *N* (%)			
TDF+FTC+DTG	–	9,515 (17.82)	–
TDF+FTC+RAL	–	1,082 (2.03)	–
BIC+FTC+TAF	–	33,685 (63.07)	–
Other	–	9,123 (17.08)	–

Note: "–" means this value is missing.

Abbreviation: MSM=men who have sex with men; TDF= tenofovir disoproxil; FTC=emtricitabine; DTG=dolutegravir; RAL=raltegravir; BIC=bictegravir; TAF=tenofovir Alafenamide Fumarate; nPEP=non-occupational post-exposure prophylaxis.

* Other people: those other than MSM, heterosexual with multiple partners, and injection drug users.

[†] The results of Human Immunodeficiency Virus (HIV) antibody testing obtained during the laboratory examination component of the nPEP clinic eligibility assessment process.

[§] Medication regimen: This variable categorizes the three primary antiretroviral therapy regimens currently in use, represented as "TDF+FTC+DTG/TDF+FTC+RAL/BIC+FTC+TAF".

63.07% of patients, with 8,233 (15.42%) low-risk individuals still requesting medication. Among all medication users, 60.34% (30,650) adhered to the standardized 28-day regimen, 57.22% (29,064) completed one-month follow-up, and 44.34% (22,521) completed three-month follow-up. Of the 703 individuals who did not initiate treatment, 66 tested HIV-positive before medication, while 136 refused treatment (101 assessed as high-risk) (Table 1 and Figure 1).

During follow-up, three users seroconverted to HIV-positive status. Upon verification, one individual engaged in high-risk behavior during treatment, while another sought care more than 72 hours post-exposure, indicating pre-medication infection. Only one case could not rule out PEP failure, yielding a failure rate of 0.0019% (1/53,405).

Analysis of Medication Adherence and Follow-up Compliance

Among medication users, 60.10% (30,509) completed either 1-month or 3-month follow-up visits, while 41.49% (21,076) completed both follow-up assessments. Multivariate logistic regression analysis revealed that high-risk men classified as "other" and those receiving the Biktarvy regimen demonstrated significantly better medication adherence and follow-up compliance compared to other groups (P<0.05) (Table 2).

DISCUSSION

This study presents the first comprehensive nationwide evaluation of HIV nPEP clinic utilization patterns and identifies key factors affecting medication adherence and follow-up compliance. Despite achieving a high treatment initiation rate of 98.70%, only 60.34% of patients completed the full 28-day regimen, and merely 60.10% attended either one-month or three-month follow-up appointments. This substantial gap between initiation and completion represents a critical weakness in effective HIV prevention implementation. These deficiencies may compromise prophylactic efficacy and prevent the timely detection of seroconversion, potentially undermining the overall public health impact. Future interventions must prioritize adherence enhancement and follow-up optimization, supported by robust monitoring systems that enable rapid program adjustments.

The nPEP clinics operate primarily within public general hospitals and designated HIV treatment facilities throughout China. With a median consultation time of 17 hours post-exposure and over half of patients seeking care within 24 hours, the system demonstrates good accessibility and timeliness. This performance reflects the extensive geographic coverage provided by 924 nationwide clinics. Many provincial facilities have expanded beyond traditional operating hours, offering both daytime and nighttime

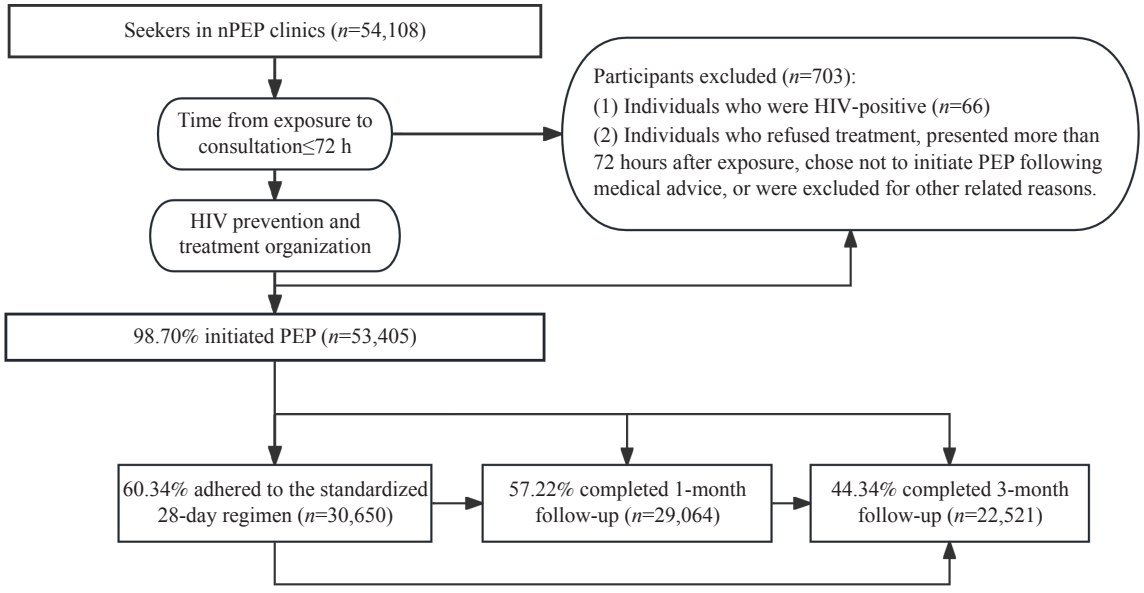

FIGURE 1. Flow chart of PEP initiation and follow-up process for nPEP clinic patients in China, 2022–2024.
Abbreviation: PEP=post-exposure prophylaxis; nPEP=non-occupational post-exposure prophylaxis.

TABLE 2. Analysis of factors influencing the standard completion of 28-day medication regimen and completion of 1-month or 3-month follow-up among attendees of nPEP clinics — China 2022–2024.

Characteristics	Adhered to the full 28-day regimen (*N*=30,650)	Adjusted *OR** (95% *CI*)	*P*	Completed 1-month/3-month follow-ups (*N*=30,509)	Adjusted *OR* (95% *CI*)	*P*
Age (years), *N* (%)						
<18	247 (0.81)	Ref		247 (0.81)	Ref	
18–23	4,102 (13.38)	1.04 (0.84, 1.27)	0.748	4,084 (13.39)	1.04 (0.85, 1.29)	0.688
24–49	24,812 (80.95)	1.02 (0.83, 1.25)	0.872	24,705 (80.97)	1.03 (0.84, 1.27)	0.757
≥50	1,489 (4.86)	1.11 (0.90, 1.39)	0.332	1,473 (4.83)	1.11 (0.90, 1.39)	0.332
Gender, *N* (%)						
Male	27,274 (88.99)	Ref		27,163 (89.03)	Ref	
Female	3,376 (11.01)	0.89 (0.84, 0.95)	<0.001	3,346 (10.97)	0.88 (0.83, 0.94)	<0.001
Exposure risk assessment result, *N* (%)						
Low risk	4,503 (14.69)	Ref		4,447 (14.58)	Ref	
High risk	26,147 (85.31)	1.45 (1.38, 1.52)	<0.001	26,062 (85.42)	1.48 (1.41, 1.56)	<0.001
Exposure population classification, *N* (%)						
MSM	6,333 (20.66)	Ref		6,326 (20.73)	Ref	
Other people†	3,974 (12.97)	1.18 (1.10, 1.27)	<0.001	3,936 (12.90)	1.15 (1.07, 1.23)	<0.001
Heterosexual	20,322 (66.30)	0.88 (0.84, 0.92)	<0.001	20,227 (66.30)	0.87 (0.83, 0.91)	<0.001
Injection drug users	21 (0.07)	1.21 (0.57, 2.59)	0.610	20 (0.07)	1.02 (0.49, 2.14)	0.954
Seeker's opinion, *N* (%)						
Refuse to take medicine	3 (0.01)	Ref		5 (0.02)	Ref	
Request to take medicine	22,652 (73.91)	7.83 (2.24, 27.28)	0.001	22,598 (74.07)	4.07 (1.43, 11.58)	0.009
Follow the doctor's advice	7,995 (26.08)	6.70 (1.92, 23.36)	0.003	7,906 (25.91)	3.32 (1.16, 9.46)	0.025
Medication regimen§, *N* (%)						
TDF+FTC+DTG	5,327 (17.38)	Ref		5,022 (16.46)	Ref	
TDF+FTC+RAL	539 (1.76)	0.81 (0.72, 0.93)	0.002	416 (1.36)	0.57 (0.50, 0.65)	<0.001
BIC+FTC+ TAF	18,955 (61.84)	1.18 (1.12, 1.23)	<0.001	18,919 (62.02)	1.35 (1.29, 1.42)	<0.001
Other	5,829 (19.02)	1.31 (1.24, 1.39)	<0.001	6,152 (20.16)	1.76 (1.66, 1.87)	<0.001

Abbreviation: *CI*=confidence interval; *OR*=odds ratio; MSM=men who have sex with men; TDF=tenofovir disoproxil; FTC=emtricitabine; DTG=dolutegravir; RAL=raltegravir; BIC=bictegravir; TAF=tenofovir alafenamide fumarate; nPEP=nonoccupational post-exposure prophylaxis.

* Adjusted *OR*: multivariate logistic regression model *OR*, adjusting for all other variables in the table.

§ Other people: those other than MSM, heterosexual with multiple partners, and injection drug users.

† Medication regimen: This variable categorizes the three primary antiretroviral therapy regimens currently in use, represented as "TDF+FTC+DTG/TDF+FTC+RAL/BIC+FTC+TAF".

services to enable prompt consultation, risk assessment, and prescription following high-risk exposures. However, since optimal nPEP administration should occur within 2 hours post-exposure and must not exceed 24 hours, the 17-hour average delay provides only a 7-hour window within the optimal timeframe. This timing constraint challenges service efficiency and underscores the need for enhanced rapid testing and evaluation capabilities. Expanding geographic coverage and clinic numbers could reduce travel distances for patients, shorten exposure-to-assessment intervals, and enable earlier medication initiation. Facilities lacking 24-hour service capacity should implement shift systems or emergency referral protocols. Medical evaluations should utilize rapid HIV testing kits for immediate assessment while collecting blood samples for confirmatory enzyme-linked immunosorbent assay testing. Liver and kidney function tests should receive urgent laboratory processing. When assessments occur at disease control institutions or social organizations, these facilities should maintain 1–2 days of emergency medication supplies before referring patients to clinics for additional drugs, ensuring medication access within the critical 72-hour window.

A small proportion of high-risk individuals (116/54,108, 0.28%) refused medication, indicating

the need for enhanced education about nPEP benefits among high-risk populations. Conversely, a substantial number of low-risk individuals (8,270/54,108, 15.25%) requested medication, likely reflecting risk overestimation and anxiety following potential exposure. Current PEP guidelines suggest nPEP may be inappropriate for low-risk exposures, and indiscriminate use could potentially increase antiviral resistance risk. Future interventions should address patients' psychological concerns while standardizing assessment procedures to enhance precision in PEP utilization and ensure rational medication use.

System data demonstrate that while the national medication initiation rate among nPEP clinic attendees reached 98.70%, medication adherence remains suboptimal — only 60.34% completed the full 28-day regimen. This finding aligns with international studies reporting 65.6% completion [adjusted odds ratio (a*OR*)=65.6%, 95% confidence interval (*CI*): 55.6%, 75.6%] (*8*). However, two Chinese studies reported significantly higher completion rates of 97% and 93.6% (*9*–*10*). This discrepancy may stem from their focus on men who have sex with men (MSM) populations, who demonstrate higher nPEP acceptance rates, benefit from effective pre-nPEP education by social organizations, receive "one-on-one" peer support, and access follow-up services through dedicated PEP platforms. These findings suggest that hospital-based nPEP services require enhanced public education, staff training, and comprehensive support services to improve adherence rates. Follow-up compliance also remains inadequate, with only 60.1% completing either 1-month or 3-month follow-ups — lower than rates reported in domestic MSM studies (*10*). The superior follow-up rates in previous research were largely attributable to peer educator support. Future studies should examine underlying reasons for medication discontinuation and follow-up interruption across diverse populations to develop targeted interventions. However, conducting PEP public education and outreach services through clinical settings may lack precision in content delivery, making it challenging to effectively reach key populations at risk for HIV infection. Innovative community-based approaches may achieve superior results through targeted outreach and adherence interventions. A cohort study examining Pre-Exposure Prophylaxis (PrEP) adherence and persistence among MSM in China found that peer-referred MSM demonstrated higher PrEP adherence and longer treatment persistence (*11*). This suggests that future community-based pilot programs could explore peer referral systems to link individuals to PEP services, potentially improving PEP adherence rates. Additional studies utilizing crowdsourcing to promote PrEP adherence or leveraging gamified smartphone interventions (O2O-PEP) to facilitate HIV PEP uptake in MSM populations provide valuable models for enhancing PEP utilization (*12*–*13*).

Multivariate analysis demonstrates that male participants, high-risk individuals, and those classified as "other people" exhibit significantly higher rates of completing the 28-day medication regimen and demonstrate superior follow-up compliance. Patients prescribed the "BIC+FTC+TAF, Biktarvy" regimen show enhanced adherence rates, likely attributable to its favorable safety profile and reduced pill burden (*14*). These predictive factors enable early identification of patients at risk for poor adherence, facilitating the development of targeted intervention strategies (*15*).

Several limitations warrant consideration in interpreting these findings. Information bias may arise from self-reported adherence data, while our analysis excludes high-risk individuals who do not seek consultation services. Additionally, our reliance on outpatient medical records prevents comprehensive analysis of socioeconomic, behavioral, and psychological determinants of adherence. Furthermore, many nPEP seekers obtain medications through online platforms and were not captured in this study, indicating that our results represent only a subset of the broader nPEP user population.

In conclusion, this study reveals that nPEP clinic attendees at public hospitals in China are predominantly young heterosexual males with multiple sexual partners. These individuals typically complete PEP medication assessment within 24 hours following exposure. However, both 28-day medication adherence rates and follow-up compliance remain suboptimal. Critical factors influencing adherence include gender, exposure assessment outcomes, risk classification, patient preferences, and prescribed medication regimen. Identifying these predictive factors enables healthcare providers to characterize individuals with poor adherence patterns and develop targeted interventions to enhance compliance. Further comprehensive investigations are essential to address these challenges and explore evidence-based strategies for improving follow-up rates and medication adherence. Such improvements will optimize nPEP intervention strategies, ensuring that high-risk

individuals can effectively prevent HIV infection and reduce HIV transmission within the community.

Conflicts of interest: No conflicts of interest.

Ethical statement: Data from the national nPEP information system were exempt from ethical review requirements.

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Methods and Applications

Auxiliary Diagnostic Value of the Interferon Gamma-Induced Protein 10 mRNA Release Assay for Tuberculosis in People Living with HIV/AIDS — Beijing Municipality, China, 2022–2024

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ABSTRACT

Introduction: Diagnosing tuberculosis (TB) in HIV-infected individuals presents significant challenges due to difficulties in obtaining specimens containing adequate quantities of *Mycobacterium tuberculosis* (*Mtb*). This study aimed to evaluate the diagnostic performance of the *IP-10* mRNA assay independently and in combination with established diagnostic tests for *Mtb* detection.

Methods: The study cohort comprised 111 HIV-infected individuals who presented with TB at Beijing Youan Hospital from 2022 to 2024. Participants were categorized into confirmed TB, probable TB, or non-TB groups according to the diagnostic criteria for tuberculosis (WS288-2017). The performance of the *IP-10* mRNA release assay was evaluated by the STARD guidelines on blood samples collected after enrollment.

Results: The *IP-10* mRNA release assay demonstrated significantly higher sensitivity than interferon-γ release assays (IGRAs) and culture methods for confirming pulmonary tuberculosis (PTB) diagnosis while maintaining comparable specificity. Receiver operating characteristic (ROC) analysis revealed that the diagnostic performance of the *IP-10* mRNA release assay used in parallel with Xpert MTB/RIF significantly exceeded that of the *IP-10* mRNA release assay alone (0.731 *vs.* 0.687, P=0.02). Among HIV-infected individuals, the *IP-10* mRNA release assay showed superior performance compared to IGRAs for diagnosing extrapulmonary tuberculosis.

Conclusions: The *IP-10* mRNA release assay exhibited excellent diagnostic performance and demonstrates substantial potential as an auxiliary tool for diagnosing TB in HIV-infected individuals. The combined application of IP-10.TB and Xpert MTB/RIF further enhance diagnostic efficacy.

Mycobacterium tuberculosis (*Mtb*) infection represents one of the most prevalent opportunistic infections and a leading cause of mortality among people living with human immunodeficiency virus (HIV, PLWH) (*1*–*2*). The Global Tuberculosis Report 2024 (*3*) documented 10.8 million new tuberculosis (TB) cases in 2023, with 662,000 cases involving HIV/*Mtb* coinfection. Notably, HIV/*Mtb* coinfection accounts for 161,000 of the 1.25 million global TB deaths (12.9%). Due to the profound immunodeficiency induced by HIV, *Mtb* coinfection typically progresses rapidly and substantially increases the incidence of disseminated tuberculosis and associated mortality. Therefore, HIV/*Mtb* coinfection has emerged as a critical global public health concern.

Mtb infection significantly amplifies HIV replication, exacerbates chronic immune activation, and accelerates the disease progression. At the same time, HIV infection substantially increases the risk of both endogenous reactivation and exogenous reinfection of TB (*4*). These two diseases create a synergistic relationship that leads to rapid clinical deterioration. Therefore, prompt and accurate diagnosis followed by effective treatment remains critical for patients with HIV/*Mtb* coinfection. Primary laboratory diagnostic approaches include sputum smears, cultures, nucleic acid amplification tests (NAATs), and immunological assays. Traditional *Mtb* culture remains the gold standard for TB diagnosis. However, this method requires extended detection periods and demonstrates limited diagnostic sensitivity. Sputum smears offer cost-effective, simple, and rapid testing but are susceptible to high false-positive rates. In HIV-infected individuals, *Mtb* infection frequently presents with atypical clinical manifestations and reduced sputum bacillary loads (*5*).

Among severely immunocompromised patients, the incidence of disseminated or extrapulmonary tuberculosis (EPTB) — including central nervous system tuberculosis, lymph node tuberculosis, tuberculous pleurisy, and skeletal tuberculosis — increases significantly. The combination of low sputum *Mtb* loads and smear-negative results may substantially reduce the sensitivity of traditional pathogen detection methods and NAATs (*6*).

Multiple strategies have been developed to enhance early diagnosis rates in HIV-infected individuals (*7*). Among these, the supplementary application of immunological testing has become a primary research focus. The interferon-gamma (IFN-γ) release assays (IGRAs), such as Wantai TB-IGRA, represent laboratory diagnostic methods based on cellular immunity (*8*) that partially address the challenge of low bacillary loads in TB patients. IGRAs have been widely implemented for auxiliary TB diagnosis and the screening of *Mtb* infection in high-risk populations. However, these assays demonstrate suboptimal diagnostic sensitivity in HIV-infected individuals (*9*). The interferon gamma-induced protein 10 (*IP-10*) has recently emerged as a promising diagnostic biomarker. Following stimulation with TB-specific peptides, *IP-10* expression levels significantly exceed those of IFN-γ. Studies have demonstrated that *IP-10* transcription increases approximately 100-fold within 2.5–8 hours after TB antigen stimulation. The elevated expression levels and stability of *IP-10* mRNA contribute to enhanced diagnostic sensitivity (*10*). Previous research has shown that *IP-10* mRNA-based assays demonstrate comparable effectiveness to IGRAs for tuberculosis diagnosis (*11*). However, the application of *IP-10* mRNA-based assays in immunocompromised populations remains insufficiently explored. Therefore, this study aimed to evaluate the diagnostic performance of *IP-10* mRNA release assays in HIV/*Mtb*-coinfected individuals and explore potential alternative methods for auxiliary TB diagnosis in HIV-infected populations.

METHODS

This prospective cohort study was conducted at Beijing Youan Hospital, Capital Medical University, Beijing, China. Between August 2022 and December 2024, we consecutively enrolled 111 HIV-infected individuals with suspected tuberculosis (Figure 1). Fasting venous blood samples were collected from all participants for *IP-10* mRNA release assays and IGRAs. Inclusion criteria comprised of 1) a confirmed positive HIV-1 test results; 2) clinical suspicion of TB; and 3) the absence of prior anti-TB treatment history. Exclusion criteria included 1) the age under 18 years, 2) incomplete medical documentation, and 3) unavailable acid-fast staining smears or culture results that precluded definitive diagnosis.

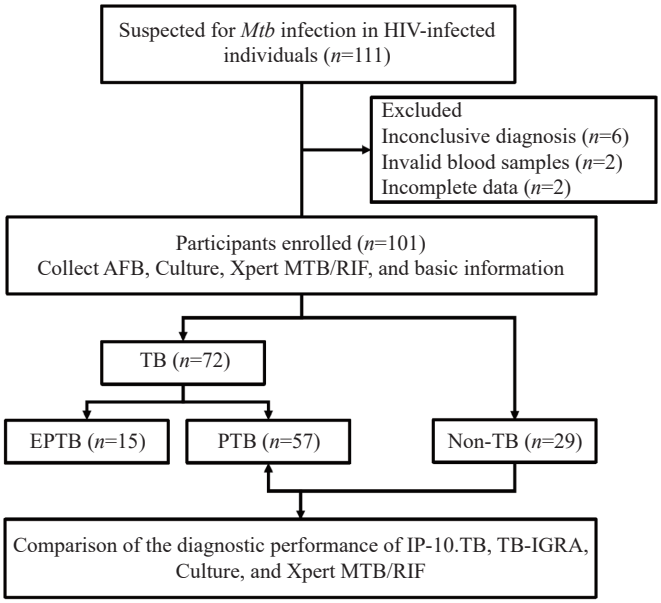

FIGURE 1. Flowchart of inclusion and grouping for the study participants.
Abbreviation: *Mtb=Mycobacterium tuberculosis*; AFB=acid-fast bacilli; TB=tuberculosis; PTB=pulmonary tuberculosis; EPTB=extrapulmonary tuberculosis.

The Research Ethics Committee of Beijing Youan Hospital approved this study and related experiments (No. 2022-115). We obtained written informed consent in accordance with the Declaration of Helsinki and conducted the study with strict adherence to approved guidelines and regulations. Study reporting followed the Standards for Reporting Diagnostic Accuracy Studies (STARD) guidelines.

Final diagnoses were determined through a comprehensive evaluation of clinical presentation, pathogenicity tests, imaging studies, and pathological findings. Participants were categorized into three groups following the Chinese guidelines for the diagnosis and treatment of human immunodeficiency virus infection/acquired immunodeficiency syndrome (*1*) and the diagnostic criteria for tuberculosis (WS288-2017) (*12*). The groups were 1) HIV with definite TB, which included positive *Mtb* culture results, nucleic acid detection in sputum or bronchoalveolar lavage fluid (BALF), or histopathological evidence; 2) HIV with probable TB, which were typical chest imaging manifestations of tuberculosis with characteristic clinical symptoms, positive tuberculin skin test, positive IGRAs results, or positive histopathology for EPTB but negative results for AFB smears, cultures, and nucleic acid tests in sputum or BALF; and 3) HIV with non-TB, which included individuals with no history of TB or TB contact who were ultimately not diagnosed with active TB. Participants with *Mtb* infections at any anatomical site other than the lungs (e.g., pleura, meninges, or bones) were classified as EPTB.

We collected demographic information and laboratory results from all participants. Approximately 4–5 mL of fasting venous blood was obtained from each participant for the simultaneous *IP-10* mRNA release assays and TB-IGRA testing. Using the final clinical diagnosis as the reference standard, we calculated and statistically analyzed the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and agreement for both detection methods. All participant samples underwent sputum smear microscopy, sputum culture, and nucleic acid testing to evaluate the diagnostic performance of these assays.

The *IP-10* mRNA release assay was conducted following the manufacturer's protocol for the IP-10.TB kit (CLR001A48, Suzhou Chuanglan Biotechnology Co., Ltd., China). Heparin-anticoagulated blood samples were distributed equally among three tubes: the negative control tube (N tube), the *Mtb* antigen tube (T tube), and the positive antigen tube (P tube). After gentle inversion to ensure thorough mixing, samples were incubated at 37 °C for 6 hours. Following incubation, RNA extraction from whole blood samples was performed, followed by reverse transcription to generate cDNA. Real-time quantitative PCR (qPCR) was conducted using an ABI 7500 qPCR system (Applied Biosystems™ 7500, Thermo Fisher, America). Target *IP-10* gene expression levels in the N, T, and P tubes were calculated using the ΔCt method, where ΔCt=Ct (target gene) – Ct (reference gene). Results were interpreted according to the following criteria: a positive result when the relative expression of *IP-10* in the T tube minus the relative expression of *IP-10* in the N tube was ≤–1.04; a negative result when the relative expression of *IP-10* in the T tube minus the relative expression of *IP-10* in the N tube was >–1.04, and the relative expression of *IP-10* in the P tube minus the relative expression of *IP-10* in the N tube was ≤–1.2; and an indeterminate results when the relative expression of *IP-10* in the T tube minus the relative expression of *IP-10* in the N tube was >–1.04 and the relative expression of *IP-10* in the P tube minus the relative expression of *IP-10* in the N tube was >–1.2.

IGRAs were performed using the Wantai TB-IGRA kit (TB-IGRA, Beijing Wantai Biological Pharmacy Enterprise) according to the manufacturer's specifications. Effector T cells underwent *in vitro* stimulation with *Mycobacterium tuberculosis*-specific antigens to induce IFN-γ secretion. Samples were then incubated at 37 °C for 22.0±2.0 hours. Following incubation, plasma samples were analyzed using ELISA to quantify secreted IFN-γ concentrations. Results were classified as positive when the difference between the test tube (T) and negative control tube (N) values (T - N) was ≥14 pg/mL and ≥N/4.

Data were collected and organized using Microsoft Excel. All statistical analyses were performed using Jamovi software (version 2.6.17), R version 4.4.0 (R Core Team R (2024), Vienna, Austria) and MedCalc Statistical Software version 23.0.8 (MedCalc Software, Ostend, Belgium). Measurement data with skewed distributions are expressed as median (interquartile range, IQR) [M (P25, P75)] and were compared using the Mann−Whitney U test. The categorical data are presented as frequencies and percentages (%) and were compared using Pearson's chi-square test. McNemar's test was employed for paired data comparisons. The sensitivity, specificity, positive predictive value (PPV),

and negative predictive value (NPV) were calculated for each diagnostic parameter. To evaluate diagnostic performance, receiver operating characteristic (ROC) curves were generated for each test. Differences in area under the curve (AUC) values between tests were assessed using the DeLong test, with statistical significance set at $P<0.05$. Agreement between methods was evaluated using the Kappa test, where Kappa≤0.4 indicated poor agreement, 0.4<Kappa<0.75 indicated moderate agreement, and Kappa≥0.75 indicated strong agreement.

RESULTS

The study enrolled 111 HIV-infected individuals with suspected TB (Figure 1). After excluding cases with incomplete diagnoses and invalid samples, 101 participants were included in the final analysis. Based on the definitive diagnosis criteria, 72 individuals were diagnosed with TB, while 29 individuals were classified as non-TB patients. The TB group comprised 57 patients with pulmonary tuberculosis (PTB) and 15 with EPTB. Among the pulmonary tuberculosis cases, 22 presented with hematogenous disseminated tuberculosis. In the non-TB group, the final diagnoses included 19 cases of nontuberculous mycobacterial infection, eight cases of bacterial pneumonia, one case of pulmonary aspergillosis, and one case of mycoplasmal pneumonia. The $CD4^+$ T-cell count was significantly elevated in the TB group compared to the non-TB group ($P=0.004$). No significant differences were observed in age, sex, or viral load between the TB and non-TB groups. Detailed demographic and clinical characteristics are presented in Table 1.

We analyzed the diagnostic performance of the *IP-10* mRNA release assay and TB-IGRA in 57 PTB patients and 29 non-TB patients. Based on clinical diagnostic criteria, the *IP-10* mRNA release assay demonstrated a diagnostic sensitivity of 68.4% [95% confidence interval (*CI*): 55.5%–79.0%] and a specificity of 69.0% (95% *CI*: 50.8%–82.7%). Contrastingly, TB-IGRA showed a diagnostic sensitivity of 36.8% (95% *CI*: 25.5%–49.8%) and a specificity of 89.7% (95% *CI*: 73.6%–96.4%). The difference in the diagnostic sensitivity between these two methods was statistically significant ($P<0.01$),

TABLE 1. Demographic and clinical characteristics of the study population [*N* (%)].

Characteristics	TB (*n*=72)	Non-TB (*n*=29)	*P*
Gender			
Male	68 (94.4)	27 (93.1)	>0.999
Female	4 (5.6)	2 (6.9)	
Age [median (P25, P75)]	36.5 (30.0, 47.0)	34 (30.0, 42.5)	0.589
$CD4^+$ T-cell count (cells/μL)	85 (29.25, 168.75)	31 (5.5, 103.5)	0.004
Viral load (copies/mL)			
>1,000	38 (52.8)	19 (65.5)	0.096
≤1,000	34 (47.2)	10 (34.5)	
Pulmonary tuberculosis	57 (79.2)	-	
Hematogenous disseminated PTB	22 (38.6)		
Extrapulmonary tuberculosis	15 (20.8)	-	
Tuberculous meningitis	10 (66.7)		
Tuberculous lymphadenitis	3 (20.0)		
Intestinal tuberculosis	1 (6.7)		
Tuberculous pleurisy	1 (6.7)		
Other diagnosis	-		
NTM infection		19 (65.5)	
Bacterial pneumonia		8 (27.6)	
Pulmonary aspergillosis		1 (3.4)	
Mycoplasmal pneumonia		1 (3.4)	

Abbreviation: TB=tuberculosis; PTB=pulmonary tuberculosis; Non-TB=other non-tuberculosis infectious diseases; NTM=non-tuberculous mycobacteria.

while no significant differences were observed in the specificity (P=0.07). The positive predictive value (PPV) and negative predictive value (NPV) of the *IP-10* mRNA assay were 81.3% (95% *CI*: 68.1%–89.8%) and 52.6% (95% *CI*: 37.3%–67.5%), respectively. For TB-IGRA, the PPV and NPV were 89.7% (95% *CI*: 73.6%–96.4%) and 87.5% (95% *CI*: 69.0%–95.7%), respectively. Among the non-TB group, the negative detection rates for nontuberculous mycobacterial (NTM) infection, bacterial pneumonia, pulmonary aspergillosis, and mycoplasmal pneumonia were 52.6% (10/19), 87.5% (7/8), 100% (1/1), and 100% (1/1), respectively (Table 2).

We evaluated the concordance between the two diagnostic methods using 86 valid samples from patients with suspected pulmonary tuberculosis. Both the *IP-10* mRNA release assay and TB-IGRA yielded positive results in 20 participants and negative results in 34 participants. The Kappa statistic for agreement was 0.292 (P=0.001), indicating poor agreement between the two diagnostic methods (Table 3).

The sensitivity, specificity, PPV, and NPV for *Mtb* culture were 24.6%, 100.0%, 100.0%, and 40.3%, respectively. The corresponding values for Xpert MTB/RIF were 52.6%, 96.6%, 96.8%, and 50.9%, respectively. The detection rate of IP-10.TB was significantly higher than that of TB-IGRA and *Mtb* cultures (P=0.012), although the difference with Xpert MTB/RIF was not statistically significant (P>0.05). Combined detection using IP-10.TB and TB-IGRA yielded a sensitivity, specificity, PPV, and NPV of 71.9%, 69.0%, 82.0%, and 55.6%, respectively, while parallel testing of IP-10.TB and Xpert MTB/RIF demonstrated corresponding values of 77.2%, 69.0%,

TABLE 2. Diagnostic performance of the IP-10.TB assay and other diagnostic methods for PTB in HIV-infected individuals.

Test	PTB (*n*=57)	Non-PTB (*n*=29)	Sensitivity/% (95% *CI*)	Specificity/% (95% *CI*)	PPV/% (95% *CI*)	NPV/% (95% *CI*)	AUC (95% *CI*)
IP-10.TB							
Positive	39	9	68.4 (55.5, 79.0)	69.0 (50.8, 82.7)	81.3 (68.1, 89.8)	52.6 (37.3, 67.5)	0.687 (58.2, 79.2)
Negative	18	20					
TB-IGRA							
Positive	21	3	36.8 (25.5, 49.8)	89.7 (73.6, 96.4)	87.5 (69.0, 95.7)	41.9 (30.5, 54.3)	0.632 (54.8, 71.7)
Negative	36	26					
Culture							
Positive	14	0	24.6 (15.2, 37.1)	100.0 (88.3, 100.0)	100.0 (78.5, 100.0)	40.3 (29.7, 51.8)	0.623 (56.6, 67.9)
Negative	43	29					
Xpert MTB/RIF							
Positive	30	1	52.6 (39.9, 65.0)	96.6 (82.8, 99.8)	96.8 (83.8, 99.8)	50.9 (38.1, 63.6)	0.746 (67.2, 82.0)
Negative	27	28					
IP-10.TB or TB-IGRA							
Positive	41	9	71.9 (59.2, 81.9)	69.0 (50.8, 82.7)	82.0 (69.2, 90.2)	55.6 (39.6, 70.5)	0.704 (60.1, 80.8)
Negative	16	20					
IP-10.TB or Xpert MTB/RIF							
Positive	44	9	77.2 (64.8, 86.2)	69.0 (50.8, 82.7)	83.0 (70.8, 90.8)	60.6 (43.7, 75.3)	0.731 (62.9, 83.3)
Negative	13	20					

Abbreviation: TB=tuberculosis; PTB=pulmonary tuberculosis; Non-PTB=other non-tuberculosis infectious diseases affecting lung tissue.

TABLE 3. IP-10.TB and TB-IGRA test concordance evaluation.

IP-10.TB	TB-IGRA		Kappa value	*P*
	Positive (*n*)	Negative (*n*)		
Positive (*n*)	20	28	0.292	0.001
Negative (*n*)	4	34		

Abbreviation: TB=tuberculosis.

83.0%, and 60.6%, respectively. The detailed results are presented in Table 2.

Further analysis was conducted by generating ROC curves (Figure 2), which enabled comparisons of the AUC values of IP-10.TB with those of other detection methods (DeLong test). AUC values for the parallel testing of IP-10.TB and Xpert MTB/RIF were significantly greater than those for IP-10.TB alone (0.731 *vs.* 0.687, *P*=0.02).

As the immunodeficient and immunocompromised populations continue to expand, the incidence of EPTB and disseminated tuberculosis has correspondingly increased. Among patients diagnosed with extrapulmonary tuberculosis, the detection rates for IP-10.TB and TB-IGRA were 60.0% and 13.3%, respectively (*P*=0.016). For patients with hematogenous disseminated tuberculosis, the positive detection rates were 72.7% and 45.5%, respectively (*P*>0.05) (Table 4).

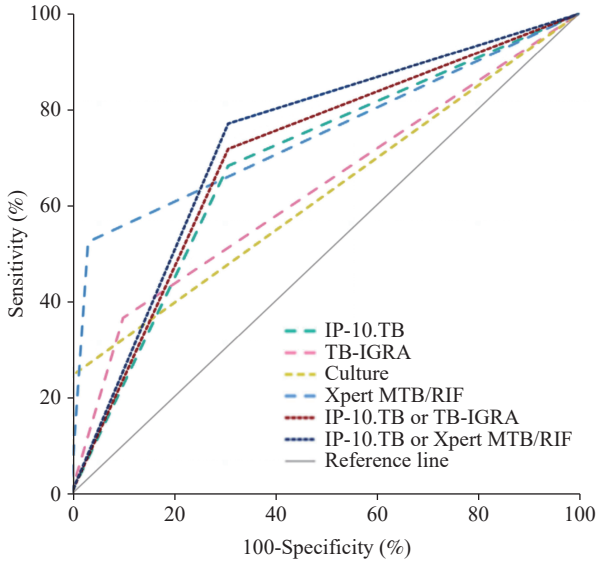

FIGURE 2. ROC curve-based PTB detection results using four individual assays and two combined diagnostic approaches.
Abbreviation: AFB=acid-fast bacilli; TB=tuberculosis; PTB=pulmonary tuberculosis; EPTB=extrapulmonary tuberculosis; ROC=Receiver operating characteristic.

DISCUSSION

Tuberculosis represents a chronic infectious disease whose clinical presentation becomes increasingly complex and atypical in HIV-infected individuals (*1*). Laboratory detection of *Mtb* often proves challenging, necessitating the integration of multiple diagnostic techniques to directly or indirectly identify evidence of *Mtb* infection — a critical step for ensuring timely diagnosis and treatment. Meta-analysis has demonstrated that the aggregated sensitivity of the *IP-10* assay reaches 85% (95% *CI*: 80%–88%), with a specificity of 89% (95% *CI*: 84%–92%) (*13*), indicating the substantial potential of *IP-10* as a biomarker for auxiliary TB diagnosis. However, evidence supporting effective diagnosis using this method in HIV-infected individuals, particularly those with severe immunosuppression, remains extremely limited.

In this study, we evaluated the diagnostic performance of the *IP-10* mRNA release assay in 101 HIV-infected individuals suspected of having TB, categorizing them into 57 cases of pulmonary TB and 29 cases of non-TB based on final diagnosis. When compared with the commonly used immunological assay TB-IGRA, our results demonstrated the sensitivity and specificity of IP-10.TB for diagnosing PTB were 68.4% and 69.0%, respectively. Notably, the sensitivity of IP-10.TB was significantly superior to that of TB-IGRA (*P*<0.01), while no statistically significant difference in specificity was observed (*P*=0.07). Meta-analysis has revealed that the aggregated sensitivity of the *IP-10* assay reaches 85% (95% *CI*: 80%–88%), with specificity at 89% (95% *CI*: 84%–92%) (*13*), indicating the substantial

TABLE 4. Diagnostic performance of the IP-10.TB assay in HIV-infected individuals with extrapulmonary tuberculosis.

	Positive cases (*n*)	Detection rate (%)	*P*
EPTB (*n*=15)			
IP-10.TB	9	60.0	0.016
TB-IGRA	2	13.3	
Hematogenous disseminated tuberculosis (*n*=22)			
IP-10.TB	16	72.7	0.070
TB-IGRA	10	45.5	

Abbreviation: EPTB=Extrapulmonary tuberculosis.

potential of *IP-10* as a biomarker for auxiliary TB diagnosis. However, evidence supporting effective diagnosis using this method in HIV-infected individuals, particularly those with severe immunosuppression, remains extremely limited.

Our findings demonstrate that the *IP-10* is predominantly secreted by monocytes and myeloid dendritic cells (*14*), with its release process being minimally affected by $CD4^+$ T cell depletion. Furthermore, previous multicenter studies have indicated that the sensitivity of *IP-10* mRNA as a biomarker remains largely uninfluenced by $CD4^+$ T cell counts (*15*). Our results align with these conclusions, demonstrating that IP-10.TB exhibits high diagnostic sensitivity even in severely immunosuppressed populations. This enhanced performance can be attributed to the fundamental differences in detection targets between TB-IGRA and IP-10.TB. The former detects IFN-γ at the protein level, whereas the latter quantifies the transient expression of *IP-10* mRNA, a downstream molecule in the IFN-γ signaling pathway (*16*), thereby substantially improving detection sensitivity.

In our study, *IP-10* mRNA release assays demonstrated lower specificity compared to TB-IGRA, although this difference was not statistically significant. This reduced specificity may be attributed to the fact that most participants had $CD4^+$ T-cell counts below 200 cells/μL, and this compromised immunity likely increased the prevalence of latent *Mtb* infection (*17*). Additionally, the limited sample size of the non-TB group may have further amplified this difference. Furthermore, false-positive cases in the non-TB group consisted mainly of NTM-infected individuals, with a negative detection rate of 52.6% (10/19). The ESAT-6, CFP-10, and PPE antigens utilized in IP-10.TB are derived from the region of difference-1 (RD-1) of *Mtb*. This region exhibits no cross-reactivity with antigens from BCG or the vast majority of NTM strains, except for a few species such as *M. kansasii*, *M. marinum*, and *M. szulgai* (*18*). Therefore, it effectively avoids interference from most NTM strains. However, when infected with NTM strains containing ESAT-6, CFP-10, or PPE antigens, these antigenic components may stimulate the host immune system, inducing a T-cell immune response similar to that elicited by *Mtb* infection. This phenomenon may result in positive *IP-10* release assay results, thereby causing false-positive outcomes. False positives may also result from differences in the TB-specific antigens employed: TB-IGRA utilizes ESAT-6 and CFP-10 antigens, whereas IP-10.TB employs ESAT-6, CFP-10, and PPE antigens. However, the precise mechanisms underlying these differences require further investigation. In the present study, concordance between IP-10.TB and TB-IGRA results were poor, which may be attributed to three factors. Firstly, the differences in assay targets and their expression levels (mRNA versus protein). Secondly, a greater variability in HIV-infected individuals with severe immunosuppression. Thirdly, the lower sensitivity of TB-IGRA. Consequently, IP-10.TB may represent an attractive alternative diagnostic method for HIV-infected individuals.

Compared with traditional IGRAs, the IP-10.TB method requires a shorter incubation time, with results available in as little as six hours. Moreover, the linear detection range of PCR technology is broader than that of ELISA. By leveraging the amplification curves to calculate the results, the variability in result interpretation is reduced, enhancing the objectivity of the detection results. The findings of this study suggest that IP-10.TB has great potential for use in the early diagnosis of tuberculosis in HIV-infected individuals. By optimizing and integrating specific tests, patients with tuberculosis can be identified earlier, thus facilitating early initiation of treatment and potentially reducing the mortality rate associated with the disease.

This study also has some limitations. First, it was a single-center, small-sample study, and the extrapolation of conclusions are challenging. Moreover, the enrolled hospitalized patients were predominantly severely immunocompromised, which may have resulted in selection bias. Lastly, it might be more objective and convincing to use a third alternative method to validate the inconsistency between the *IP-10* mRNA release assay and the TB-IGRA test results. This part of our work is in progress.

Therefore, multicenter studies with larger and more diverse samples are necessary to validate the diagnostic performance of *IP-10* mRNA release assay. Additionally, although IP-10.TB has a high sensitivity, it is not effective in differentiating between latent infection with *Mtb* and active tuberculosis, and cannot predict the transition from latent infection to active tuberculosis. Besides, the IP-10.TB results could not reflect the relationship with the *Mtb* bacterial load, thus limiting its application in evaluating the efficacy of anti-tuberculosis treatment.

IP-10 mRNA release assays have significant clinical value and potential as an auxiliary tool for diagnosing TB in HIV-infected individuals. Furthermore, the combined use of IP-10.TB and Xpert MTB/RIF can

increase the diagnostic efficacy of TB. In the cases of EPTB with insufficient diagnostic evidence, *IP-10* mRNA release assays provide complementary and auxiliary diagnostic benefits.

Conflicts of interest: No conflicts of interest.

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Preplanned Studies

Assessment of Intercultural Communication Competence for China Field Epidemiology Training Program (CFETP) Trainees — China, 2025

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Summary

What is already known about this topic?

Trainees in the China Field Epidemiology Training Program (CFETP) constitute a vital workforce in addressing global public health emergencies. Developing intercultural communication competence is essential for their future participation in international public health efforts. However, within China's existing public health training system, this aspect has not yet received adequate attention or been systematically strengthened.

What is added by this report?

This study is the first to evaluate and investigate the intercultural communication competence of domestic CFETP trainees. There are 77 trainees that demonstrated strong cognitive (Score rates: 86.57%) and emotional (87.22%) competencies. However, behavioral (79.42%) competence, particularly language proficiency, can be improved. Further analysis indicated that international experience, duration of time spent abroad, and foreign language proficiency had a significant impact on their intercultural communication competence.

What are the implications for public health practice?

This study examined the current state of intercultural communication competence among public health professionals and the factors influencing it. It highlights the key obstacles and practical challenges trainees face in intercultural communication while providing essential data to inform the development of targeted strategies for improving competence and refining training programs.

ABSTRACT

Introduction: Advancements in global public health have increased the competency demands for public health professionals engaged in global health work in China. Intercultural communication competence, an integral component of global public health capabilities, enables trainees to build trust, collaborate effectively in multicultural contexts, and maintain cultural sensitivity and effectiveness in public health interventions.

Methods: China Field Epidemiology Training Program (CFETP) trainees with an expressed interest in global health work were selected for this study. A questionnaire was used to evaluate their intercultural communication competence through a combination of subjective self-assessments and objective testing.

Results: A total of 77 CFETP trainees completed the survey. Self-assessment scores indicated a relatively high level of intercultural communication competence (scoring rate: 84.86%), whereas objective test scores were moderately lower (scoring rate: 72.21%). Key influencing factors included previous international experience, duration of time spent abroad, and proficiency in foreign languages.

Conclusion: The participating CFETP trainees demonstrated above-average intercultural communication competence, although performance varied across specific dimensions. Future research should focus on addressing weaker aspects of intercultural skills among public health professionals through targeted training efforts.

The China Field Epidemiology Training Program (CFETP), a cornerstone of China's public health workforce development established in October 2001, has trained 448 highly skilled field epidemiologists through its 2-year program as of February 2025. These professionals are central to domestic outbreak investigations, major public health events, epidemic prevention and control, and public health

policymaking. They also serve as key talent pools for global public health efforts (*1*). Although CFETP graduates possess professional expertise, those who perform well in domestic settings may not necessarily be equipped to navigate the complexities of public health in intercultural environments. Public health issues are often intertwined with cultural factors (*2*) shaped by the customs, traditions, and social behaviors of target populations (*3*). Intercultural communication competence is therefore a core requirement, enabling professionals to build trust, facilitate collaboration and ensure that public health interventions are culturally appropriate and effective in diverse settings.

This study drew on domestic and international intercultural competence models (*3*), scales (*4*), and domestic intercultural competence test guidelines (*5*), incorporating insights from in-depth interviews with professionals, to design a Global Public Health Personnel Intercultural Communication Competence Survey Questionnaire. The questionnaire comprised three main sections: 1) basic personal information; 2) a self-evaluation scale for intercultural communication competence, employing a 5-point Likert scoring system measuring intercultural cognitive competence (10 items, 50 points), intercultural emotional competence (9 items, 45 points), and intercultural behavioral competence (8 items, 40 points); and 3) scenario-based test questions, consisting of 15 multiple-choice questions (10 points each) based on three work-related scenarios: public health assistance abroad, employment in international health organizations, and participation in global health projects. The score rate (%) was determined using the following formula: average score/total score × 100%. Score rates <60% were categorized as low, 60.00%–80.00% as medium, >80.00% as relatively high, and > 90.00% as high level. This study conducted an online questionnaire survey. Data were analyzed using SPSS (version 25.0, IBM SPSS Inc., Armonk, NY, USA).

The survey was administered to all 448 graduated CFETP trainees, with 77 responses received (response rate: 17.19%). The respondents were selected from multi-tiered disease prevention and control centers across 22 provincial-level administrative divisions in China, with an average age of 41.40 years. Approximately 51.95% were male, and 87.01% held postgraduate degrees. A majority (66.23%) had overseas experience, although 60.78% of that subgroup had spent less than 6 months abroad, primarily for brief professional visits (Table 1). The self-assessment scale demonstrated strong reliability, with an overall Cronbach's α coefficient of 0.95. Exploratory factor analysis yielded a Kaiser-Meyer-Olkin (KMO) value of 0.84, and Bartlett's test of sphericity was significant (P<0.01). Six factors were extracted, aligning with the expected three-dimensional structure (Table 2). The self-assessment results indicated that CFETP trainees exhibited a relatively high overall level of intercultural communication competence. By contrast, the objective test results showed that the score rates across the three scenarios and the total score were all below 80%, indicating a moderate level of performance (Table 2). Overall, Self-assessment scores slightly exceeded objective test scores, suggesting a possible overestimation of competence..

The consistency between self-assessment and objective test results was relatively weak (Table 3). A comparative analysis based on demographic characteristics was conducted across these dimensions (Table 1). Trainees with overseas experience had better intercultural cognitive and behavioral competence. Those with longer durations of stay abroad achieved significantly higher scores in behavioral competence. English proficiency had a notable influence on all three dimensions of cognitive, emotional, and behavioral competence, while educational level had no significant effect, though doctoral degree holders scored slightly higher in cognitive and behavioral competence. Sex, age, and professional title were not significant factors.

The main barriers to intercultural competence were cultural background differences, limited language proficiency, and insufficient communication opportunities. In terms of training needs, cultural knowledge, language proficiency, and understanding of cultural taboos were the top three priorities. Most trainees possessed extensive experience in domestic disease prevention through profession-focused training. However, available international opportunities were typically brief and provided minimal cultural exposure. This limited immersion impedes the development of intercultural competence, highlighting the need to incorporate such training into public health programs.

DISCUSSION

High-quality professionals are essential for China's active role in global public health governance and serve as a driving force in advancing a global community focused on health for all (*6*). Intercultural communication competence, a key component of global public health capacity, is indispensable for both long-term health aid initiatives and short-term

TABLE 1. Comparative analysis of cross-cultural communication competence across dimensions under different characteristics.

Item	Numbers (%)	Self-assessment			Test questions
		Cognitive ability	Emotional competence	Behavioral competence	
Sex					
Male	40 (51.95)	4.44±0.54	4.32±0.51	3.99±0.64	102.00±23.99
Female	37 (48.05)	4.21±0.57	4.41±0.50	3.95±0.60	115.14±21.81
T		1.78	−0.75	0.29	−2.51
P		0.08	0.46	0.77	0.01*
Age (years)					
20−29	2 (2.60)	4.35±0.21	4.22±0.16	3.50±0.00	115.00±7.07
30−39	29 (37.66)	4.33±0.58	4.28±0.58	3.96±0.70	105.86±22.92
40−49	36 (46.75)	4.29±0.59	4.42±0.47	3.99±0.56	111.94±23.76
≥50	10 (12.99)	4.45±0.55	4.42±0.43	4.04±0.68	101.00±28.07
F		0.19	0.49	0.42	0.75
P		0.90	0.69	0.74	0.53
Overseas experience					
Yes	51 (66.23)	4.44±0.49	4.37±0.44	4.09±0.57	106.27±23.06
No	26 (33.77)	4.11±0.64	4.34±0.61	3.73±0.65	112.31±25.03
T		2.53	0.26	2.50	1.06
P		0.01*	0.80	0.01*	0.30
Cumulative time spent overseas (years)					
<0.5	30 (60.00)	4.41±0.54	4.33±0.47	3.98±0.57	106.33±23.41
0.5−1	15 (30.00)	4.47±0.44	4.46±0.45	4.13±0.56	111.33±21.00
>1	5 (10.00)	4.62±0.36	4.44±0.28	4.67±0.41	88.00±23.87
F		0.40	0.47	3.37	2.00
P		0.67	0.63	0.04*	0.15
English proficiency					
Basic English for daily communication	26 (33.77)	4.07±0.68	4.20±0.58	3.59±0.61	107.69±28.75
Sufficient for basic work communication	27 (35.06)	4.31±0.45	4.30±0.47	3.91±0.49	110.37±20.09
Proficient, capable of handling most work communication	22 (28.57)	4.59±0.40	4.61±0.36	4.40±0.41	109.09±21.58
Use English like a native speaker	2 (2.60)	5.00±0.00	4.61±0.24	5.00±0.00	80.00±14.14
F		4.89	3.22	12.77	1.03
P		0.00**	0.03*	0.00**	0.39
Educational background					
Bachelor's degree or below	10 (12.99)	4.31±0.43	4.48±0.53	3.94±0.60	100.00±23.09
Master's degree	55 (71.43)	4.28±0.61	4.29±0.51	3.89±0.63	110.18±24.07
Doctoral degree	12 (15.58)	4.57±0.42	4.57±0.40	4.35±0.49	106.67±23.09
F		1.28	1.89	2.87	0.81
P		0.28	0.16	0.06	0.45
Professional title					
Senior professional title	27 (35.06)	4.47±0.59	4.48±0.42	4.06±0.61	107.78±26.36
Associate senior professional title	35 (45.45)	4.25±0.54	4.30±0.56	4.01±0.57	111.14±21.11
Intermediate professional title	12 (15.58)	4.20±0.61	4.23±0.51	3.63±0.71	103.33±26.05
Junior professional title or other	2 (2.60)	4.65±0.21	4.67±0.47	4.25±1.06	95.00±35.36
F		0.93	0.91	1.40	0.41
P		0.45	0.46	0.24	0.81

* $P<0.05$;
** $P<0.01$, the difference is significant.

TABLE 2. Descriptive statistics of each dimension.

Item	Meaning	Mean	SD	Score rate (%)	Level
Self-assessment scale					
Cognitive ability		43.29	5.66	86.57	Relatively high
Cultural knowledge	The communicator's understanding of cultural knowledge and common sense of both their own country and other countries, including cultural background, social norms, and cultural taboos. This encompasses three subordinate indicators: material culture, institutional culture, and spiritual culture.	21.42	3.57	85.66	Relatively high
Intercultural awareness	Sensitivity to and insight into differences, interaction patterns, and values across cultures, encompassing three subordinate indicators: cultural differences, cultural identity, and critical awareness.	21.87	2.64	87.48	Relatively high
Emotional competence		39.25	4.53	87.22	Relatively high
Personal characteristics	The proactive guidance of human behavior, manifesting relatively stable traits across diverse situations, encompasses two subordinate indicators: qualities and character.	26.14	3.06	87.14	Relatively high
Motivation	The ability to stimulate and sustain the communicator's willingness to engage in cross-cultural contexts and to direct behavior toward specific objectives. It consists of three subordinate indicators: willingness to communicate, task-driven motivation, and self-driven motivation.	13.10	1.80	87.36	Relatively high
Behavioral competence		31.77	4.97	79.42	Moderate
Communication skills	Selecting appropriate cultural resources based on specific situations and using verbal and non-verbal forms of expression to ensure effective communication. This includes three subordinate indicators: cultural resource utilization ability, linguistic skills, and non-linguistic skills.	10.64	2.40	70.91	Moderate
Executive ability	The ability to integrate resources, apply communication strategies, and achieve communication goals. It consists of four subordinate indicators: observational and critical thinking skills, interaction management skills, adaptability, and teamwork skills.	21.13	3.08	84.52	Relatively high
Total score		114.56	13.12	84.86	Relatively high
Test questions					
Public health foreign aid	Communication issues are designed around emergency response, health project collaboration, and local work engagement. These include intercultural coordination in the local work environment, emergency management, meeting preparation, proactive communication for assistance, team integration, and trust building.	35.20	11.69	70.39	Moderate
Employment in international health organizations	Communication issues are based on the daily operations and interpersonal interactions within international organizations. These include communication methods, problem-solving, conflict management, and emergency response in the specific working environment of international organizations to ensure a smooth workflow and maintain positive professional relationships.	38.05	10.94	76.10	Moderate
Participation in international health projects	Questions focus on real-life scenarios involving international exchange and cooperation. Topics include effective communication, adaptability, respect, and inclusiveness in intercultural environments to facilitate problem-solving and strengthen collaboration.	35.07	10.52	70.13	Moderate
Total score		108.31	23.75	72.21	Moderate

Abbreviation: SD=standard deviation.

emergency responses to international public health crises. It extends beyond language proficiency to include the ability to understand, adapt, and respect diverse cultural contexts while effectively navigating complex intercultural environments. Given its significance, this study focused on CFETP trainees, recognized for their strong public health expertise, to assess the current state of intercultural communication competence among domestic public health professionals, identify gaps across multiple dimensions, and provide insights for future capacity-building efforts (*7*).

The self-assessment results suggest that CFETP trainees generally possess high intercultural

TABLE 3. Correlation analysis of each dimension.

Item	Cognitive ability	Emotional competence	Behavioral competence	Cultural knowledge	Intercultural awareness	Personal characteristics	Motivation	Communication skills	Executive ability	Overall Self-assessment	Test Questions
Dimension											
Cognitive ability	1										
Emotional competence	0.496**	1									
Behavioral competence	0.697**	0.602**	1								
Extracted factor											
Cultural knowledge	0.936**	0.432**	0.632**	1							
Intercultural awareness	0.878**	0.479**	0.640**	0.653**	1						
Personal characteristics	0.461**	0.961**	0.512**	0.402**	0.444**	1					
Motivation	0.465**	0.882**	0.643**	0.404**	0.450**	0.717**	1				
Communication skills	0.653**	0.524**	0.879**	0.611**	0.574**	0.480**	0.503**	1			
Executive ability	0.616**	0.562**	0.928**	0.543**	0.585**	0.453**	0.645**	0.638**	1		
Overall self-assessment	0.875**	0.794**	0.895**	0.799**	0.794**	0.731**	0.755**	0.803**	0.819**	1	
Test questions	−0.185	0.154	−0.084	−0.167	−0.172	0.087	0.242*	−0.223	0.039	−0.059	1

Note: The questionnaire items were mapped to specific competency domains as follows: Cultural Knowledge: Items 1–1 to 1–5, intercultural Awareness: Items 1–6 to 1–10, Personal characteristics: Items 2–1 to 2–6, Motivation: Items 2–7 to 2–9, Communication Skills: Items 3–1 to 3–3, Executive ability: Items 3–4 to 3–8.

* $P<0.05$;

** $P<0.01$, the difference is significant.

communicative competence. However, noticeable differences emerged across certain items, and scores were notably lower in areas related to knowledge of religion, traditional ceremonies, social etiquette, customs (mean score 4.08), and intercultural knowledge, both within one's own country and abroad (mean 3.95). This trend aligns with trainees' expressed need for more cultural knowledge. Limited opportunities for intercultural exchange may have contributed to a lack of awareness regarding the intricate relationship among religion, traditional customs, and health. Furthermore, the trainees also scored lower on intercultural initiative for two main reasons. First, weak professional language skills. Second, China's predominant communication style, which favors indirect expression, may encourage passivity. Supported by intrinsic motivations such as task-oriented demands (mean 4.40) and self-improvement goals (mean 4.48), participants' communicative initiative (mean 4.23) exhibited an upward trend. These motivations may help individuals overcome psychological barriers in real-world situations, ultimately strengthening their initiative and adaptability in intercultural contexts.

The overall score on the self-assessment scale was slightly higher than that of the objective test, particularly in cultural knowledge and behavior. Trainees with higher self-assessment scores exhibited greater confidence in their ability to navigate intercultural communication. This finding is consistent with those of international studies, which indicate that even without formal intercultural training, participants often assume they possess the necessary skills to function effectively in multicultural work environments (*8*). Intercultural communication is inherently complex and encompasses a broad range of competencies. Even with similar levels of cultural knowledge and communicative initiative, individuals' actual behavior may vary owing to personal characteristics. Therefore, assessments should distinguish between competence gaps resulting from modifiable factors such as knowledge and language proficiency and those influenced by intrinsic traits such as personality.

Analysis across different backgrounds revealed that women outperformed men in objective testing and scored higher on intercultural emotional competence. From a sex-based perspective, women are often thought to have stronger empathy, increased cultural awareness, and greater aptitude for foreign language learning. These strengths likely helped them avoid missteps in test scenarios and make more thoughtful decisions. In the self-assessments, trainees with stronger English proficiency reported better intercultural communication capabilities, particularly in terms of cultural understanding, initiative, inclusiveness, communication, and teamwork. Trainees with overseas experience demonstrated stronger cognitive and behavioral competence. Firsthand intercultural exposure improves both cultural understanding and practical communication skills while encouraging a broader worldview. These abilities tend to strengthen with longer stays abroad. Moving forward, English proficiency and international experience should be prioritized in selecting and training of professionals for global health work.

To enhance intercultural communication competence, it should be continuously taught and reinforced through medical education, training, and practice (*9*). For in-service personnel, increasing opportunities for international health exchanges and integrating training programs can strengthen their intercultural communication competence (*10*). Trainees prefer face-to-face lectures, in-depth case studies, global public health emergency response scenarios, and practical experiences related to medical missions and international public health initiatives (*11*). The development of cultural knowledge and language proficiency is a long-term process that requires continuous support from the educational system. Integrating intercultural competence into public health education and research can yield more substantial and lasting improvements (*12*).

This study has certain limitations. First, its exclusive focus on trainees interested in global health activities introduces sampling bias, which may limit the representativeness and generalizability of the findings. Second, although the objective test questions were developed with expert guidance, the complexity of intercultural communication behaviors makes it challenging for existing assessment tools to capture all dimensions of intercultural communication competence.

In conclusion, the participating CFETP trainees demonstrated above-average intercultural communication competence, which was mainly influenced by English proficiency and overseas experience. The significance of our study lies not only in providing public health professionals with a comprehensive understanding of their cross-cultural communication skills—enabling them to assess their knowledge, attitudes, and abilities when encountering

cultural differences — but also in clarifying essential directions for selecting and training international health professionals. Future efforts should focus on more specific areas within public health and addressing weaker aspects of intercultural skills.

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Outbreak Reports

An Outbreak of Dermatitis Caused by *Redoa leucoscela* Larvae in A Scenic Area — Tongren City, Guizhou Province, China, July–August 2024

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Summary

What is already known about this topic?

Redoa leucoscela (*R. leucoscela)* Collenette (Lepidoptera: Erebidae), releases urticating setae during larval molting. These setae disperse through aquatic and aerial pathways and can trigger allergic reactions upon dermal contact. Clinical manifestations include pruritic dermatitis with stinging sensations and papular lesions; untreated cases may progress to systemic reactions or secondary infections.

What is added by this report?

Between July 10 and August 16, 2024, a dermatitis outbreak caused by *R. leucoscela* occurred in Y Village, Tongren City, Guizhou Province. A total of 32 cases were identified, including 30 residents and 2 tourists. This report provides the first epidemiological evidence linking *R. leucoscela* larvae to dermatitis outbreaks through rigorous case-control methodology.

What are the implications for public health practice?

During peak *R. leucoscela* larvae infestation periods, local authorities must implement integrated dermatitis surveillance and larval eradication programs, coupled with prominent warning signage in high-risk zones (riversides, swimming areas) advising against water contact and minimizing exposure to *P. stenoptera* tree foliage to prevent outbreak recurrence. Concurrently, health promotion campaigns must prioritize eco-awareness education for tourism stakeholders and the public, advocating for eco-conscious tourism behaviors to minimize anthropogenic habitat disruption, thereby achieving sustainable tourism-conservation synergy.

ABSTRACT

Introduction: On August 13, 2024, the X County CDC reported that multiple villagers in Y Village within a scenic area had developed unexplained generalized pruritic rashes since July 10. Preliminary investigations revealed that most patients had swum in the river prior to symptom onset. The incident generated public concern and negatively impacted local tourism. To identify the cause and control the outbreak, our center conducted an on-site investigation.

Methods: Cases were defined as residents or visitors in Y Village presenting with rash and pruritus without other identifiable causes between July 10 and August 16, 2024. We identified cases through interviews with village doctors, household surveys, and medical record reviews. Thirty village cases comprised the case group, while 60 asymptomatic residents from the same period were randomly selected as controls (1∶2 ratio). Household interviews collected exposure and allergy histories.

Results: We identified 32 cases (30 villagers, attack rate 9.29%; 2 tourists). Village cases ranged from 3 to 77 years of age. The 0–14-year age group exhibited the highest attack rate (26.92%), with a decreasing trend observed as age increased (χ^2 for trend=16.45, $P < 0.001$), and rates declining significantly in older groups (χ^2=20.86, $P<0.001$). Symptom onset clustered between July 10 and August 16, peaking on July 20. The median symptom duration was 6 days (range: 3–14 days). All cases presented with rash and pruritus (100%). Village Group A had the highest attack rate at 32.08% (χ^2=34.25, $P<0.001$). Environmental investigation revealed Redoa leucoscela larvae (expert-identified) parasitizing riverside Pterocarya stenoptera trees. Urticating setae from R. leucoscela larvae were detected in river water. Univariate analysis identified significant risk factors as staying under P. stenoptera trees [odds ratio (OR)=14.03, 95% confidence interval (CI): 4.29, 45.87] and swimming in the river (OR=4.60, 95% CI: 1.71, 12.38).

Conclusion: This dermatitis outbreak resulted from dermal contact with *R. leucoscela* larval urticating setae.

On July 10, 2024, Y Village residents in X County, Tongren City, Guizhou Province, developed cutaneous pruritus and erythematous rashes after river swimming. Affected individuals sought treatment at the village clinic, receiving antihistamine therapy. Subsequently, the X County government received successive reports from local and surrounding residents documenting that visitors to the area developed pruritic rashes after their visits, prompting concerns regarding potential environmental triggers. Additional tourists reported similar dermatological symptoms through digital platforms, generating public concern and impacting regional tourism. Given escalating public health implications, local authorities designated this a priority response, mobilizing the X County CDC for comprehensive epidemiological investigations. This investigation retrospectively identified unreported cases among village residents dating to July 10, confirming multiple residents and tourists developed generalized pruritic dermatitis following direct river exposure. On August 13, the X County CDC reported comprehensive findings — including case timelines, tourist complaints, public sentiment impacts, and preliminary results — to the Tongren City CDC. Upon notification, the Tongren City CDC deployed a multidisciplinary investigative team comprising epidemiologists, clinical specialists, and laboratory scientists to conduct a field investigation aimed at verifying the outbreak, elucidating the etiology, and implementing appropriate public health control measures.

INVESTIGATION AND RESULTS

We defined suspected cases as individuals within Y Village presenting with unexplained pruritus and skin rash between July 10-August 16, 2024, excluding cases with confirmed alternative etiologies. The start date corresponded to symptom onset in the index case, confirmed as the first autochthonous case within Y Village without travel history or documented allergen exposure.

Cases were identified through hospital record reviews, clinician interviews, and active case-finding. All cases met predefined inclusion criteria: symptom consistency, exclusion of alternative dermatoses, and dermatologist-verified diagnoses. We investigated all cases using a Cluster Dermatitis Case Investigation Form collecting clinical manifestations, exposure histories, and demographics. River water quality was assessed per Environmental Quality Standards for Surface Water (GB 3838-2002). We conducted a 1:2 unmatched case-control study to identify risk factors. Associations were analyzed using chi-square or Fisher's exact tests. We calculated relative risk (*RR*) with 95% confidence intervals (*CI*) for age groups (reference: ≥65 years) and odds ratios (*OR*) with 95% *CI* for categorical exposures. Statistical significance was $P<0.05$ using SPSS (version 26.0, IBM Corporation, Armonk, NY, USA).

The outbreak occurred in a scenic area in Y Village, Tongren City, Guizhou Province. The village has seven administrative groups with 323 permanent residents along the river. Boasting a beautiful environment and a temperate climate (mean annual temperature 16 °C), it attracts a large number of tourists .

We identified 30 confirmed cases among Y Village residents, yielding an attack rate of 9.29% (30/323, 95% *CI*: 6.37, 13.00). Two tourists with similar symptoms were excluded due to insufficient documentation. All 30 cases were investigated using a standardized "Cluster Dermatitis Case Investigation Form". Contact tracing identified two index cases: Index Case A swam in the river for 30 minutes, then barbecued beneath riverside trees. At 17:00, red rashes with pruritus appeared on limbs and torso. They received a clinical diagnosis of allergic contact dermatitis at X County People's Hospital and improved with anti-allergy treatment. Index Case B operated a local guesthouse and experienced recurring rashes on torso and limbs with pruritus since mid-July. They reported no river swimming but noted their guesthouse's proximity to *P. stenoptera* trees with numerous "caterpillars" congregating — a phenomenon not observed previously. Verified betamethasone use achieved partial symptom resolution.

The primary presentation was pruritic maculopapular rashes predominantly affecting limbs and trunk (Figure 1B). No cases exhibited fever, lymphadenopathy, or systemic involvement.

Among 30 confirmed cases, symptom onset occurred between July 10 and August 16, 2024. The epidemic peaked on July 20 (n=5, 16.7%; Figure 1A), with an epidemic curve characteristic of continuous common-source exposure. Cases clustered within five residential groups: a, b, c, d, and e (Figure 1D). Attack rates varied significantly across groups (χ^2=34.25, $P<0.001$), with the highest in a (32.08%) and lowest in e (2.48%).

Case ages ranged from 3 to 77 years. Attack rates

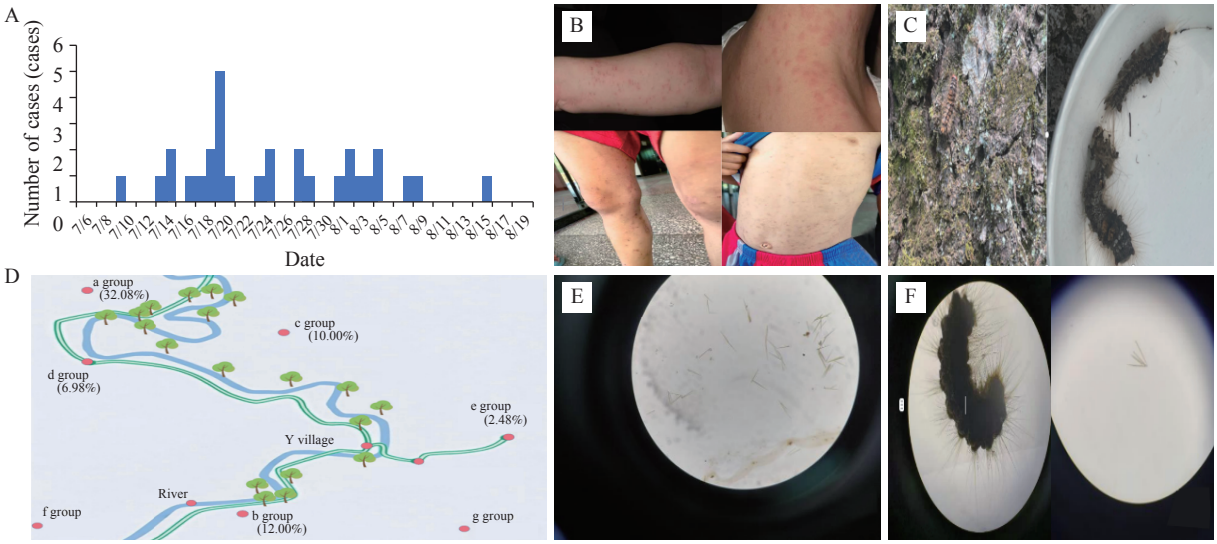

FIGURE 1. Overall overview of the 2024 dermatitis outbreak caused by *R. leucoscela* larvae in a scenic area of Tongren City. (A) Epidemic curve of rash cases in Y Village, July–August 2024; (B) Clinical manifestations of rash cases in Y Village; (C) *R. leucoscela* larvae observed at the investigation site; (D) Distribution of village groups by disease incidence in Y Village; (E) Morphology of suspected urticating setae from *R. leucoscela* larvae detected in river water samples; (F) Water sample containing *R. leucoscela* larvae after one-hour soaking period.

showed significant heterogeneity across age groups (χ^2=20.86, df=3, P<0.001). The 0–14-year group had the highest attack rate (26.92%), followed by 15–44-year group (20.93%). The 45–64-year and ≥65-year groups showed lower rates (5.88% and 5.08%, respectively). Using RR analysis with ≥65-year group as reference, the 0–14-year group demonstrated highest risk (*RR*=5.28, P< 0.001), while 15–44-year group showed second-highest risk (*RR*=4.11, P<0.05). No significant difference emerged between 45–64-year and ≥65-year groups (P>0.05) (Table 1). Sex-based attack rates showed no significant difference: 12.07% in males (21/174) *vs.* 6.04% in females (9/149) (χ^2=3.46, df=1, P>0.05).

Based on field observations and preliminary findings, we developed two etiological hypotheses for the clustered dermatitis outbreak in Y Village: 1) waterborne exposure through direct contact with contaminated river water, and 2) dermal contact with urticating setae from "caterpillars" parasitizing *P. stenoptera* trees.

Environmental surveys revealed no industrial pollution sources near Y Village. The adjacent river contained clear water, with *P. stenoptera* trees, willows, and other species along both banks. Only *P. stenoptera* trees exhibited "caterpillar" activity (Figure 1C). Villagers reported unprecedented larval density on riverside trees beginning July 2024 — not observed previously — with larval morphology consistent with documented descriptions. During pre-outbreak tourism development, investigations documented concurrent increases in: 1) visitor density; 2) nighttime illumination duration.

Guizhou Provincial CDC entomology experts identified "caterpillars" inhabiting *P. stenoptera* trees as *R. leucoscela* larvae. Two investigators conducted controlled exposure by applying river water to their arms. Within two minutes, both developed red rashes and papules with burning sensations and pruritus — symptoms matching outbreak cases. Symptoms resolved spontaneously upon leaving the contaminated area.

Water quality analysis demonstrated compliance with Surface Water Class II standards (GB 3838-2002). Microscopic examination revealed structures morphologically consistent with *R. leucoscela* urticating setae (Figure 1E). *R. leucoscela* larvae immersed in sterile water for one hour shed urticating setae morphologically identical to structures in river samples (Figure 1F).

We conducted a case-control study with all 30 confirmed cases (Y Village residents) and 60 randomly selected unaffected controls (1∶2 ratio). Controls satisfied: 1) absence of target disease confirmed by clinical examination; 2) continuous village residence ≥6 months before outbreak; 3) no immunocompromising conditions or active infections. Demographics were not matched to preserve population heterogeneity.

Univariate analysis evaluated associations between

TABLE 1. Age-specific attack rates of dermatitis in Y Village, 2024.

Age group (years)	Population	Cases	Attack rate (%)	*RR* (95% *CI*) *vs.* ≥65 years	*P*
0–14	26	7	26.92	5.30 (1.94, 14.50)	<0.001
15–44	43	9	20.93	4.12 (1.56, 10.88)	0.002
45–64	136	8	5.88	1.56 (0.41, 3.24)	0.78
≥65	118	6	5.08	1.00	

Note: Attack rate calculated as (cases/population)×100%. *RR* (95% *CI*) *vs.* ≥65 years: Relative risk and 95% confidence interval calculated using the ≥65 years group as reference. *RR*=attack rate of target age group ÷ attack rate of ≥65 years group. Statistical significance defined as *P*<0.05.
Abbreviation: *CI*=confidence interval; *RR*=relative risk.

rash development and exposures [river swimming, *P. stenoptera* trees exposure (>1 minute under trees), home flower cultivation, allergic history]. Significant associations emerged for *P. stenoptera* trees exposure (*OR*=14.03, 95% *CI*: 4.29, 45.87) and river swimming (*OR*=4.60, 95% *CI*: 1.71, 12.38) (Table 2), while allergic history (*OR*=1.00, 95% *CI:* 0.09, 11.49) and flower cultivation (*OR*=0.38, 95% *CI*: 0.04, 3.40) showed no significance. Exclusive *P. stenoptera* exposure increased rash risk 6.25-fold (*OR*=6.25, 95% *CI*: 1.04, 37.67). Combined exposure to *P. stenoptera* trees and river swimming showed 26.25-fold increased risk (*OR*=26.25, 95% *CI*: 5.17, 133.34) (Table 3). River-swimming-only exposure indicated 3.33-fold increased risk, though not statistically significant due to limited sample size (*OR*=3.33, 95% *CI*: 0.54, 20.45).

PUBLIC HEALTH RESPONSE

Patients presenting with dermatitis received comprehensive anti-allergic and anti-inflammatory treatment protocols. Healthcare providers counseled patients to avoid scratching affected areas to prevent secondary bacterial infections and skin damage. Patients experiencing symptom progression or complications were advised to seek immediate specialized dermatological care at appropriate medical facilities. Targeted insecticide applications were systematically implemented to eliminate *R. leucoscela* populations throughout the affected area. Concurrent community health education initiatives were delivered to residents, emphasizing the critical importance of avoiding river swimming and prolonged exposure to *P. stenoptera* trees during peak hazard periods (July–August). These educational efforts promoted enhanced personal protective measures during outdoor recreational activities to minimize direct contact with urticating setae and reduce future exposure risks.

DISCUSSION

This dermatitis outbreak resulted from human exposure to urticating setae of *R. leucoscela* larvae through direct contact. The epidemiological evidence supports this causal relationship. The outbreak period (July 10 to August 16, 2024) coincided precisely with peak *R. leucoscela* larval activity (*1*). The epidemic curve exhibits characteristics consistent with intermittent common-source exposure. During peak larval period (July–August) (*1*), tourism seasonality increased high-risk behaviors (river swimming, *P. stenoptera* tree exposure), concentrating human activity in setae-contaminated areas. This temporal convergence of peak exposure and setal density with peak disease incidence strengthens the exposure-disease association. Logistic regression confirmed that exclusive *P. stenoptera* exposure conferred 6.25 times higher risk (*OR*=6.25, 95% *CI*: 1.04, 37.67), while combined exposure increased risk 26.25-fold (*OR*=26.25, 95% *CI*: 5.17, 133.34) (Table 3), indicating synergistic effects. In the river-swimming-only subgroup (*n*=19), association was non-significant (*OR*=3.33, 95% *CI*: 0.54, 20.45) due to limited power.

Converging ecological, clinical, and exposure evidence explains this outbreak mechanistically. *R. leucoscela* larvae exclusively inhabit *P. stenoptera* trees along Y Village's riparian zones, feeding on foliage and releasing urticating setae during development (*1*). These setae contaminate air (wind dispersal) and water (direct shedding), with peak contamination in July–August aligning with larval activity (*1–2*). Cases presented pruritus, erythema, and papules, consistent with previous studies and the 2009 *R. leucoscela*-associated outbreak in Daxijiang, Guangxi Zhuang Autonomous Region (*2*).

All cases presented localized pruritic rashes without fever or exudative lesions, excluding infectious etiologies such as rubella and measles. Laboratory analysis was ruling out general contamination.

TABLE 2. Univariate logistic regression analysis of risk factors for dermatitis in Y Village, 2024.

Risk factors	Number of exposures (cases)		Exposure rate (%)		*OR* (95% *CI*)
	Case	Control	Case	Control	
Exposure to *P. stenoptera* trees	26	19	86.67	31.67	14.03 (4.29, 45.87)
River swimming	23	25	76.67	41.67	4.60 (1.71, 12.38)
History of allergies	1	2	3.33	3.33	1.00 (0.09, 11.49)
Flower cultivation at home	1	5	3.33	8.33	0.38 (0.04, 3.40)

Abbreviation: *OR*=odds ratio; *CI*=confidence interval.

TABLE 3. Association between environmental exposures and dermatitis in Y Village.

Exposure to *P. stenoptera* trees	River swimming	Cases	Controls	*OR* (95% *CI*)
+	+	21	10	26.25 (5.17, 133.34)
+	−	5	10	6.25 (1.04, 37.67)
−	+	4	15	3.33 (0.54, 20.45)
−	−	2	25	1.00

Note: "+" indicates presence of exposure (individuals were exposed to *P. stenoptera* trees or engaged in river swimming); "−" indicates absence of exposure.
Abbreviation: *OR*=odds ratio; *CI*=confidence interval.

Critically, microscopic examination established direct causal linkage between setae exposure during swimming and subsequent rash development.

Pronounced age-related risk gradients align with established physiological susceptibility patterns and behavioral exposure differences. The 0–14-year age group demonstrated highest attack rates, consistent with pediatric dermatological vulnerability characterized by thinner stratum corneum, elevated transepidermal water loss, and diminished capacity for neutralizing environmental irritants (*3*). Prolonged aquatic exposure through recreational swimming substantially increased disease risk among younger participants. The 15–44-year age group exhibited elevated risk through frequent river contact during occupational activities (agricultural work) and recreational pursuits. Reduced risk in the 45–64-year and ≥65-year groups likely reflects decreased participation in high-risk aquatic behaviors.

This outbreak exemplifies a critical nexus between tourism development, ecological disruption, and public health. Anthropogenic factors — particularly tourism infrastructure including persistent nighttime illumination, recreational activities, and riverside barbecuing — disrupt ecosystem equilibrium. The phototactic behavior of *R. leucoscela* adults toward artificial light sources (*4*–*5*) expands geographic distribution and elevates reproductive density. These perturbations (anthropogenic habitat modification) create optimal conditions for R. leucoscela population explosions, culminating in elevated human exposure risks. This reveals eco-tourism dynamics as upstream determinants of disease emergence, extending beyond conventional vector-control frameworks..

This study had several limitations. First, recall bias may have influenced self-reported exposures, potentially inflating odds ratios. Second, case under-ascertainment of mild cases among residents and tourists could have underestimated attack rates while overestimating odds ratios. Third, absence of quantitative exposure metrics (e.g., setae concentration) precluded dose-response analysis, limiting ability to define intervention thresholds. Fourth, incomplete baseline data on meteorological conditions and vegetation dynamics compromised capacity for spatiotemporal risk prediction and targeted intervention planning.

The dermatitis outbreak generated substantial long-term community impacts across multiple domains. First, ecological disruption from *R. leucoscela* proliferation indicated disrupted interspecies equilibrium, potentially triggering cascading threats to species sharing ecological niches. Prolonged imbalance may reduce biodiversity, simplify ecosystem structure, and compromise environmental resilience. Second, tourism economic recession resulted from diminished attractiveness and declining visitation rates. Peak-season revenue losses strained cash flow, particularly challenging small operators and increasing closure risks. Third, downstream sectoral contraction affected linked industries including hospitality and transport, with reduced hotel occupancy, restaurant patronage,

and underutilized infrastructure precipitating broader regional economic destabilization. Fourth, health and demographic consequences included elevated dermatitis risks from chronic exposure to urticating setae, while recurrent outbreaks undermined environmental safety confidence. Prolonged health threats may impair quality of life, exacerbate psychological distress, and accelerate population out-migration.

To achieve a sustainable balance between tourism benefits and ecological conservation, comprehensive multidimensional coordination is essential. We propose integrated approaches: First, strengthen ecological protection through defined conservation boundaries and zoned management strategies. Core ecological areas (including water sources and natural habitats) must be strictly protected by prohibiting high-risk activities such as camping and barbecuing. Scientific boundary delineation between tourist zones and protected areas ensures development activities do not interfere with critical habitats. Second, implement biological monitoring systems utilizing big data analytics to track larval breeding cycles and identify high-risk periods. During these periods, sensitive zones should be temporarily closed to minimize anthropogenic interference while maintaining conservation-tourism balance. Third, enhance regulatory frameworks and strengthen enforcement mechanisms. Establish joint enforcement systems across environmental protection, cultural tourism, and urban management sectors. Target violations such as illegal barbecuing and littering through collaborative governance. Promote "Leave No Trace" principles and advocate behavioral guidelines including eco-equipment use and complete waste removal. Fourth, strengthen public education through comprehensive warning signage at entrances and camping sites to enhance visitors' understanding of ecological risks and conservation requirements. Fifth, develop comprehensive contingency plans including protocols for rapid case identification, environmental risk assessment, targeted vector control, and public communication for sudden ecological events. These plans should integrate rapid medical-environmental agency coordination to mitigate negative impacts promptly. Through these measures, sustainable equilibrium between economic gains and ecological conservation can be established, securing long-term tourism viability and ecosystem stability.

Conflicts of interest: No conflicts of interest.

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Ethical statement: This outbreak investigation was conducted as part of routine public health surveillance activities and does not require formal ethical approval.

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