

Recent HIV Infection Surveillance Using a Rapid Test for Recent Infection among Persons Newly Diagnosed with HIV in Thailand: Establishment, Implementation, Initial outcomes, and Lessons Learned

Kriengkrai Srithanaviboonchai, Thitipong Yingyong, Theerawit Tasaneeyapan, Supaporn Suparak, Supiya Jantaramanee, Benjawan Roudreo, Suvimon Tanpradech, Jarun Chuayen, Apiratee Kanphukiew, Thananda Naiwatanakul, Suchunya Aungkulanon, Michael Martin, Chunfu Yang, Bharat Parekh, Sanny Chen Northbrook

Submitted to: JMIR Public Health and Surveillance on: August 06, 2024

Disclaimer: © **The authors. All rights reserved.** This is a privileged document currently under peer-review/community review. Authors have provided JMIR Publications with an exclusive license to publish this preprint on it's website for review purposes only. While the final peer-reviewed paper may be licensed under a CC BY license on publication, at this stage authors and publisher expressively prohibit redistribution of this draft paper other than for review purposes.

Table of Contents

Original Manuscript.......5

Recent HIV Infection Surveillance Using a Rapid Test for Recent Infection among Persons Newly Diagnosed with HIV in Thailand: Establishment, Implementation, Initial outcomes, and Lessons Learned

Kriengkrai Srithanaviboonchai^{1, 2}; Thitipong Yingyong³; Theerawit Tasaneeyapan⁴; Supaporn Suparak⁵; Supiya Jantaramanee³; Benjawan Roudreo³; Suvimon Tanpradech⁴; Jarun Chuayen²; Apiratee Kanphukiew⁴; Thananda Naiwatanakul⁴; Suchunya Aungkulanon⁴; Michael Martin⁶; Chunfu Yang⁶; Bharat Parekh⁶; Sanny Chen Northbrook⁴

Corresponding Author:

Kriengkrai Srithanaviboonchai Faculty of Medicine Chiang Mai University 110 Intavaroros road, Sriphum, Maung, Chiang Mai TH

Abstract

Background: A recent infection testing algorithm (RITA) incorporating case surveillance (CS) with the rapid test for recent HIV infection (RTRI) was integrated into HIV testing services in Thailand.

Objective: To describe the establishment of the recent HIV infection surveillance and report lessons learned and initial outcomes from April through August 2022

Methods: We conducted desk reviews, developed a surveillance protocol and manual, selected sites, trained staff, implemented surveillance, and analyzed outcomes. Remnant blood specimens of consenting newly diagnosed individuals were tested using the AsantéTM HIV-1 Rapid Recency® Assay. Duration of HIV infection was classified as RTRI-recent or RTRI-long-term. Individuals testing RTRI-recent with CD4<200 or opportunistic infections were classified as RITA-CS-long-term.

Results: Two hundred and one hospitals in 14 high-burden HIV provinces participated in surveillance. Of these, 69 reported ?1 HIV diagnosis during the surveillance period. Of 1,053 newly diagnosed cases, 64 (6.1%) were classified as RITA-CS-recent. Self-reporting as transgender women (Adjusted Odds Ratio [AOR]: 7.41, 95% CI: 1.59-34.53) and men who have sex with men (AOR: 2.59, 95% CI: 1.02-6.56) compared to heterosexual, and students compared to office worker or employer (AOR: 3.76, 95% CI: 1.25-11.35) were associated with RITA-CS-recent infection in multivariate analysis. Proper selection of surveillance sites, utilizing existing surveillance tools and systems, and conducting frequent follow up and supervision visits were most commonly cited as lessons learned to inform the next surveillance phase.

Conclusions: Recent HIV infection surveillance can provide an understanding of current epidemiologic trends to inform HIV prevention interventions to interrupt ongoing or recent HIV transmission. Key success factors of the HIV recent infection surveillance in Thailand include a thorough review of the existing HTS service delivery system, a streamlined workflow, strong laboratory and health services, and regular communication between sites and the Provincial Health Offices.

(JMIR Preprints 06/08/2024:65124)

DOI: https://doi.org/10.2196/preprints.65124

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

¹Faculty of Medicine Chiang Mai University Chiang Mai TH

²Research Institute for Health Sciences Chiang Mai University Chiang Mai TH

³Department of Disease Control Ministry of Public Health Nonthaburi TH

⁴Division of Global HIV/TB U.S. Centers for Disease Control and Prevention Nonthaburi TH

⁵Department of Medical Sciences Ministry of Public Health Nonthaburi TH

⁶Division of Global HIV/TB U.S. Centers for Disease Control and Prevention Atlanta US

✓ Please make my preprint PDF available to anyone at any time (recommended).

Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users. Only make the preprint title and abstract visible.

- No, I do not wish to publish my submitted manuscript as a preprint.
- 2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?
- ✓ Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).

Original Manuscript

Recent HIV Infection Surveillance Using a Rapid Test for Recent Infection among Persons Newly Diagnosed with HIV in Thailand: Establishment, Implementation, Initial outcomes, and Lessons Learned

Kriengkrai Srithanaviboonchai^{1,2}, Thitipong Yingyong^{3,§}, Theerawit Tasaneeyapan⁴, Supaporn Suparak⁵, Supiya Jantaramanee³, Benjawan Roudreo³, Suvimon Tanpradech⁴, Jarun Chuayen¹, Apiratee Kanphukiew⁴, Thananda Naiwatanakul⁴, Suchunya Aungkulanon⁴, Michael Martin⁶, Chunfu Yang⁶, Bharat Parekh⁶, Sanny Chen Northbrook⁴

Department of Disease Control 88/21 Tiwanon Rd. Talard-Kwan Nonthaburi, 11000, Thailand Tel. +66 02 5903000

Email: thity_24@yahoo.com

Abstract

¹Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand

² Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

³ Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand

⁴Division of Global HIV/TB, U.S. Centers for Disease Control and Prevention, Nonthaburi, Thailand

⁵ Department of Medical Sciences, Ministry of Public Health, Nonthaburi, Thailand

⁶ Division of Global HIV/TB, U.S. Centers for Disease Control and Prevention, Atlanta, United States

[§] Corresponding author: Thitipong Yingyong

Background: A recent infection testing algorithm (RITA) incorporating case surveillance (CS) with the rapid test for recent HIV infection (RTRI) was integrated into HIV testing services in Thailand.

Objectives: To describe the establishment of the recent HIV infection surveillance and report lessons learned and initial outcomes from April through August 2022

Methods: We conducted desk reviews, developed a surveillance protocol and manual, selected sites, trained staff, implemented surveillance, and analyzed outcomes. Remnant blood specimens of consenting newly diagnosed individuals were tested using the Asanté[™] HIV-1 Rapid Recency[®] Assay. Duration of HIV infection was classified as RTRI-recent or RTRI-long-term. Individuals testing RTRI-recent with CD4<200 or opportunistic infections were classified as RITA-CS-long-term.

Results: Two hundred and one hospitals in 14 high-burden HIV provinces participated in surveillance. Of these, 69 reported ≥1 HIV diagnosis during the surveillance period. Of 1,053 newly diagnosed cases, 64 (6.1%) were classified as RITA-CS-recent. Self-reporting as transgender women (Adjusted Odds Ratio [AOR]: 7.41, 95% CI: 1.59-34.53) and men who have sex with men (AOR: 2.59, 95% CI: 1.02-6.56) compared to heterosexual, and students compared to office worker or employer (AOR: 3.76, 95% CI: 1.25-11.35) were associated with RITA-CS-recent infection in multivariate analysis. Proper selection of surveillance sites, utilizing existing surveillance tools and systems, and conducting frequent follow up and supervision visits were most commonly cited as lessons learned to inform the next surveillance phase.

Conclusions: Recent HIV infection surveillance can provide an understanding of current epidemiologic trends to inform HIV prevention interventions to interrupt ongoing or recent HIV transmission. Key success factors of the HIV recent infection surveillance in Thailand include a thorough review of the existing HTS service delivery system, a streamlined workflow, strong laboratory and health services, and regular communication between sites and the Provincial Health Offices.

Keywords: rapid test, surveillance, HIV, AIDS, diagnosis, Thailand

Introduction

Early detection and treatment of newly infected persons is crucial for infectious disease control. In the case of HIV, people are more likely to pass on the virus to others due to high ongoing risk and unawareness of the infection (Ambrosioni et al., 2012; Paraskevis et al., 2011; Wawer et al., 2005). The United States Centers for Disease Control and Prevention (U.S. CDC) developed assays that can detect recent HIV infections, which included the less-sensitive EIA (Janssen et al., 1998) then the BED-Capture Enzyme Immunoassay (BED-CEIA) (Parekh et al., 2002), followed by the Limiting Antigen (Lag) Avidity EIA (Duong et al., 2012). These laboratory tests have been widely used to estimate HIV-1 incidence in cross-sectional surveys. However, these laboratory-based assays must be performed centrally, and the test results are not available immediately. This limits the assays' value in identifying those most likely to spread the infection.

Rapid testing can provide timely and useful information regarding recent HIV infections for surveillance purposes. Recent infection surveillance aids in locating hotspots of recent HIV infections, and when triangulated with data from other surveillance systems and program data may help identify populations and geographic areas where ongoing or recent transmission is occurring (Kim et al., 2019; Telford et al., 2022). In 2013, the U.S. CDC developed a novel rapid test (Granade et al., 2013), which later became commercially available as Asanté™ HIV-1 Rapid Recency® Assay (Sedia BioSciences, Beaverton, OR, USA). It can be used to simultaneously verify HIV infections and distinguish between long-term and recent HIV infections (Yufenyuy et al., 2022). This lateral flow assay (Sadeghi et al., 2021) was a format modification of the Limiting Antigen (Lag) Avidity EIA assay which distinguished long-term and recent HIV infections based on differential antibody binding at limiting antigen concentrations. The results can be interpreted both visually and with a strip reader. With this rapid test for recent HIV infection (RTRI), there is a potential to verify HIV diagnosis and detect recent infections on-site within minutes. To date, there are two commercially available point-of-care RTRI assays (WHO and UNAIDS: 2022 technical guidance, 2022); Alere Ag/ Ab Combo (Abbott Laboratory, Abbott Park, IL) that claims to detect acute infection before development of HIV antibodies and Asante Recency Assay which detects recent infection post seroconversion. The Asanté™ HIV-1 Rapid Recency® Assay has been validated in the laboratory as well as in the field and can detect more new infections due to longer recency duration (Agyemang et al., 2022; Yufenyuy et al., 2022).

The TRACE initiative (Tracking with Recency Assays to Control the Epidemic) was launched in

2019. The surveillance was funded by the United States President's Emergency Plan for AIDS Relief (PEPFAR) and implemented in several PEPFAR-supported countries (Kim et al., 2019). Through TRACE, one of the recent infection testing algorithms (RITA) was implemented, which includes RTRI testing as an additional test in HIV testing services (HTS). The integration of RTRI into routine HTS offers an opportunity for program-based surveillance in persons with new HIV diagnoses in facility- and community-based testing sites (Rwibasira et al., 2021).

Thailand joined the TRACE initiative in 2020. The project started as a demonstration project in Bangkok and expanded to include two additional provinces in 2021. During the first two years, RITA comprised of RTRI and viral load (VL) testing for those RTRI-recent, in combination with case surveillance (CS), was used to characterize HIV infections as recent or long-term (Kassanjee et al., 2016). In 2022, Thailand established the surveillance of recent HIV infections using RITA-CS. The use of VL testing as a proxy for antiretroviral treatment (ART) use was discontinued after results from the demonstration project showed that the use of RITA-CS gave equal/more accurate recency classification outcomes when comparing to RITA-VL (Suraratdecha et.al.,2023). Using CS to exclude or reclassify those who were previously diagnosed, on ART, or had advanced HIV disease before or after RTRI testing, respectively, improved classification of recency status. In this article, we describe the establishment of Thailand's HIV-1 recent infection surveillance system using the RTRI test and CS, report the lessons learned, and initial results from April through August 2022.

Methods

1. Desk review and gathering of relevant information

A review of the findings and challenges/lessons from earlier TRACE projects conducted in Thailand and other nations was performed. The related service delivery and data management systems were also reviewed through a series of discussions with relevant organizations. These included the service delivery systems at HTS and ART clinics, national algorithm of HIV diagnosis, logistics of CD4 and HIV VL laboratory testing, and current HIV-related data collection and data management system models.

2. Development of surveillance protocol and manual

The essential components of the protocol were drafted based on information gathered and the goals established. The protocol's overall draft, inclusion and exclusion criteria, service flow at the HTS, case record form, and data management system were handled by the Chiang Mai University Research Health Institute for Health Sciences (RIHES). It was the responsibility of the Thai Ministry

of Public Health to draft the information regarding the supplies and logistics of the RTRI test kits, as well as the method of staff time and effort reimbursement. The RTRI laboratory training curriculum, procedure and the laboratory QA/QC protocol were the responsibility of the Thai National Institute of Health (NIH). The U.S. CDC was responsible for drafting the informed consent and counseling process. The team meetings considered all inputs before developing the manual and staff training curriculum.

3. Selection of surveillance sites

Provinces with >20% annual increase of new HIV diagnoses and new HIV diagnoses among men who have sex with men (MSM) and transgender women (TGW) from 2017 to 2020 were selected to participate. After selecting the provinces, all public hospitals within each selected province were invited to participate. Laboratory hubs were assigned based on the district of each participating hospital by the Provincial Health Office, except in Bangkok where each hospital had its own laboratory hub.

4. Ethical Clearance

The underlying protocol was deemed a surveillance activity by the Thai Ministry of Public Health Ethics Committee and reviewed by CDC, deemed not research and was conducted with applicable federal law and CDC policy. See e.g., 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.

5. Staff training

There were two different types of training for the personnel involved in this project. The nurse counselor and laboratory staff were trained on the project overview, RTRI, service flow, data management, data use, and logistics of blood samples. The overall project training was a full 1-day training, and hospitals were grouped into 6 groups for 6 separate trainings. Laboratory staff members were trained in RTRI laboratory techniques as well as associated internal quality control (IQC) and external quality assessment (EQA) procedures. This was a half-day training, and the sites were grouped into 3 groups for 3 separate trainings. Due to the COVID-19 situation at the time, the training was conducted online in March 2022.

6. Implementation

The first-year implementation began in April 2022 and ended in August 2022. The project team went to all provincial sites to meet with staff in person to discuss progress and problems with regard to the implementation and management of the project. The team also went to selected hospitals and laboratories reporting newly diagnosed HIV cases to gain firsthand information about the sites.

These site visits served to monitor activities, address any problems delaying the commencement of activities, and address any queries that the sites had. The RIHES staff kept track of the data entered in the system and communicated with the sites of any missing data. Throughout this implementation phase, a series of online meetings with the provincial site coordinators were also held.

7. Service flow

- a. *Checking eligibility criteria:* Using the national identification number, the HIV counselor checked whether the client had a previous HIV diagnosis or ART history in the National AIDS Program database (NAP). Information on opportunistic infections (OI) and CD4 count at the time of HIV diagnosis was retrieved from medical records once available and was used to improve the accuracy of the test as part of CS.
- b. *Verbal Informed Consent:* During post-test HIV counseling, clients who tested positive for HIV following the national 3-test algorithm at specific clinics (HIV, TB, STI, and antenatal), aged ≥15 years old, no previous HIV diagnosis or <28 days of antiretroviral treatment, residing in selected provinces, and able to communicate in Thai were asked for their consent to use remnant blood collected for HIV testing for RTRI. The RTRI result was only used for surveillance purposes and was not returned to the client.
- c. *RTRI testing:* The RTRI test was performed on the left-over blood samples for those RTRI-consented clients who tested HIV-positive. The RTRI results were classified as RTRI-recent (infection acquired in the past 12 months), RTRI-long-term (infection acquired more than 12 months ago) or RTRI-inconclusive and recorded in the project's data management system by laboratory staff. We used case surveillance (CS) as part of a recent infection testing algorithm (RITA) to identify late presenters. Individuals with a RTRI-recent result and CD4<200 or OIs were reclassified as RITA-CS- long-term. All other RTRI-recent individuals were classified as RITA-CS-recent. To reduce the cost of the recency surveillance program, eligible blood samples from community hospitals that had a small number of clients were sent to the laboratory hubs for RTRI testing.
- d. *Data collection:* The team designed a 1-page RTRI-1 case record form to collect individual client information: 1) demographics: age, sex, ever registered in NAP, nationality, residential postal code, marital status, and occupation; 2) HIV risk: key population, risk behaviors, risk venue, timing of the last risk behavior; and 3) RTRI result.
- e. *Data management system:* Alongside the data collection tools, a specific online data management system was created. Healthcare workers had two options for entering data: directly into the

system or first writing it down on the paper form before entering it into the online system. Demographics and risk behaviors already entered into other data systems (hospital information system and laboratory data system) were transferred to the project's data management system. Project staff checked the data in the system regularly for data inconsistencies and missing data before contacting the provincial health officer to assist with problem-solving.

8. Data analysis

Data were entered, cleaned, and analyzed using the Statistical Package for the Social Sciences (SPSS), version 22.0 (IBM Corporation, Armonk, NY, USA). Frequencies, percentages, and means were given in descriptive statistics when applicable. The chi-square test was performed to compare categorical variables. The primary outcome was the proportion of RITA-CS- recent HIV infection among newly diagnosed individuals after excluding those with OI, CD4<200/mm3, previous HIV diagnoses, or ART history in NAP. Crude Odds Ratios (COR) were calculated to determine risk factors for RITA-CS-recent HIV infection. All predictor variables with significant associations were included in multiple logistic regression after accounting for any potential multicollinearity. Adjusted Odds Ratios (AOR) were calculated to determine independent risk factors for RITA-CS-recent HIV infection. We calculated 95% confidence intervals (CIs) for both simple and multivariate logistic regressions. For all analyses, a p-value of less than 0.05 was regarded as statistically significant.

9. Lessons Learned:

A meeting was held with 26 co-investigators and participating staff and moderated by Department of Disease Control after completing data collection to share lessons learned and inform planning and implementation of the next round of recency surveillance in 2023.

Results

Study sites

There were 14 provincial sites participating in the surveillance. Only one province per health region was selected for the 13 health regions, except in region 7 which had 2 provinces. Altogether, 201 hospitals and 41 laboratory hubs volunteered to participate in recency surveillance (Table 1).

Table 1. Distribution and proportion of participating hospitals and corresponding laboratory hubs within each province by geographic region and health region, Thailand, April – August 2022.

Geographi c Region	Health region	Province	% Participating Hospitals % (n/N)	No. of Corresponding Laboratory Hubs
North	1	Chiang Rai	100 (18/18)	2
	2	Phitsanulok	22.2 (2/9)	2
	3	Kamphaeng Phet	100 (12/12)	3
Central	4	Nonthaburi	87.5 (7/8)	1
	5	Ratchburi	100 (11/11)	4
	6	Chon Buri	8.3 (1/12)	1
Northeast	7	Maha Sarakham	7.7 (1/13)	1
		Khon Kaen	7.7 (2/26)	2
	8	Udon Thani	4.5 (1/22)	1
	9	Buri Ram	100 (23/23)	2
	10	Mukdahan	53.8 (7/13)	1
South	11	Surat Thani	100 (21/21)	7
	12	Songkhla	100 (17/17)	4
Bangkok	13	Bangkok	83.9 (78/93)	11
	Total		67.4 (201/298)	41

Of the 201 participating public hospitals, 69 reported at least one newly diagnosed HIV infection (ranging from 17-260 newly diagnosed HIV individuals per facility) during the surveillance period. Among 1,794 newly diagnosed HIV individuals, 1,053 consented to the RTRI test. After excluding 14 inconclusive results, 96 (9.2%) were classified as RTRI-recent. Of these, 32 (33.3%) had an OI or CD4 < 200 cells/mm³ at the time of HIV diagnosis and were reclassified as RITA-CS-long-term. A total of 64 (6.2%) were classified as RITA-CS-recent and 975 (93.8%) were classified as RITA-CS-long-term infections (Figure 1).

Figure 1. Flow diagram of reclassified RTRI-recent and reclassified RTRI-long-term HIV infections among newly diagnosed persons living with HIV in 14 selected provinces, Thailand, April – August 2022 (N=1,784).

Notes: PLHIV: persons living with HIV, RTRI: rapid test for recent infection, RITA: recent infection testing algorithm, OI: opportunistic infections.

Demographic comparisons between RITA-CS-recent and RITA-CS-long-term infections are shown in Table 2. Age, gender, marital status, geographic region of residence, and type of employment were statistically associated with duration of HIV infection. Among RITA-CS- recent infections, the modal categories were persons aged ≥20 years (82.8%), male (78.1%), MSM (48.4%), single (56.3%), residing in the Northeast region (46.9%), Thai (98.4%), and students (26.6%). Similar demographic characteristics were reported among RITA-CS-long-term infections, except for type of employment with the majority reporting as laborers (36.0%).

Table 2. Demographic characteristics of RITA-CS-recent and RITA-CS-long term HIV infections among newly diagnosed persons living with HIV in 14 selected provinces, Thailand, April – August 2022 (N=1,039)

	3	Duration of HIV infection status				
Demographic characteristics	Total N = 1,039	RITA-CS- Recent n = 64 n (%)	RITA-CS-Long term n = 975 n (%)	<i>P</i> -value		
Age in years (mean \pm SD) = 34.7 \pm 12.5						
15-19	76 (7.3)	11 (17.2)	65 (6.7)	.005		
≥20	963 (92.7)	53 (82.8)	910 (93.3)			
Sex						
Male	781 (75.2)	50 (78.1)	731 (75.0)	.572		
Female	258 (24.8)	14 (21.9)	244 (25.0)			
Gender/sexuality						
Heterosexual	357 (34.4)	9 (14.1)	348 (35.7)	.004		

		Duration of HIV infection status			
Demographic characteristics	Total N = 1,039	RITA-CS- Recent	RITA-CS-Long term	Darahaa	
	·	n = 64 n (%)	n = 975 n (%)	<i>P</i> -value	
Men who have sex with men	397 (38.2)	31 (48.4)	366 (37.5)		
Transgender	27 (2.6)	4 (6.3)	23 (2.4)		
Bisexual	24 (2.3)	3 (4.7)	21 (2.2)		
Other	168 (16.2)	10 (15.6)	158 (16.2)		
Missing	66 (6.4)	7 (10.9)	59 (6.1)		
Marital status					
Single	448 (43.1)	36 (56.3)	412 (42.3)	.032	
Married	275 (26.5)	9 (14.1)	266 (27.3)		
Widow/Separate	56 (5.4)	1 (1.6)	55 (5.6)	(5)	
Missing	260 (25.0)	18 (28.1)	242 (24.8)		
Geographical region of reside	nce				
Central	211 (20.3)	5 (7.8)	206 (21.1)	8.9)	
North	92 (8.9)	5 (7.8)	87 (8.9)		
Northeast	319 (30.7)	30 (46.9)	289 (29.6)		
South	157 (15.1)	6 (9.4)	151 (15.5)		
Bangkok	260 (25.0)	18 (28.1)	242 (24.8)		
Nationality			<u></u>		
Thai	1,002 (96.4)	63 (98.4)	939 (96.3)	.373	
Non-Thai	37 (3.6)	1 (1.6)	36 (3.7)		
Employment					
Unemployed	81 (7.8)	0 (0.0)	81 (7.8)	< .001	
Office worker, government officer, employer	181 (17.4)	9 (14.1)	172 (17.6)		
Laborer	366 (35.2)	15 (23.4)	351 (36.0)		
Student	88 (8.5)	17 (26.6)	71 (7.3)		
Missing	323 (31.1)	23 (35.9)	300 (30.8)		

Notes: SD: standard deviation, RITA: recent infection testing algorithm, CS: case surveillance

A significantly higher odds of RITA-CS-recent HIV infections were seen among those aged 15-19 years old (14.5%) compared to \geq 20 years old (5.5%), MSM (7.8%) and TGW (14.8%) compared to heterosexual (2.5%), residing in the Northeast (9.4%) and Bangkok (6.9%) compared to the Central region (2.4%), and being a student (19.3%) compared to office worker/government officer or employer (5.0%), In multivariate analysis, self-reporting as MSM (AOR: 2.59, 95% CI: 1.02 – 6.56), TGW (AOR: 7.41, 95% CI: 1.59 – 34.53), and being a student (AOR: 3.76, 95% CI: 1.25-11.35) were independent risk factors for RITA-CS-recent HIV infection after controlling for age and other

variables (Table 3).

Table 3. Risk factors associated with RITA-CS-recent HIV infection among newly diagnosed persons living with HIV in 14 selected provinces, Thailand, April–August 2022 (N = 1,039)

	RITA-CS-recent HIV infection (n = 64)			
Characteristics	% (n/N)	Crude Odds Ratio COR (95% CI)	Adjusted Odds Ratio AOR (95% CI)	
Age in years				
15-19	14.5 (11/76)	2.91 (1.45-5.83)*	1.53 (0.49-4.75)	
≥20	5.5 (53/963)	1	1	
Sex				
Male	6.4 (50/781)	1.19 (0.65-2.19)	a	
Female	5.4 (14/258)	1	Co	
Gender/sexuality	1			
Heterosexual	2.5 (9/357)	1	1	
Men who have sex with men	7.8 (31/397)	3.28 (1.54-6.98)*	2.59 (1.02-6.56)*	
Transgender	14.8 (4/27)	6.73 (1.93-23.50)*	7.41 (1.59-34.53)*	
Bisexual	12.5 (3/24)	5.52 (1.39-21.93)*	4.43 (0.84-23.47)	
Marital status		0.6		
Single	8.0 (36/448)	4.81 (0.65-35.75)	a	
Married	3.3 (9/275)	1.86 (0.23-14.99)		
Widow/Separate	1.8 (1/56)	1		
Geographical region of reside	ence			
Central	2.4 (5/211)	1	a	
North	5.4 (5/92)	2.34 (0.67-8.39)		
Northeast	9.4 (30/319)	4.28 (1.63-11.21)*		
South	3.8 (6/157)	1.64 (0.49-5.46)		
Bangkok	6.9 (18/260)	3.06 (1.12-8.40)*		
Nationality				
Thai	6.3 (63/1,002)	2.83 (0.38-20.93)	a	
Non-Thai	2.7 (1/37)	1		
Employment				
Unemployed	0.0 (0/81)	n/a	n/a	
Office worker, government officer, employer	5.0 (9/181)	1	1	
Laborer	4.1 (15/366)	1.34 (0.61-2.95)	0.90 (0.35-2.28)	
Student	19.3 (17/88)	4.58 (1.95-10.75)*	3.76 (1.25-11.35)*	

Notes: *Statistically significant (p<0.05), a = not included in the analysis

Lessons learned

A number of lessons learned were identified to inform the next phase of recency surveillance: a)

exclude hospitals that do not report newly diagnosed HIV-positive infections in future plans; b) utilize existing surveillance database, data management system, and dashboards in the next phase; c) conduct frequent follow up and supervision of sites to identify issues, challenges, and best practices that can be shared with others; d) continue to provide laboratory trainings to ensure accuracy, reliability, and quality of RTRI testing; and e) continue to monitor the accuracy of results across all laboratories and ensure robust quality control and external quality assurance systems are in place.

Discussion

HIV recent infection surveillance combining CS and RTRI tests has been established and integrated into Thailand's HIV surveillance system. Several factors contributed to the successful implementation of this project: a) thorough review of existing related service delivery and data management systems, b) development of a project workflow that was integrated into existing HTS, c) strong existing foundation of laboratory and health services, d) early site visits to gather feedback for system improvement, e) regular communication with the sites, and f) development of dashboard for visualization of key indicators.

Use of recent infection testing assays alone can yield false recent results due to potential misclassification of recent infection cases with advanced HIV disease, ART, or elite suppressors (Hladik et al., 2012; Laeyendecker et al., 2008). The World Health Organization and populations-based HIV impact assessment surveys have combined recency assays with additional parameters such as VL and/or checking for ARVs in blood, in lowering the false recent rate (FRR) for HIV incidence estimates (Kassanjee et al., 2016; Voetsch et al., 2021). In Thailand, the initial demonstration project showed that combining CS data and RTRI testing (RITA-CS) was more accurate in classifying recent infection status than RTRI with VL testing (RITA-VL) (These data will be published in a separate report). Our recency surveillance results indicated that those with AHD, when misclassified, could not be identified by RITA-VL due to their high VL but CS information helped improve their classification. The streamlined process of RTRI testing at HTS and CS data use has enabled Thailaind to integrate the HIV recent infection surveillance into the routine surveillance system as reported here.

In addition to RTRI results, history of NAP registration, OI, and CD4 information were incorporated into the analysis. By excluding or reclassifying clients with evidence of long-term HIV infection (presence of OIs, CD4<200, prior HIV diagnosis, ART history), our results showed an accurate

proportion of recent infections among newly diagnosed persons living with HIV. The proportion of recent HIV infection dropped from 10.2% to 6.2% after reclassifying RTRI-recent clients with history of HIV diagnosis, OI, and CD4 <200 as RITA-CS-long-term HIV infections. When determining RTRI-recent infections, this algorithm should be considered in countries with a strong CS as it is more precise than utilizing RTRI results alone or with RITA-VL. Both RITA-CS and RTRI data were able to identify gender minority populations, such as TGW and MSM, as risk groups for recent HIV infection outside of students.

To increase the efficiency of the surveillance program, future plans should only include hospitals that are sufficient in size and have high risk populations within their jurisdiction. To reduce the probability of misclassification, known cases of longstanding HIV infection should be screened out first using information from health records, both locally and nationally. These include clients who have previously registered for HIV, received an OI diagnosis, and had low CD4. Additional information is needed to recommend whether Thailand should implement RTRI surveillance in HTS as one of its long-term country-wide HIV surveillance systems since there are potential biases when interpreting recency results from HTS programs (*WHO and UNAIDS: 2022 technical guidance*, 2022). However, this program-based surveillance can complement cross-sectional surveys and provide additional data for triangulation.

There are several limitations to this analysis. First, since participation was voluntary and not all HTS sites within large hospitals or hospitals within a selected province participated in this surveillance round, HIV diagnoses identified during the surveillance period may not be representative of the catchment area or province. Second, only one or two sites were selected to represent each province and results may not be generalizable to the entire province. Third, use of NAP has its limitations as it does not include newly diagnosed HIV cases in the private sector. Fourth, we gathered self-reported information on demographics. Fifth, individuals who frequently retest may be more likely to receive a recent infection test result than individuals who rarely test due to self-stigma, low perception of HIV risk, and other factors (i.e., long travel distance to clinic, low HIV knowledge, etc.). Finally, we were not able to re-test newly diagnosed PLHIV with an RTRI-inconclusive result and excluded them from the analysis.

In conclusion, through recent infection surveillance, we identified newly diagnosed individuals aged 15-19 years old, who self-reported as MSM or TGW, and students to be at higher risk for HIV

acquisition. Key factors contributing to the establishment and implementation of the HIV recent infection surveillance in Thailand include a thorough review of the existing HTS service delivery system, a streamlined workflow, strong foundation of laboratory and health services, and regular communication between sites and the Provincial Health Offices. When triangulated with other programs and surveillance data sources, RTRI-recency data may provide better understanding of current epidemiologic trends. Targeted interventions to prevent new infections among youth, TGW and MSM may help interrupt ongoing transmission in Thailand in near real-time.

Acknowledgments

This project was supported by the President's Emergency Plan for AIDS Relief through the U.S. Centers for Disease Control and Prevention under the terms of cooperative agreement CDC-RFA-GH16-1676. It was also partially supported by Chiang Mai University.

Conflict of interests

The authors declare that they have no competing interests.

Authors' contributions

K.S., T.Y., T.T., S.S., S.J., B.R., S.T., J.C., A.K., T.N., S.A., M.M., C.Y., B.P. and S.N., designed the research study. K.S., T.Y., T.T., S.S., S.J., B.R., S.T., J.C., and S.N. collected the data. M.M., C.Y., B.P., and S.N. contributed essential test kits. K.S. and J.C. analysed the data. K.S. and S.N. wrote the paper. All authors contributed to the article, have read, and approved the final manuscript.

Disclaimer

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the funding agencies.

Data Availability Statement

Data available on request due to privacy/ethical restrictions.

References

Abdool Karim, Q., Macklin, R., Gruskin, S., Klucking, S., Lockett, L., Maxwell, C. J., Mayer, K. H., Sanders, E., & Sawe, F. (2020). HIV recency testing: should results be disclosed to individuals tested? *J Int AIDS Soc*, 23(8), e25584. https://doi.org/10.1002/jia2.25584

Agyemang, E. A., Kim, A. A., Dobbs, T., Zungu, I., Payne, D., Maher, A. D., Curran, K., Kim, E., Kwalira, H., Limula, H., Adhikari, A., Welty, S., Kandulu, J., Nyirenda, R., Auld, A. F., Rutherford, G. W., & Parekh, B. S. (2022). Performance of a novel rapid test for recent HIV infection among newly-diagnosed pregnant adolescent girls and young women in four high-HIV-prevalence districts-Malawi, 2017-2018. *PloS One*, *17*(2), e0262071. https://doi.org/10.1371/journal.pone.0262071

Ambrosioni, J., Junier, T., Delhumeau, C., Calmy, A., Hirschel, B., Zdobnov, E., Kaiser, L., & Yerly, S. (2012). Impact of highly active antiretroviral therapy on the molecular epidemiology of newly diagnosed HIV infections. *Aids*, *26*(16), 2079-2086. https://doi.org/10.1097/QAD.0b013e32835805b6

Duong, Y. T., Mavengere, Y., Patel, H., Moore, C., Manjengwa, J., Sibandze, D., Rasberry, C., Mlambo, C., Li, Z., Emel, L., Bock, N., Moore, J., Nkambule, R., Justman, J., Reed, J., Bicego, G., Ellenberger, D. L., Nkengasong, J. N., & Parekh, B. S. (2014). Poor performance of the determine HIV-1/2 Ag/Ab combo fourth-generation rapid test for detection of acute infections in a National Household Survey in Swaziland. *J Clin Microbiol*, 52(10), 3743-3748. https://doi.org/10.1128/jcm.01989-14

Duong, Y. T., Qiu, M., De, A. K., Jackson, K., Dobbs, T., Kim, A. A., Nkengasong, J. N., & Parekh, B. S. (2012). Detection of recent HIV-1 infection using a new limiting-antigen avidity assay: potential for HIV-1 incidence estimates and avidity maturation studies. *PloS One*, *7*(3), e33328. https://doi.org/10.1371/journal.pone.0033328

Granade, T. C., Nguyen, S., Kuehl, D. S., & Parekh, B. S. (2013). Development of a novel rapid HIV test for simultaneous detection of recent or long-term HIV type 1 infection using a single testing device. *AIDS Res Hum Retroviruses*, *29*(1), 61-67. https://doi.org/10.1089/aid.2012.0121

Hladik, W., Olara, D., Mermin, J., Moore, D., Were, W., Alexander, L., & Downing, R. (2012). Effect of CD4+ T cell count and antiretroviral treatment on two serological HIV incidence assays. *AIDS Res Hum Retroviruses*, *28*(1), 95-99. https://doi.org/10.1089/aid.2010.0347

Janssen, R. S., Satten, G. A., Stramer, S. L., Rawal, B. D., O'Brien, T. R., Weiblen, B. J., Hecht, F. M., Jack, N., Cleghorn, F. R., Kahn, J. O., Chesney, M. A., & Busch, M. P. (1998). New testing strategy to detect early HIV-1 infection for use in incidence estimates and for clinical and prevention purposes. Jama, 280(1), 42-48. https://doi.org/10.1001/jama.280.1.42

Kassanjee, R., Pilcher, C. D., Busch, M. P., Murphy, G., Facente, S. N., Keating, S. M., McKinney, E., Marson, K., Price, M. A., Martin, J. N., Little, S. J., Hecht, F. M., Kallas, E. G., & Welte, A. (2016). Viral load criteria and threshold optimization to improve HIV incidence assay characteristics. *Aids*, *30*(15), 2361-2371. https://doi.org/10.1097/qad.0000000000000001209

Kim, A. A., Behel, S., Northbrook, S., & Parekh, B. S. (2019). Tracking with recency assays to control the epidemic: real-time HIV surveillance and public health response. *Aids*, *33*(9), 1527-1529. https://doi.org/10.1097/qad.0000000000002239

Laeyendecker, O., Rothman, R. E., Henson, C., Horne, B. J., Ketlogetswe, K. S., Kraus, C. K., Shahan, J., Kelen, G. D., & Quinn, T. C. (2008). The effect of viral suppression on cross-sectional incidence testing in the johns hopkins hospital emergency department. *J Acquir Immune Defic Syndr*, *48*(2), 211-215. https://doi.org/10.1097/QAI.0b013e3181743980

Suraratdecha, C., Jirajariyavej, S., Tanpradech, S., Na Autthaya, N.I., Tasaneeyapan, T., Chaiphosri, P., Naiwatanakul, T., Northbrook, S., Baker-Goering, M., Ussavarojpong, S. Economic evaluation of HIV infection recency at four health facilities in Bangkok, Thailand. In Abstracts of the 12th IAS Conference on

HIV Science, Brisbane, Australia, July 2023.

Paraskevis, D., Nikolopoulos, G., Tsiara, C., Paraskeva, D., Antoniadou, A., Lazanas, M., Gargalianos, P., Psychogiou, M., Malliori, M., Kremastinou, J., & Hatzakis, A. (2011). HIV-1 outbreak among injecting drug users in Greece, 2011: a preliminary report. *Euro Surveill*, *16*(36). https://doi.org/10.2807/ese.16.36.19962-en

Parekh, B. S., Kennedy, M. S., Dobbs, T., Pau, C. P., Byers, R., Green, T., Hu, D. J., Vanichseni, S., Young, N. L., Choopanya, K., Mastro, T. D., & McDougal, J. S. (2002). Quantitative detection of increasing HIV type 1 antibodies after seroconversion: a simple assay for detecting recent HIV infection and estimating incidence. *AIDS Res Hum Retroviruses*, *18*(4), 295-307. https://doi.org/10.1089/088922202753472874

Rwibasira, G. N., Malamba, S. S., Musengimana, G., Nkunda, R. C. M., Omolo, J., Remera, E., Masengesho, V., Mbonitegeka, V., Dzinamarira, T., Kayirangwa, E., & Mugwaneza, P. (2021). Recent infections among individuals with a new HIV diagnosis in Rwanda, 2018-2020. *PloS One*, *16*(11), e0259708. https://doi.org/10.1371/journal.pone.0259708

Sadeghi, P., Sohrabi, H., Hejazi, M., Jahanban-Esfahlan, A., Baradaran, B., Tohidast, M., Majidi, M. R., Mokhtarzadeh, A., Tavangar, S. M., & de la Guardia, M. (2021). Lateral flow assays (LFA) as an alternative medical diagnosis method for detection of virus species: The intertwine of nanotechnology with sensing strategies. *Trends Analyt Chem*, *145*, 116460. https://doi.org/10.1016/j.trac.2021.116460

Telford, C. T., Tessema, Z., Msukwa, M., Arons, M. M., Theu, J., Bangara, F. F., Ernst, A., Welty, S., O'Malley, G., Dobbs, T., Shanmugam, V., Kabaghe, A., Dale, H., Wadonda-Kabondo, N., Gugsa, S., Kim, A., Bello, G., Eaton, J. W., Jahn, A., . . . Auld, A. F. (2022). Geospatial Transmission Hotspots of Recent HIV Infection – Malawi, October 2019-March 2020. *MMWR Morb Mortal Wkly Rep*, *71*(9), 329-334. https://doi.org/10.15585/mmwr.mm7109a1

WHO and UNAIDS. Using Recency Assays for HIV Surveillance: 2022 technical guidance. (2022). (978-92-4-006438-6).

Wawer, M. J., Gray, R. H., Sewankambo, N. K., Serwadda, D., Li, X., Laeyendecker, O., Kiwanuka, N., Kigozi, G., Kiddugavu, M., Lutalo, T., Nalugoda, F., Wabwire-Mangen, F., Meehan, M. P., & Quinn, T. C. (2005). Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. *J Infect Dis*, *191*(9), 1403-1409. https://doi.org/10.1086/429411

Yufenyuy, E. L., Detorio, M., Dobbs, T., Patel, H. K., Jackson, K., Vedapuri, S., & Parekh, B. S. (2022). Performance evaluation of the Asante Rapid Recency Assay for verification of HIV diagnosis and detection of recent HIV-1 infections: Implications for epidemic control. PLOS Glob Public Health, 2(5), e0000316. https://doi.org/10.1371/journal.pgph.0000316