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Original Article

# Assessment of the performance regarding confirmatory diagnosis and initiation of antiretroviral therapy under a modified national HIV testing algorithm and pay-for-performance program in Taiwan

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**KEYWORDS**
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Time to ART initiation

**Abstract** *Background:* A pay-for-performance plan for rapid antiretroviral therapy (ART) commencement was initiated in 2018, while a modified testing algorithm offers immunochromatographic test (ICT) to replace Western blot (WB), and simultaneous testing with ICT and Nucleic Acid Amplification Test (NAAT) for HIV-positive sera was adopted in 2019 in Taiwan.
*Methods:* Serum specimens collected from 1117 suspected or confirmed HIV infection cases in 2016—2019 were reassessed the performance of WB, ICT, and NAAT. We reviewed the medical records of 10,732 individuals diagnosed with HIV in 2015—2021 to determine the time from screening to confirmatory diagnosis, followed by ART commencement.
*Results:* All 860 WB-positives were also positive by ICT and NAAT. The positive detection percentages were 37.0% by ICT and 51.4% by NAAT for 257 WB-indeterminate and -negative sera.

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The sensitivity for WB and ICT was 93.8% and 95.5%, respectively. In the people living with HIV (PLHIV) cohort, the median time from initial positive to confirmatory diagnosis decreased from 5 to 6 days before 2019 to 1 day in 2021. The median time from initial positive to ART initiation decreased from 37 days in 2015, 14 days in 2018, to 6 days in 2021. Compared to 2015—2017, the time to ART initiation was 91.48 days lower in 2018 ($P < 0.001$) and 100.66 days lower in 2019—2021 ($P < 0.001$) by the adjusted linear regression model.
*Conclusion:* A significant decrease in the time to ART initiation was observed after initiation of the pay-for-performance program and optimized testing algorithm in Taiwan.


## Introduction

The World Health Organization (WHO) announced its 95-95-95 treatment goal in hopes of ending AIDS by 2030.[1] Previous studies have indicated that HIV treatment is highly effective in reducing the transmission of HIV, and the evidence is now clear that people living with HIV with an undetectable viral load cannot transmit HIV sexually.[2] Therefore, identifying undiagnosed cases and increasing the coverage of HIV testing is crucial. The first target of the 95-95-95 plan is to have 95% of all people living with HIV (PLHIV) know their HIV status.[3] A rapid and accurate diagnosis is one of the key strategies for achieving the first target.[4,5] Specifically, an accurate diagnosis of early HIV infection would detect and efficiently control disease transmission because individuals have higher HIV viral loads during the acute infection stage.[6] The Western blot (WB) assay is the standard test for an HIV confirmatory diagnosis, but WB analysis has several limitations including low sensitivity and delayed test results by more than a week.[7,8] The WHO report in 2019 also noted that the WB method is time-consuming and requires professionals to judge the results; patients may delay taking their medicine or lose contact and refuse to come back.

In 2014, the US Centers for Disease Control and Prevention recommended the use of an HIV-1/2 antibody differentiation immunoassay, a single-use immunochromatographic test (ICT) to diagnose HIV infections.[9] The WHO strongly suggested replacing WB with simpler and more rapid diagnostic tests in 2019.[10] As of 2020, Japan also modified HIV confirmatory testing protocols using ICT as a replacement for WB, and ICT and simultaneous testing with ICT and NAAT for initial HIV-positive sera[11]; however, assessments of real-world outcomes on overall HIV diagnostic turnaround time and the initiation of antiretroviral therapy (ART) using the modified testing algorithm are limited.[12—14]

The Central Laboratory in the Taiwan Centers for Disease Control (TCDC) provides confirmatory tests for samples that were initially positive from local health bureaus. The TCDC has provided NAATs since 2009 for patients who have HIV-negative or -indeterminate results but are still under high clinical suspicion from. Hence, the TCDC has since collected many sera that were initially positive, but WB-negative or -indeterminate. In addition, the TCDC started to set the policy of rapid ART initiation in 2016 and the Taiwan Food and Drug Administration approved an ICT for an HIV confirmatory diagnosis in 2017. A pay-for-performance program to improve HIV-related healthcare has been established since 2018. This plan focuses on greater financial incentives towards ART initiation within 7 days of HIV diagnosis. A modified HIV testing algorithm was endorsed since 2019, including ICT as a replacement for WB method and the initial positive results have been simultaneously tested with ICT and NAAT. Herein, we further evaluated the implementation of these strategies.

## Methods

### Study population and resources

This research included sera and PLHIV cohort studies. The sera study involved 1117 surplus serum samples from the Central Laboratory at the TCDC collected between 2016 and 2019. The PLHIV cohort were diagnosed and reported to the TCDC between January 2015 and December 2021. The data were from the HIV/AIDS reporting/case management system. The information included the date of the sample collection for the confirmatory diagnosis testing, the date of the HIV reporting, testing results, and the date of ART prescription; however, information on the confirmatory assay kit utilized was lacking. This study (IRB-107108 and IRB-108301) was approved by the Institutional Review Board of the TCDC.

### Laboratory measurements

WB analysis was performed using MP Diagnostics HIV BLOT 2.2 (MP Biomedicals Asia Pacific Pte Ltd., Singapore, Singapore), which detects HIV-1 and HIV-2 antibodies. We used the Genius HIV-1/2 confirmatory assay (Bio-Rad Laboratories, Redmond, WA, USA) as the ICT. HIV-1 NAAT was performed using the mSample Preparation System RNA (Abbott, Chicago, IL, USA) for specimen preparation, and PCR was performed using the Abbott RealTime HIV-1 assay kit (Abbott) and m2000 RealTime System (Abbott).

### The pay-for-performance program

Implemented in 2018, the pay-for-performance program motivates case managers to encourage patients to initiate treatment by compensating the healthcare facilities according to the interval between the date of diagnosis and the date of HIV treatment initiation. Intervals were calculated and categorized into multiple groups that correspond to different compensation rates and the facilities received the funding at the end of the year. Every year, these groups

and rates were re-discussed and adjusted based on the policy implementation and their previous performance.

### Measurements

The primary measurement included a comparison of agreement between ICT and WB results, the consistency between ICT and NAAT results, and the consistency between WB and NAAT results. The NAAT results are referred to as the "true result."

The secondary measurement included the time from initial positive to a confirmatory diagnosis, followed by ART initiation. Here, we defined the date of sample collection for the confirmatory testing as the date of initial positive result. The 2015–2021 study period was divided into 3 periods based on the interventions, as follows: 2015–2017 was designated the before intervention stage; 2018 was the start of the pay-for-performance program stage; and 2019–2021 as the modified testing algorithm combined with the pay-for-performance program stage.

### Statistics

Cohen's kappa (κ) was calculated to determine agreement between the WB and ICT results. The crosstabs chi-square test of independence was performed to determine the Cramer coefficient V value and the agreements between the WB and NAAT results, and the ICT and NAAT results.

The mean, median, and variability were calculated by year, time from initial positive to confirmatory diagnosis, and initiation of ART. We constructed adjusted linear regression models to evaluate the association between these strategies and time to the confirmatory diagnosis, followed by initiation of ART. The models were adjusted for age, gender, mode of transmission, and AIDS status at the time of HIV diagnosis. All analyses were performed using SAS 9.4.

## Results

### Study population

In the serum study, a total of 1117 sera were tested. Group A consisted of 917 specimens including 860 WB positives, 28 indeterminate, and 29 negatives. Group B consisted of 257 specimens with 57 indeterminate or negative results from group A and 200 specimens with WB negative or intermediate results, but still considered to be of high clinical suspicion by physicians.

The PLHIV cohort in this research consisted of records from 10,732 PLHIV (79%) that included the dates of sample collection for the confirmatory testing among 13,591 PLHIV who were diagnosed and reported to the TCDC between January 2015 and December 2021.

### Description of the PLHIV cohort

The PLHIV cohort of 10,732 individuals included 10,460 males (97.5%) and 272 females (2.5%). Most of the subjects (n = 9216 [85.9%]) were men who have sex with men (MSM). The median age on the day of diagnosis was 29 years (interquartile range [IQR], 25–36 years). One-third of the subjects had AIDS at the time of HIV diagnosis (n = 3538 [33.0%]; Table 1).

### Consistency among WB, ICT, and NAAT results in group A

To summarize, all 860 WB-positive samples were further confirmed as ICT- and NAAT-positive in the A group. In the 57 WB-negative or -indeterminate samples, 16 (28.1%) and 22 (38.6%) were ICT-positive and NAAT-positive, respectively. In addition, among 41 ICT-negative or -indeterminate results, 6 (14.6%) were NAAT-positive.

The kappa value between the WB and ICT results was 0.5116. The Cramer value between the WB and NAAT results was 0.7971. The Cramer value between the ICT and NAAT results was 0.9225 (Fig. 1). Overall, the sensitivity for WB and ICT among this cohort was 93.8% (860/917) and 95.5% (876/917), respectively.

### Consistency among WB, ICT, and NAAT results in group B

Group B consisted entirely of WB-indeterminate and -negative results. Of 133 WB-indeterminate samples, there were 81 ICT-positive and 39 ICT-negative results. Among the 13 ICT-indeterminate samples, 7 were NAAT-positive. Among the 39 ICT-negative samples, 7 were NAAT-positive. Among 124 WB-negative samples, 14 were ICT-positive, 7 were ICT-indeterminate, and 103 were ICT-negative. Among the 7 ICT-indeterminate samples, 3 were NAAT-positive. Among the 103 ICT-negative samples, 20 were NAAT-positive. Further analysis of the NAAT results reconfirmed the 81 ICT-positive samples to be positive (Fig. 2).

**Table 1** Demographic status of the study population.

| Characteristics | Total | |
|---|---|---|
| | n | % |
| **Number** | **10,732** | **100** |
| **Age at HIV diagnosis(years)** | | |
| ≧14 | 7 | 0.1 |
| 15–24 | 2647 | 24.7 |
| 25–34 | 4820 | 44.9 |
| 35–44 | 2081 | 19.4 |
| 45–54 | 830 | 7.7 |
| ≦55 | 347 | 3.2 |
| Median (IQR) | **31.6** | |
| **Sex** | | |
| Female | 272 | 2.5 |
| Male | 10,460 | 97.5 |
| **Transmission category** | | |
| MSM | 9216 | 85.9 |
| Heterosexual | 1055 | 9.8 |
| IDU | 261 | 2.5 |
| Others | 200 | 1.9 |
| **AIDS status at HIV diagnosis** | | |
| No AIDS | 7194 | 67.0 |
| Yes, within 3 months | 3538 | 33.0 |

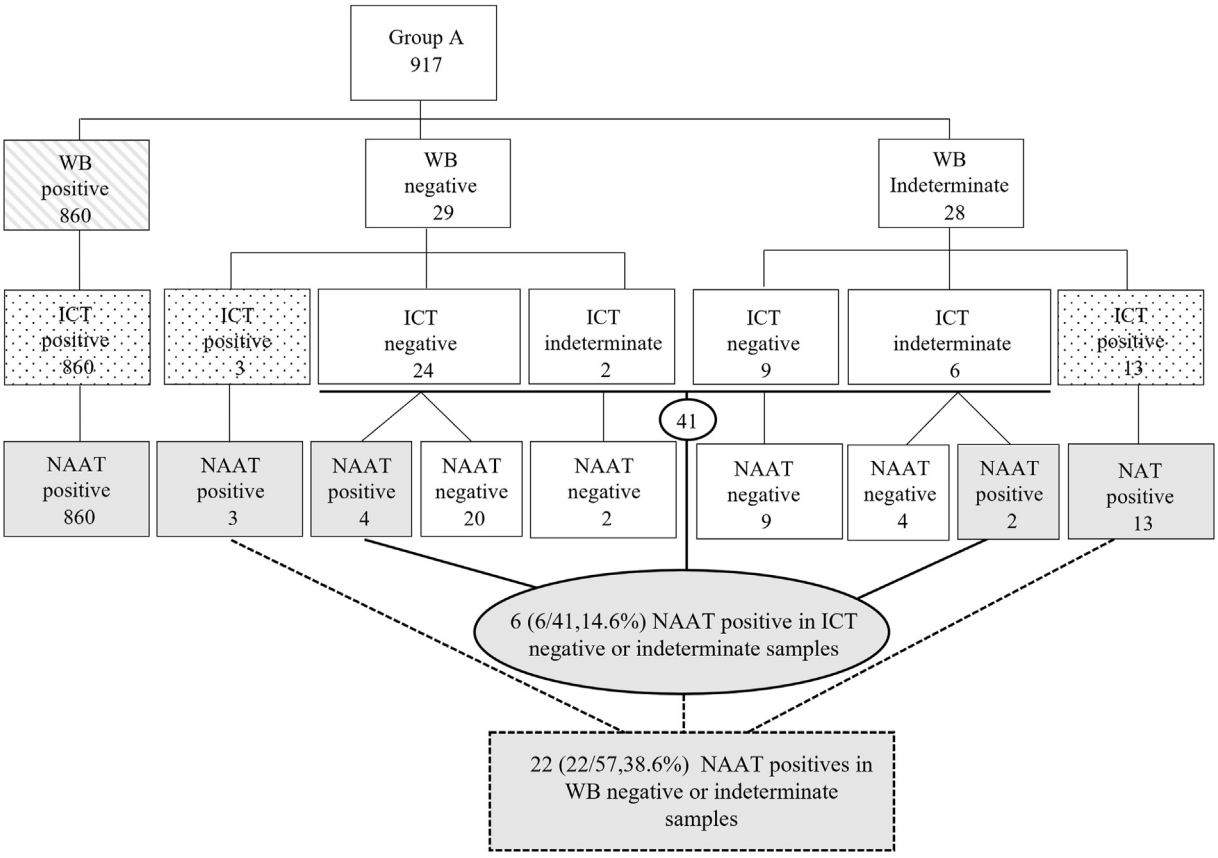


**Figure 1.** Comparison of WB, ICT, and NAAT HIV confirmatory diagnoses in 917 sera with initial HIV-positive results from the local health bureaus. WB, Western blot; ICT, immunochromatographic test; NAAT, nucleic acid amplification test.

In summary, NAAT detected 132 positive samples (51.4%) and ICT detected 95 positive samples (37.0%) of 257 WB-intermediate or -negative samples. In addition, among 162 ICT-negative or -indeterminate results, 37 (22.8%) were NAAT-positive (Fig. 2).

## Time to HIV confirmatory diagnosis and initiation of ART

The proportion of HIV cases with the date of initial positive results ranged from 74.9% in 2015 to 81.8% in 2021. In our PLHIV cohort study, the median time from the initial HIV-positive results to the HIV confirmatory test before the modified HIV testing algorithm (2015—2018) was 5 days (IQR, 2—8 days) to 6 days (IQR, 2—8 days). During the modified HIV testing algorithm period (2019—2021), the median time to confirmatory diagnoses were 4 days (IQR, 1—7 days) in 2019 to 1 days (IQR, 0—3 days) in 2021 (Table 2).

The proportion of PLHIV who received ART within 1 year after an HIV diagnosis was around 97—98% during 2015—2021. The median time from the initial HIV-positive result to initiation of ART prior to 2018 was 27 days (IQR, 16—42 days) to 37 days (IQR, 20—202 days). The pay-for-performance program was implemented in 2018, at which time the median time to initiation of ART was 2 weeks (median: 14 days; IQR, 7—28 days). The median time to initiation of ART had a decreasing trend between 2019 and 2021 (median: 6 days; IQR, 1—15 in 2021; Table 2) under the modified HIV testing algorithm combined with the pay-for-performance program.

## Rapid confirmatory diagnosis in association with the algorithm transition

Based on the fully adjusted linear regression model, the time to diagnosis was 2.8 days lower in 2019—2021 with the modified HIV testing algorithm compared with the time to diagnosis in 2015—2017 ($P < 0.001$). Other factors, including non-MSM transmission and non-AIDS status at the time of HIV diagnosis, were positive predictors of a longer time to an HIV confirmatory diagnosis. Variables, such as age, gender did not significantly predict the time to diagnosis (Table 3).

## Early initiation of ART in association with the pay-for-performance program and the testing algorithm transition

In the fully adjusted linear regression model for the time from the initial positive results to the initiation of ART (Table 4), when compared with 2015—2017, the time was 91.48 days lower in 2018 during the pay-for-performance program ($P < 0.001$) and 100.66 days lower from 2019 to 2021 during the pay-for-performance program with testing algorithm transition ($P < 0.001$). The other variables did not predict the duration to initiation of ART significantly. Only

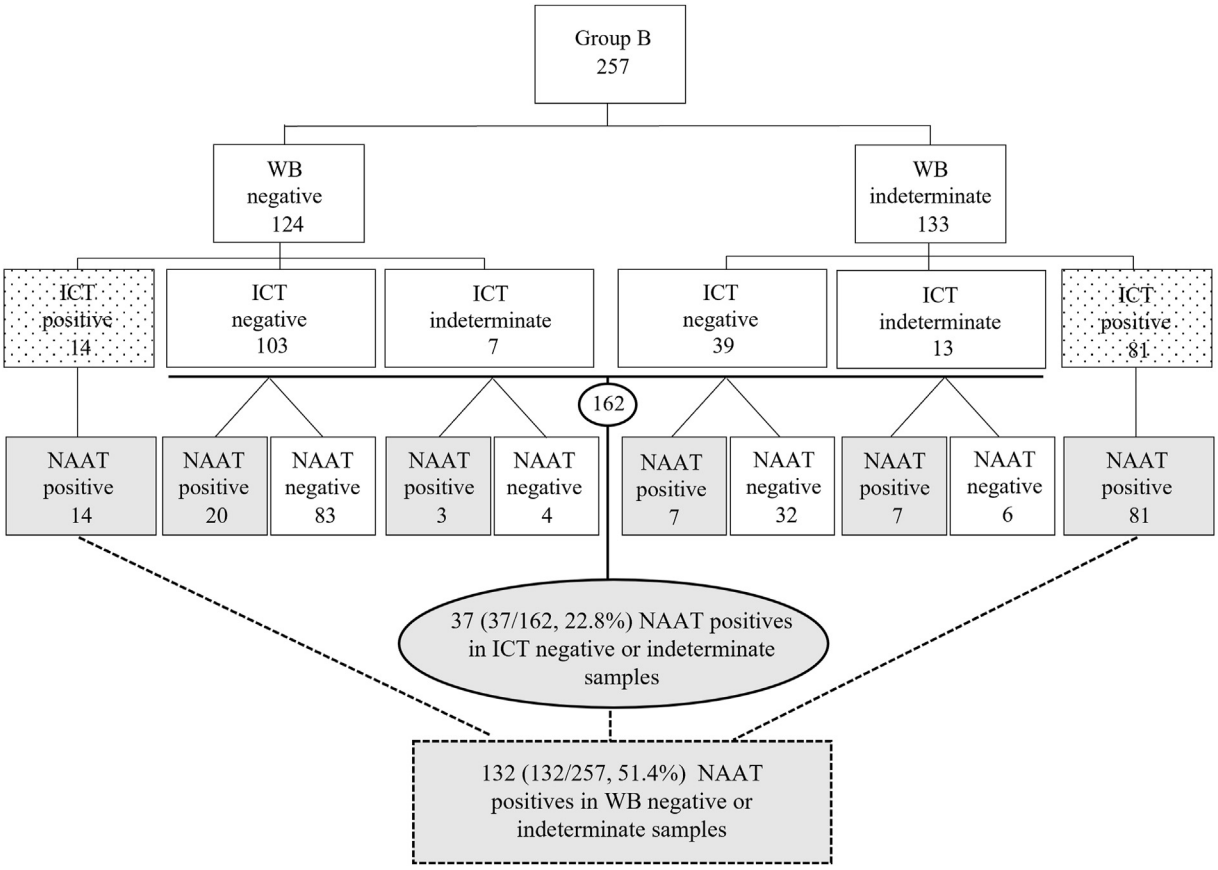


**Figure 2.** Comparison of WB, ICT, and NAAT results and HIV confirmatory diagnoses in 257 serum samples with WB-indeterminate and -negative results. WB, Western blot; ICT, immunochromatographic test; NAAT, nucleic acid amplification test.

**Table 2** Distribution of the study population, time to confirmatory diagnoses, and initiation of ART by year in Taiwan.

| Year | AIDS designated Hospitals | Hospitals with ICT | Reported cases | cases with the dates of initial positive results | | PLHIV with receiving ART | | Time from initial positive results to confirmatory diagnosis (days) | | Time from initial positive to on-ART (days) | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | n | n | n | % | n | % | Median | IQR | Median | IQR |
| total | — | — | 13,591 | 10,732 | 79.0% | 10,446 | 97.3% | — | — | — | — |
| 2015 | 57 | — | 2324 | 1740 | 74.9% | 1689 | 97.1% | 5 | 3,8 | 37 | 20,202 |
| 2016 | 62 | — | 2394 | 1749 | 73.1% | 1702 | 97.3% | 5 | 2,8 | 29 | 17,63 |
| 2017 | 69 | — | 2508 | 1982 | 79.0% | 1919 | 96.8% | 5.5 | 3,8 | 27 | 16,42 |
| 2018 | 77 | — | 1982 | 1635 | 82.5% | 1593 | 97.4% | 6 | 2,8 | 14 | 7,28 |
| 2019 | 78 | 21 | 1748 | 1470 | 84.1% | 1437 | 97.8% | 4 | 1,7 | 10 | 5,21 |
| 2020 | 83 | 27 | 1389 | 1137 | 81.9% | 1114 | 98.0% | 2 | 0,5 | 7 | 3,18 |
| 2021 | 83 | 79 | 1246 | 1019 | 81.8% | 992 | 97.4% | 1 | 0,3 | 6 | 1,15 |

non-AIDS status at the time of HIV diagnosis positively predicted a longer time to initiation of ART in both models.

## Discussion

In this study we have shown that the ICT assay is a reliable and superior alternative to WB analysis. This finding is consistent with most previous reports.[15—20] ICT has better sensitivity than WB (95.5% & 93.8%) when used as a confirmatory test. With NAAT as the gold standard in HIV testing, the results of ICT and NAAT compared to WB and NAAT were more consistent in our study; however, when comparing ICT and NAAT, the former failed to identify all HIV-positive sera. According to the results, the TCDC has endorsed the ICT assay as a replacement for traditional WB analysis since 2019. The initial positive results were tested with ICT and NAAT simultaneously since 2019. Hence, our testing protocol was modified from a 3-step to a 2-step procedure. Furthermore, our study showed that improvements in HIV care can be summed up in two ways. First,

**Table 3** Unadjusted and adjusted linear regression models for time from the initial positive to confirmatory diagnosis.

| Variables | Unadjusted model n = 10,732 | | Adjusted model n = 10,732 | |
|---|---|---|---|---|
| | b ± S.E. | P-value | β ± S.E. | P-value |
| Year | | | | |
| 2015–2017 | referent | | referent | |
| 2018 | −0.059 ± 0.19 | 0.7580 | −0.05 ± 0.19 | 0.7867 |
| 2019–2021 | −2.85 ± 0.15 | <0.001 | −2.81 ± 0.15 | <0.001 |
| Age | – | | 0.01 ± 0.01 | 0.5234 |
| Sex | – | | | |
| Female | – | | referent | |
| Male | – | | −0.01 ± 0.45 | 0.9876 |
| Transmission mode | – | | | |
| MSM | – | | referent | |
| Heterosexual | – | | 0.77 ± 0.25 | 0.0019 |
| Other | – | | 1.18 ± 0.49 | 0.0161 |
| AIDS status at HIV diagnosis | – | | | |
| No | – | | referent | |
| Yes | – | | −1.66 ± 0.14 | <0.0001 |

**Table 4** Unadjusted and adjusted linear regression models for time from initial positive to initiation of ART.

| Variables | Unadjusted model n = 10,446 | | Adjusted model n = 10,446 | |
|---|---|---|---|---|
| | b ± S.E | P-value | β ± S.E | P-value |
| Year | | | | |
| 2015–2017 | referent | | Referent | |
| 2018 | −92.46 ± 5.71 | <0.0001 | −91.48 ± 5.64 | <0.0001 |
| 2019–2021 | −104.29 ± 4.34 | <0.0001 | −100.66 ± 4.32 | <0.0001 |
| Age | – | | 0.013 ± 0.21 | 0.9532 |
| Sex | – | | | |
| Female | – | | Referent | |
| Male | – | | 0.52 ± 13.67 | 0.9695 |
| Transmission mode | – | | | |
| MSM | – | | Referent | |
| Heterosexual | – | | 3.46 ± 7.40 | 0.6399 |
| Other | – | | 0.20 ± 17.89 | 0.9911 |
| AIDS status at HIV diagnosis | – | | | |
| No | – | | Referent | |
| Yes | – | | −67.83 ± 4.24 | <0.0001 |

upon replacement of WB analysis with ICT, the time from initial positive results to confirmatory diagnosis has significantly decreased. Second, the concurrent use of NAAT has further facilitated shortening of the interval between the initial positive results and initiation of treatment, thus allowing same-day testing and initiation of ART. This simultaneous testing algorithm also allowed instant availability of data on viral load, thus giving physicians greater confidence to diagnose and prescribe antiretroviral therapy.

The HIV diagnostic testing algorithm is a 3-step sequence of tests for detection, differentiation, and confirmation of HIV-1 and HIV-2 in the USA.[9] A recent study in the US reported that one-fourth of all tests had discordant results between the ICT and initial screening assay in 2017.[12] Among the serum samples with indeterminate or negative ICT results, 7% of patients were NAAT-positive. The study suggested that the 3-step current HIV diagnostic algorithm is complex and inefficient.[12] In addition, two other recent studies suggested the sole use of HIV-1 NAAT, rather than ICT, after an initial HIV Ag/Ab immunoassay.[21,22] Our study also showed that NAAT could detect a portion of positives among ICT-negative or -indeterminate samples. Furthermore, our real-world cohort study exemplifies how the simultaneous utilization of ICT and NAAT may be a feasible testing algorithm according to the decline in overall duration from initial positive results to confirmatory diagnosis. In consideration of public health approaches and monitoring the HIV epidemic, the concurrent use of NAAT and ICT is essential to differentiate both acute and non-acute HIV infections.[23]

Taiwan has a population of approximately 23 million people. The estimated HIV prevalence was 27,455 (1.58 per 1000 people) in 2019 with an undiagnosed rate of 12.1%.[24–26] The rapid ART initiation policy has been endorsed in Taiwan since 2016. This pay-for-performance plan has, since 2018, focused on greater financial incentives towards initiating ART within 7 days of diagnosis.

The shorter the time interval between the HIV confirmatory diagnosis and ART initiation, the higher the financial incentive. As a result, there was a steep decline in the time from HIV initial positive testing to the initiation of ART in 2018. By 2019, 92% of all patients diagnosed with HIV infection received sustained ART, while 95% of those receiving ART had viral suppression.[24—26] A past study in San Francisco also reported the time from diagnosis to ART between 2013 and 2017 showed a decreasing trend from 37 to 6 days due to their RAPID ART Program Initiative,[27] a retrospective cohort study between 2014 and 2018 in Taiwan also reported that rapid ART initiation increased from 33.8% in 2014 to 68.3% in 2017, and the median interval between HIV diagnosis and viral suppression decreased from 138 to 47 days.[28] One systematic review paper concluded that rapid of ART as within 1 week of diagnosis could improve health outcomes.[29] Some studies also concluded that pragmatic research to identify feasible packages for shortening the interval from diagnosis to initiation of ART in complex health systems is necessary.[29,30] In our study, with optimization of testing algorithms and transition to incorporate NAAT and ICT in the diagnostic procedure and the pay-for-performance program, the goal towards a continuous decrease in the time from diagnosis to initiation of ART would be more successful and the reimbursement for HIV care from CDC has an impact in shortening the interval between diagnosis and treatment.

The inability to identify the exact confirmatory testing method used on each individual was our study limitation. Also, our analysis relies on a dataset on limited characteristic variables such as co-morbidities that might influence the model of statistical analysis. In addition, the specificity cannot be calculated owing to the lack of true negative samples from sample collection, which is also a limitation of our data. Despite these limitations, our study had some unique strengths. Our study used multiple interlinked data sources consists of 7 years of data. Most other published studies on HIV testing algorithms did not obtain such detailed information.

## Conclusions

Combining the pay-for-performance program and the modified HIV testing algorithm may be useful to help rapid ART initiation. Henceforth, we plan to follow-up on this cohort study and undertake further analyses of long-term follow-up research associated with viral suppression, adherence, morbidity, and mortality. Consequently, in 2021 the ICT and NAAT for HIV confirmatory diagnoses were approved to receive reimbursement from the National Health Insurance in Taiwan. Our findings, overall, suggest that the modified HIV testing algorithm offers the ICT assay as a replacement for WB analysis, and initial positive results are simultaneously tested with ICT and NAAT.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## References

1. UNAIDS. *Fast track: ending the AIDS epidemic by 2030*. 2015. https://www.unaids.org/sites/default/files/media_asset/201506_JC2743_Understanding_FastTrack_en.pdf.
2. Eisinger RW, Dieffenbach CW, Fauci AS. HIV viral load and transmissibility of HIV infection: undetectable equals untransmittable. *JAMA* 2019;**321**(5):451—2.
3. WHO. *Consolidated guidelines on HIV testing services for a changing epidemic*. 2019.
4. Ford N, Geng E, Ellman T, Orrell C, Ehrenkranz P, Sikazwe I, et al. Emerging priorities for HIV service delivery. *PLoS Med* Feb 2020;**17**(2).
5. Cornett JK, Kirn TJ. Laboratory diagnosis of HIV in adults: a review of current methods. *Clin Infect Dis* Sep 2013;**57**(5):712—8. https://doi.org/10.1093/cid/cit281.
6. Martin TCS, Abrams M, Anderson C, Little SJ. Rapid antiretroviral therapy among individuals with acute and early HIV. *Clin Infect Dis* Jul 1 2021;**73**(1):130—3. https://doi.org/10.1093/cid/ciaa1174.
7. Huang X, Liu X, Chen J, Bao Y, Hou J, Lu X, et al. Evaluation of blood-based antibody rapid testing for HIV early therapy: a meta-analysis of the evidence. *Front Immunol* 2018;**9**:1458.
8. Parekh BS, Ou CY, Fonjungo PN, Kalou MB, Rottinghaus E, Puren A, et al. Diagnosis of human immunodeficiency virus infection. *Clin Microbiol Rev* 2018;**32**(1):e00064.
9. Prevention CfDCa. *Laboratory testing for the diagnosis of HIV infection: updated recommendations*. Updated June 27, 2014, http://stacks.cdc.gov/view/cdc/23447.
10. WHO. *WHO recommends countries move away from the use of western blotting and line immunoassays in HIV testing strategies and algorithms*. 2019. https://www.who.int/publications/i/item/WHO-CDS-HIV-19.30. [Accessed 27 November 2019].
11. The Japanese Society for AIDS Research. 診療における*HIV-1*2感染症の診断ガイドライン*2020*版. 2020. Available from: https://jaids.jp/wpsystem/wpcontent/uploads/2021/01/guideline2020.pdf.
12. Burudpakdee C, Near AM, Tse J, Faccone J, Rodriguez PL, Karichu JK, et al. Real-world HIV diagnostic testing patterns in the United States. *Am J Manag Care* 2022;**28**(2):e42—8.
13. Wesolowski LG, Chavez PR, Cardenas AM, Katayev A, Slev P, Valsamakis A, et al. Routine HIV test results in 6 US clinical laboratories using the recommended laboratory HIV testing algorithm with genius HIV 1/2 supplemental assay. *Sex Transm Dis* 2020;**47**(5S Suppl 1):S13—7.
14. Nasrullah M, Wesolowski LG, Ethridge SF, Cranston K, Pentella M, Myers RA, et al. Acute infections, cost and time to reporting of HIV test results in three U.S. State Public Health Laboratories. *J Infect* 2016;**73**(2):164—72.
15. Friedrichs I, Buus C, Berger A, Keppler OT, Rabenau HF. Evaluation of two HIV antibody confirmatory assays: geenius HIV1/2 confirmatory assay and the recomLine HIV-1 & HIV-2 IgG line immunoassay. *J Virol Methods* 2015;**224**:91—4.
16. Montesinos I, Eykmans J, Delforge ML. Evaluation of the Bio-Rad Genius HIV-1/2 test as a confirmatory assay. *J Clin Virol* 2014;**60**(4):399—401.

17. Moon HW, Huh HJ, Oh GY, Lee SG, Lee A, Yun YM, et al. Evaluation of the bio-rad Genius HIV 1/2 confirmation assay as an alternative to western blot in the Korean population: a multi-center study. *PLoS One* 2015;**10**(9):e0139169.
18. Hawthorne Hallen A, Samuelson A, Nordin M, Albert J, Bogdanovic G. Evaluation of bio-rad genius HIV-1 and -2 assay as a confirmatory assay for detection of HIV-1 and -2 antibodies. *Clin Vaccine Immunol* Aug 2014;**21**(8):1192—4. https://doi.org/10.1128/CVI.00153-14.
19. Herssens N, Beelaert G, Fransen K. Discriminatory capacity between HIV-1 and HIV-2 of the new rapid confirmation assay Genius. *J Virol Methods* Nov 2014;**208**:11—5.
20. Serhir B, Desjardins C, Doualla-Bell F, Simard M, Tremblay C, Longtin J. Evaluation of the bio-rad geenius HIV 12 assay as part of a confirmatory HIV testing strategy for quebec, Canada comparison with western blot and inno-lia assays. *J Clin Microbiol* 2019;**57**(6). e01398—18.
21. Pitasi MA, Patel SN, Wesolowski LG, Masciotra S, Luo W, Owen SM, et al. Performance of an alternative laboratory-based HIV diagnostic testing algorithm using HIV-1 RNA viral load. *Sex Transm Dis* 2020;**47**(5S Suppl 1):S18—25.
22. Masciotra S, Luo W, Rossetti R, Smith T, Ethridge S, Delaney KP, et al. Could HIV-1 RNA testing be an option as the second step in the HIV diagnostic algorithm? *Sex Transm Dis* 2020;**47**(5S Suppl 1):S26—31.
23. Mor O, Mileguir F, Michaeli M, Levy I, Mendelson E. Evaluation of the Bio-Rad Genius HIV 1/2 assay as an alternative to the INNO-LIA HIV 1/2 assay for confirmation of HIV infection. *J Clin Microbiol* 2014;**52**(7):2677—9.
24. Wu SB, Huang YC, Huang YF, Huang JC. Estimating HIV incidence, prevalence, and percent of undiagnosed infections in Taiwan using CD4 data. *J Formos Med Assoc* Feb 2022;**121**(2):482—9.
25. Huang YF, Huang YC, Lo YC, Latkin C, Huang HY, Lee CC, et al. Towards the first 90: impact of the national HIV self-test program on case finding and factors associated with linkage to confirmatory diagnosis in Taiwan. *J Int AIDS Soc* 2022;**25**(3):e25897.
26. Huang YF, Yang JY, Nelson KE, Kuo HS, Lew-Ting CY, Yang CH, et al. Changes in HIV incidence among people who inject drugs in Taiwan following introduction of a harm reduction program: a study of two cohorts. *PLoS Med* 2014;**11**(4):e1001625.
27. Bacon O, Chin J, Cohen SE, Hessol NA, Sachdev D, Coffey S, et al. Decreased time from human immunodeficiency virus diagnosis to care, antiretroviral therapy initiation, and virologic suppression during the citywide RAPID initiative in San Francisco. *Clin Infect Dis* 2021;**73**(1):e122—8.
28. Huang YC, Sun HY, Chuang YC, Huang YS, Lin KY, Huang SH, et al. Short-term outcomes of rapid initiation of antiretroviral therapy among HIV-positive patients: real-world experience from a single-centre retrospective cohort in Taiwan. *BMJ Open* 2019;**9**(9). e033246.
29. Bacon O, Chin J, Cohen SE, Hessol NA, Sachdev D, Coffey S, et al. Decreased time from human immunodeficiency virus diagnosis to care, antiretroviral therapy initiation, and virologic suppression during the citywide RAPID initiative in San Francisco. *Clin Infect Dis* 2021;**73**(1):e122—8.
30. Esber AL, Coakley P, Ake JA, Bahemana E, Adamu Y, Kiweewa F, et al. Decreasing time to antiretroviral therapy initiation after HIV diagnosis in a clinic-based observational cohort study in four African countries. *J Int AIDS Soc* 2020;**23**(2):e25446.