Early Diagnosis and Same-Day ART

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- How to get people tested early with the most sensitive test platform (at least 4th generation rapid test)
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Benefits of early HIV diagnosis

- Earlier initiation of antiretroviral therapy (ART)
- HIV-related morbidity and mortality can be prevented (with ART)
- Reaching the status of U=U (Undetectable=Untransmissible) sooner
- Less chance of transmitting HIV & TB to others (less transmission)
- Possibility of functional cure
- Ease the life for the treating doctor

❖ To fully benefit from **early diagnosis**, early diagnosis must always be accompanied by **rapid ART initiation**, termed **'Test and Treat'**

➢ **Rapid ART initiation** is defined by ART initiation within 7 days of diagnosis, preferably on the same day (**Same-day ART, SDART**)

Definition of early HIV diagnosis

- High CD4 is generally considered as the most reliable marker of early diagnosis although the rapidity of its decline depends on the level of viral load (rapid progressor with high VL vs. slow progressor with low VL)
- **Baseline (Pre-treatment) CD4 of <350 is globally accepted as 'Late diagnosis'.** However, baseline CD4 of <350 is normally seen after an average of 5 or more years of infection, thus, it is not truly 'early'. Patient's immune system has already been severely destroyed and HIV has already been transmitted to many others.
- **Therefore, for practical purpose, early diagnosis is diagnosis made as soon as possible after HIV acquisition or after risk exposure.**

Many patients throughout the world are diagnosed late

Case of Thailand: Baseline CD4 of patients newly diagnosed between July – December 2021 (7 years after Treat All Guideline) **in representative provinces**

Provinces	# Newly Dx pts	Median baseline CD4	Ranges	% CD4<200
Bangkok	1298	232	(0, 1641)	45
Chiang Mai	214	187	(2, 966)	52
Chiang Rai	203	210	(2, 1067)	48
Udorn Thani	239	179	(2, 1587)	52
Ubol Rachthani	151	204	(1, 1071)	48
Pitsanuloke	151	205	(4, 1022)	48
Phuket	124	224	(2, 1360)	45

Factors contributing to early diagnosis

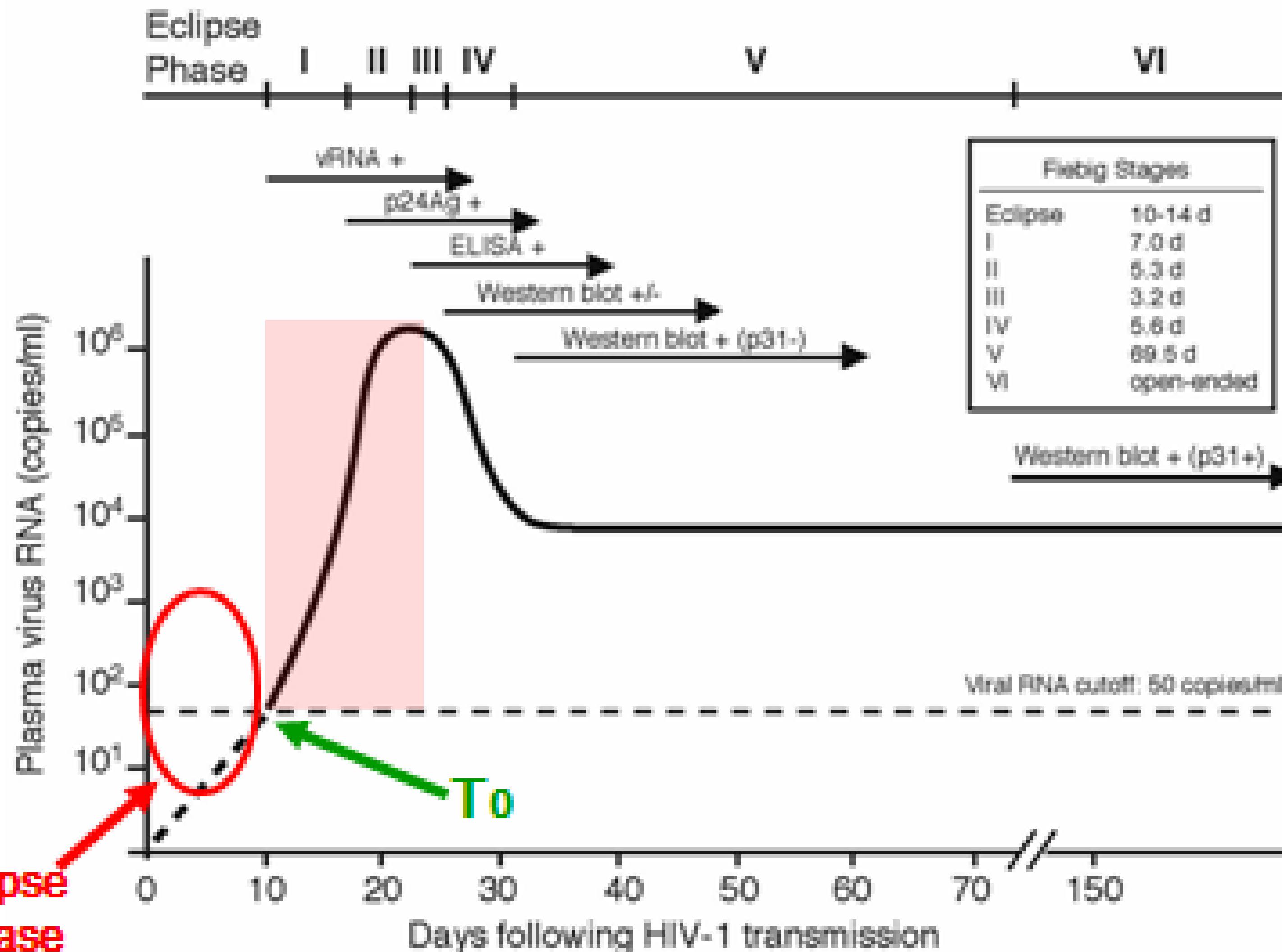
1. **Volunteer to test early** after risk exposure due to high risk awareness / consciousness
2. **Being advised by HCP to have test early,** especially when encountered with acute HIV symptoms which frequently misdiagnosed as "URI or viral infection". Some patients know it better than doctors that they should have an HIV test. Thus, doctors need to be more aware.

PLUS

A sensitive test platform, i.e., 4th Generation test or beyond

- ➢The more sensitive the test is, the better preventive and therapeutic outcomes.
- ➢What is the most sensitive test available and what is its window period?

Laboratory Staging of Acute HIV-1 Infection



The HIV eclipse phase is the time after acquisition of HIV when no existing diagnostic test is capable of detecting HIV. The HIV nucleic acid test (NAT) is the first test that can detect HIV following HIV acquisition.

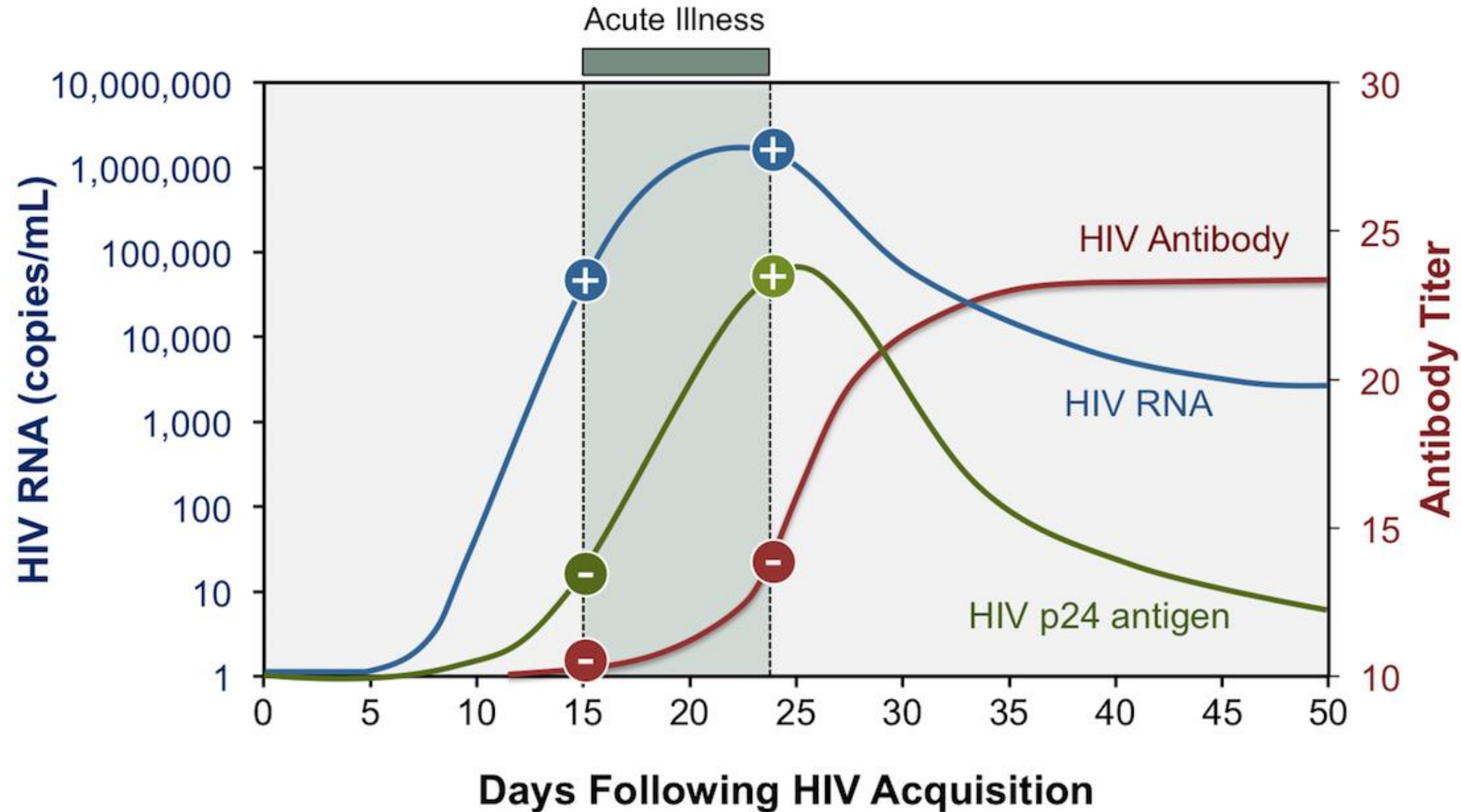
Eclipse Phase

CHAVI

(Fiebig *et al*, *AIDS* 2003)

Global HIV Vaccine Enterprise

HIV RNA is positive earliest



With acute HIV, the typical pattern is a positive HIV RNA, positive HIV p24 antigen, and negative anti-HIV antibodies. Note that with very early acute HIV, the p24 antigen test may be negative. Illustration: David H. Spach, MD

National HIV Curriculum, accessed January 2022

Most sensitive test device, whatever available, should be used for people who come to test (early)

- HIV-RNA: Qualitative (Aptima) & Quantitative (Viral load): not widely available
- p24 antigen testing: also not widely available
- 4th generation (Ag/Ab) test devices, both machine-based & rapid test
- 3rd or 2nd generation test devices should no longer be used as screening test either in the laboratory or as self-test since **4th generation rapid test (self-test) is now available and its price should be forced internationally to come down to the same level as 3rd generation tests**
  - Alere™ HIV Combo test
  - The *OnSite* HIV Ag/Ab 4th Gen Rapid Test (detection of IgG, IgM, IgA)
  - TRUSTline HIV-Ab/Ag 4th Gen Rapid Test

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APJAI

ORIGINAL ARTICLE

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Ability of Alere™ HIV Combo to diagnose acute HIV infection is based mainly on HIV-1 p24 antigen detection

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Abstract

Background: Alere™ HIV Combo is the only rapid and sensitive point-of-care 4th generation (antigen/antibody) HIV

- Although Alere^{TM} HIV Combo, the newly available rapid 4th Gen test is less sensitive than machine-based 4th generation test but still can detect three quarters of AHI individuals missed by conventional 3rd Gen Ab tests.
- In a setting with high HIV incidence where machine-based 4th generation test is not always available, rapid Alere^{TM} HIV Combo is preferred as the first test in HIV testing algorithm over 3rd Gen Ab test.
- Even for Ab detection, Alere^{TM} HIV Combo is more sensitive than conventional Ab tests. Therefore, it should replace the conventional Ab tests if the price is equal.

-50 stored plasma samples of subjects with **acute HIV infection** which were positive by machine-based 4th generation screening test but negative by both confirmatory antibody tests. All samples were positive by qualitative and quantitative HIV-RNA assays.

Results: Alere^{TM} HIV Combo was non-reactive (NR) in 13 (26%) and **reactive (R) in 37 (74%),** categorized into:

- Antibody positive only (R1) = 5
- p24 antigen positive only (R2) = 26
- Both p24 antigen and antibody positive (R3) = 6

- 32/50 (64%) p24 antigen detection & 11/50 (22%) Ab detection

How to get people diagnosed (tested) early

- Public education and public campaign are essential but not enough
- Skill of self-risk assessment is essential but usually biased for self
- Attitude towards healthy life such as U=U or PrEP use is a good incentive for testing, similar to FBS check to prevent overt diabetes
- Legal and social barriers of ‘risk behaviors’ have to be removed including stigma and discrimination of testing and of being positive
- Convenient & client-friendly **testing facilities** and **testing procedures**
- Client-centered with multi-services of need under one roof such as STI, anal Pap smear, gender-affirming and harm reduction services
- HIV self-test
- Testing led and provided by the peers of the key population themselves (KPLHS)

Key Population-Led Health Services (KPLHS):

designed and co-delivered by KPs

- A defined **set of HIV-related health services**, focusing on specific key populations
- Services are identified by the community itself and are, therefore, **needs-based, demand-driven, and client-centered**
- Delivered by trained and qualified **lay providers**, who are often members of the key populations

Vannakit R, et al. JIAS 2020; 23(6):e25535.
USAID LINKAGES project and USAID Community Partnership project

Key population-led health services (KPLHS): filling service gaps for key populations

ACCESSIBILITY

- Located in **hot spots**
- **Flexible service hours** suitable for KP's lifestyle
- **One-stop** service

AVAILABILITY

- **Needs-based** and **client-centered** services, such as hormone monitoring, STI, legal consultation, harm reduction

ACCEPTABILITY

- **Staff are members of KP communities** who truly understand KP's lifestyle
- Services are gender-oriented, and **free from stigma and discrimination**

QUALITY

- Staff are **trained and qualified** in accordance with national standards
- Strong **linkages** with and **high acceptance** from **public health sectors**

KPLHS: significant contribution to HIV testing, HIV diagnosis and PrEP services among KPs in Thailand

HIV incidence (by Mar 2017)

MSM
6.19
PER 100 PY

TG
2.4
PER 100 PY

MSW in Pattaya
11.69
PER 100 PY

TGSW in Pattaya
4.06
PER 100 PY

55% of MSM & TGW tested for HIV nationwide in 2018

36% of newly diagnosed HIV-positive cases among MSM & TGW nationwide in 2018

55% of Thai PrEP users in 2018

received services at 10 community health centers in 6 provinces

USAID LINKAGES project and Thai Red Cross AIDS Research Centre, December 2018.

Transgender-led, integrated gender affirming and sexual health services at Tangerine Clinic

HORMONE SERVICES

- Counseling on gender transition
- Hormone prescription
- Hormone level monitoring

SEXUAL HEALTH SERVICES

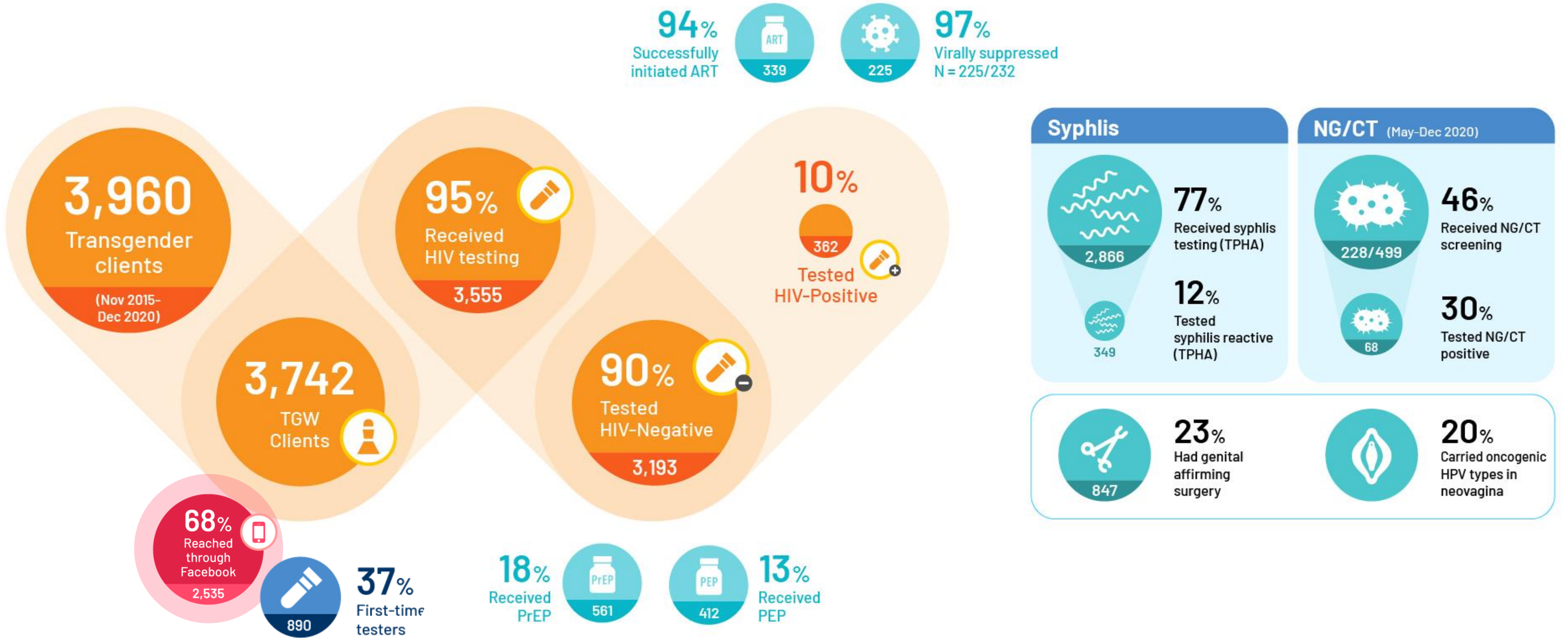
- HIV testing, syphilis testing
- Condom and lubricant
- Anal and neovaginal Pap smears
- High Resolution Anoscopy and Neovaginoscopy
- PrEP and PEP
- Same-day ARV treatment, CD4 count and viral load testing
- STI treatment
- Vaccination for hepatitis A, B and HPV
- Neovagina care

WELL-BELING SERVICES

- Mental health support and referrals
- Counseling for gender affirming surgery and referrals
- Referrals for legal assistance

Source: Tangerine Clinic, IHRI, USAID EpiC Thailand, 2020.

Tangerine Clinic's Service Data: Transgender women



USAID LINKAGES project and EpiC project

Benefits of same-day ART

- **Reduce the chance of loss to follow up**
- Reduce the chance of HIV-related morbidity and mortality as well as other co-morbidities (CVD, CVA, liver and kidney diseases, malignancy)
- Higher chance of normalized CD4 and normal life span
- Reduce transmission of HIV and TB to others
- Reach U=U faster and enjoy more on physical and psychological benefits of U=U

Undetectable = Untransmissible (U=U): FACT

- Evidence from 3 serodiscordant studies (N=2,000 couples): PARTNER 1 (M-F), PARTNER 2 (MSM) and Opposites Attract (MSM), where infected individuals had been on ART with VL<200 copies/mL (Undetectable)
- Seronegative couples were followed every 1-2 months with record of frequency of sex and condom use as well as anti-HIV and STI tests
- After 3,000 couple-years of follow-up (average 1.5 years of follow-up), NONE was infected in spite of 130,000 condomless sex (av. 43/person), i.e., **100% protection** or zero transmission (=Untransmissible)
- 40% of seronegative individuals continued to have unprotected sex with others, resulting in 14 infections in this study, all unrelated to partner's virus
- **Understanding U=U** will enhance acceptance for HIV testing, HIV treatment, HIV disclosure, **autonomy of sexual act** (which does not always mean condomless sex) and can reduce self and public stigma. **HCPs need to understand this fact and regularly communicate with their patients.**

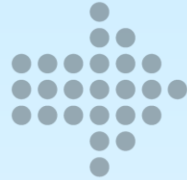
How to start ART on the same day of HIV Diagnosis

- National guideline should recommend same-day ART, if possible.
- Treat All Guideline already allows SDART initiation without having to know the results of CD4 or other labs. including CXR provided patients are asymptomatic (80-90%). Only exception is TB and cryptococcal meningitis.
- Physician (not necessary to be ID) should be available every day to authorize the first 2-4 week prescription of ART via telemedicine to nurses or CBOs who are the first to encounter the patients of which 80-90% are eligible.
- On-site CXR helps but not absolutely needed.
- TLD is the preferred regimen.
- **Patients need to come back in 1-2 weeks** to review all test results and any adverse effects of ART, then placed on eligible ART site.

Same-day ART initiation through CBO-hospital partnership

Newly diagnosed/ re-engage clients, accompanied by KP lay provider

Willing to start ART (non-coercive)



First visit at ART site

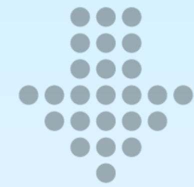
1. Confirm HIV-positive status and draw blood for baseline lab test
2. Psychosocial support
3. CXR
4. Medical history and physical examination
5. ART initiation (2-4 weeks ART supply)

Exclude suspected TB (by symptom/CXR), crypto meningitis, serious OIs

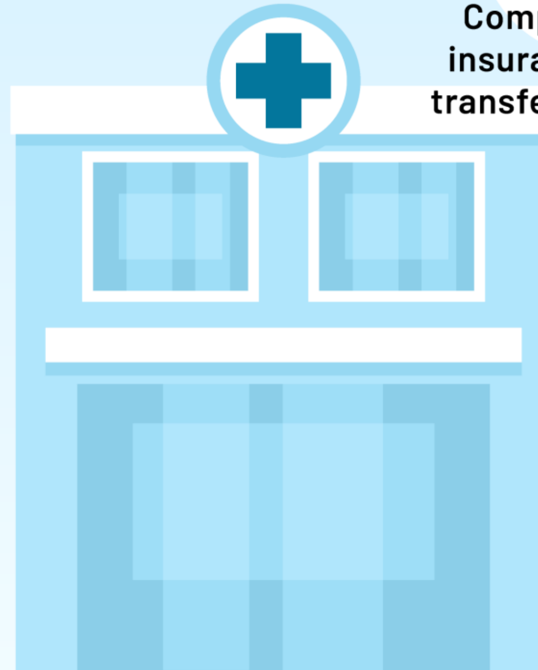
Complete health insurance scheme transfer (as needed)

Follow-up visit at ART site

1. Notify baseline lab results
2. Assess adverse event/IRIS
3. 1-3 months ART supply



"U=U as key motivational message to start and maintain ART"



3-6 months DSD

Seekaew P. et al, JIAS 2021, 24:e25869

Start ART for PLHIV with suspected TB, except for meningitis, while rapidly investigating for TB

Box 5. Clinical considerations for people living with HIV being evaluated for rapid ART initiation

The Guideline Development Group suggested the following update to existing guidance on rapid ART initiation *(2)*:

- **previous clinical consideration:** brief delay in ART initiation while investigating for TB symptoms; and
- **new clinical consideration:** among people living with HIV with signs and symptoms suggesting TB, except for central nervous system disease (meningitis), initiate ART while rapidly investigating for TB, with close follow-up within seven days to initiate TB treatment if TB is confirmed.

WHO Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery and Monitoring: Recommendations for a Public Health Approach, July 2021.

Need to rule out clinical signs and symptoms of “meningitis” before ART initiation

Critical to rule out clinical signs and symptoms of meningitis*, as initiation of ART in this group of results in increased mortality and morbidity.

*For e.g., either TB or cryptococcal meningitis

Box 4.1. Importance of screening for signs and symptoms of meningitis

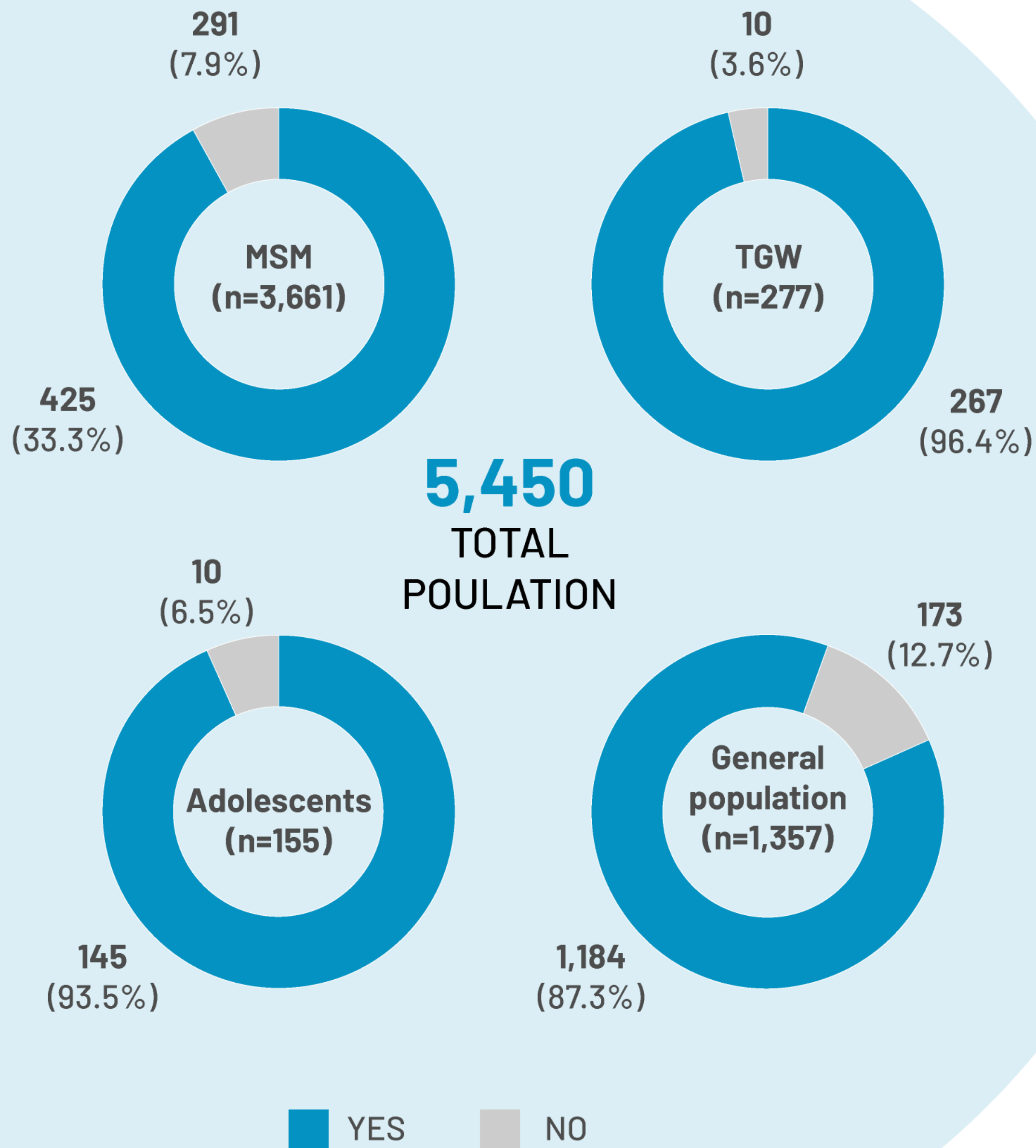
Among people living with HIV with TB meningitis or other forms of meningeal infection such as cryptococcal meningitis, earlier ART is associated with more severe adverse events and increased mortality with cryptococcal meningitis. For people living with HIV and TB meningitis, immediate ART is associated with more severe adverse events compared with initiating ART two months after the start of TB treatment.[a]

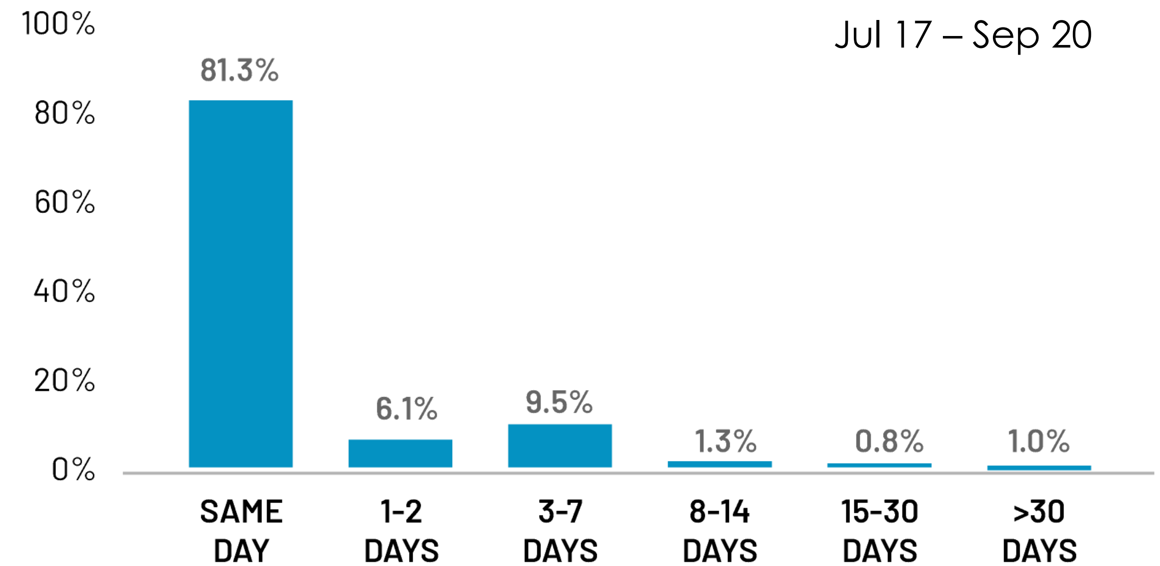
- ART should be delayed by 4–6 weeks of ART following initiation of treatment for cryptococcal meningitis. Use of steroids is not recommended.[a]
- ART should be delayed at least four weeks (and initiated within eight weeks) after treatment for TB meningitis is initiated. Corticosteroids should be considered adjuvant treatment for TB meningitis.[b]

Sources: [a] *Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy (1).* [b] *Guidelines for treatment of drug-susceptible tuberculosis and patient care – 2017 update (59).*

WHO Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery and Monitoring: Recommendations for a Public Health Approach, July 2021.

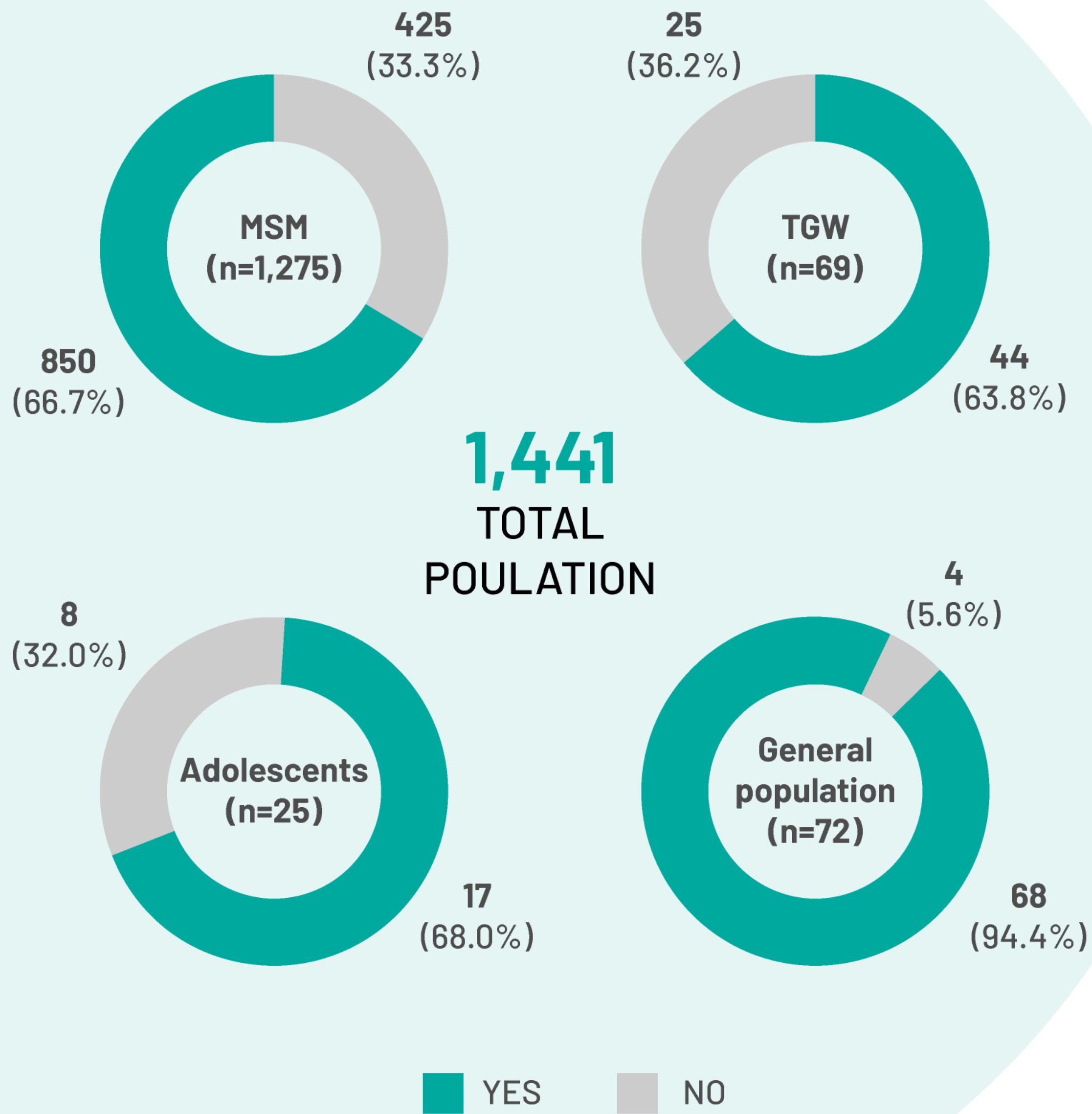
Same-day ART initiation, Bangkok site

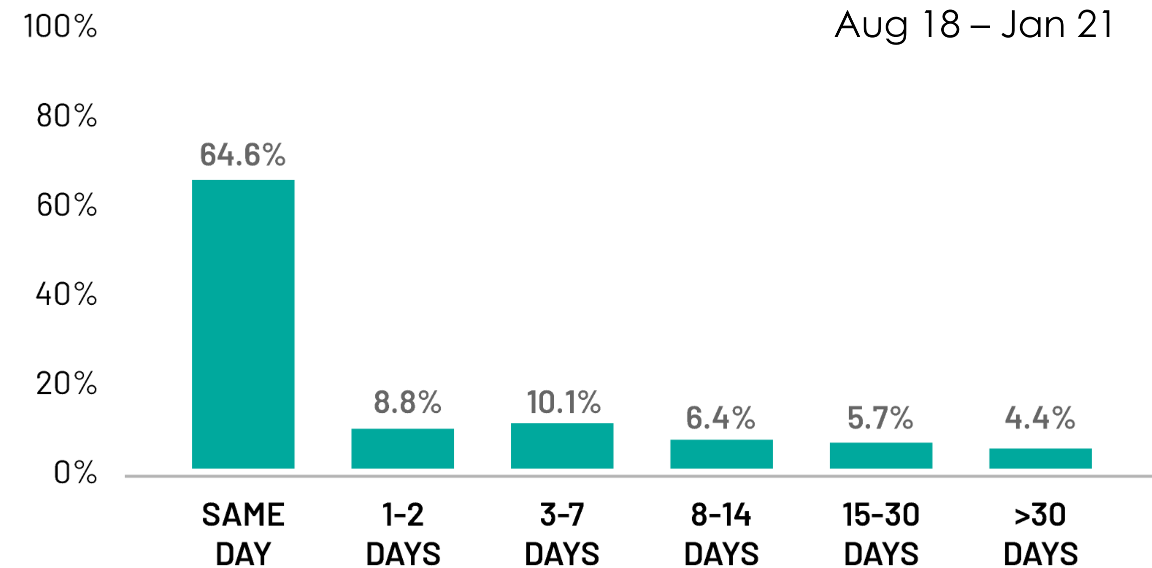




USAID LINKAGES project, September 2020

Same-day ART initiation, non-Bangkok sites





USAID LINKAGES project, January 2021

Days post HIV diagnosis that ART in initiated: July-December 2021

Prov.	N	SD	1	2	3	4	5	6	7	8-14	15-28	>28	Perf. score /Pt
BKK	1298	64	107	35	25	35	21	52	57	171	274	411	3.56
CM	214	30	13	4	3	5	6	8	6	20	34	52	3.90
CR	203	12	8	5	5	3	9	8	10	29	50	50	3.40
UDOR	239	7	22	6	7	21	12	9	11	34	47	56	4.05
UBOL	151	15	9	3	3	2	2	0	5	17	30	48	3.38
PHUK	124	15	11	14	10	7	4	3	1	12	16	12	5.27

Tips for Same-day ART initiation: Perspectives from HCPs who have successfully implemented SDART in Thailand

- SDART is feasible if all healthcare providers in the ART clinic have the common goal of SDART.
- Coordination within the ART team is essential as well as reducing ‘self-centered’ while focusing on ‘patient-centered’.
- A good and effective follow-up plan after ART initiation will ensure prescribing physicians that any adverse events will be detected early and managed properly.

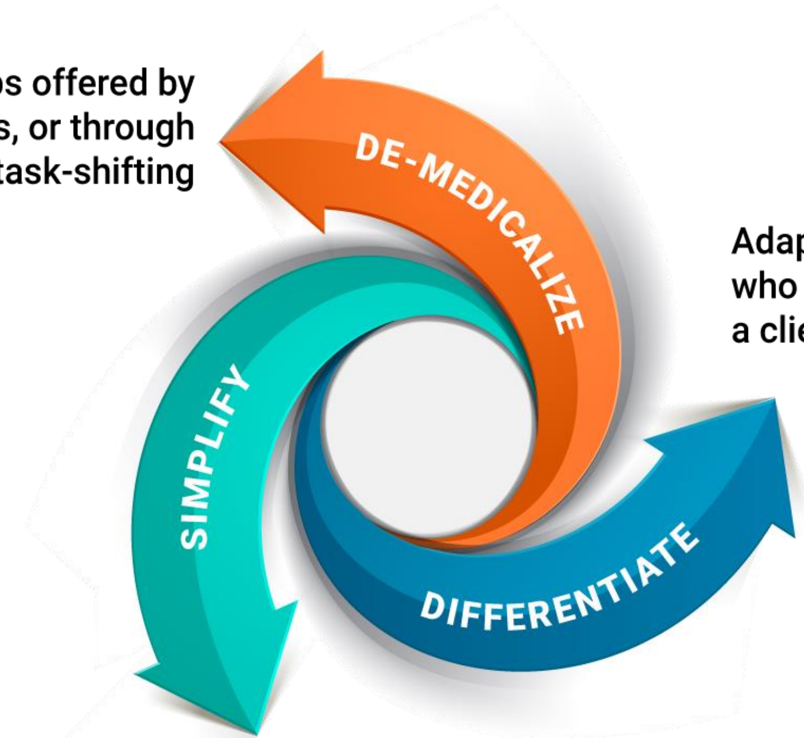
➢ If these 3 factors are met, SDART can be implemented in any big or small hospitals, clinics or community centers.

Dr. Pratana Leenasirimakul, Dr. Supannee Jirajariyavej,
Ms. Yaowarak Siriwarothai: Dec 3, 2021 WAD Conference

Same-day ART Initiation:

De-medicalize, Simplify & Differentiate

Different steps offered by lay providers, or through HCW task-shifting



Adapting the when, where, who and what based on a client-centered approach

Finding less complex ways to deliver care, to promote increased access and lower cost, while retaining efficacy and quality

Kimberly Green, et al. 2020.

Summary

- Patient's awareness of HIV risk events and the benefit of early HIV diagnosis is the prerequisite for the patient to show up for HIV testing early. Client-centered, non-stigmatized testing site is needed, such as that operated by key populations (KPLHS).
- The most available sensitive test platform (HIV-RNA or 4th Gen tests) should be used without the fear that the reactive screening test cannot be confirmed. It can either later or sooner.
- All the 3rd Gen tests currently used in many small laboratories should be replaced at least by rapid 4th Gen test. We must collectively force the price down to be equal.
- Once diagnosed, ART should be started on the same day. This is feasible in about 80-90% of patients with the use of telemedicine and more effective team effort.
- Such an approach will maximize the value for the money invested in national HIV testing and ART program.
- Early diagnosis, followed by same-day ART and same-day PrEP is the only hope that country can end AIDS on time (by 2030)

THANK YOU VERY MUCH