

EpiC advanced HIV disease (AHD) program in Jakarta, Indonesia

Background

The Meeting Targets and Maintaining Epidemic Control (EpiC) program is funded by the United States Agency for International Development (USAID) and strives to deliver efficient, affordable, results-based technical assistance and direct service delivery tailored to context and epidemiology that is effective in surging, scaling, and sustaining HIV services and systems for long-term epidemic control among key populations. EpiC supports a national coordinated effort led by the Government of Indonesia (GOI) to accelerate treatment coverage in Jakarta and Greater Jakarta and build capacities to institutionalize and scale HIV service key strategies. Since 2021, this has included advanced HIV disease (AHD) diagnosis and package management following national policies and World Health Organization (WHO) recommendations.

WHO defines AHD for adults, adolescents, and children 5 years and older as a CD4 cell count <200 cells/mm³, or having WHO clinical stage 3 or 4 findings. All children younger than 5 who are not on effective ART are considered to have advanced disease because, in the absence of effective treatment, children with HIV have higher viremia and more rapid disease progression with high mortality.¹

In 2017, WHO issued specific recommendations to identify AHD and proposed an evidence-based comprehensive package of interventions for countries and HIV programs to actively address AHD among PLHIV to reduce morbidity and mortality.^{2,3} In 2020, WHO published guidance to address AHD among children and adolescents.³ A full chapter about AHD was newly incorporated in the consolidated guidelines on HIV prevention, testing, treatment, service

¹ World Health Organization. Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy, July 2017. Geneva: WHO; 2017. Available from: <https://www.who.int/publications/i/item/9789241550062>

² Ford N, Meintjes G, Calmy A, Bygrave H, Migone C, Vitoria M, et al. Managing advanced HIV disease in a public health approach. *Clinical Infectious Diseases*; 2018;66 (Suppl 2): S106-S110.

³ World Health Organization. Package of care for children and adolescents with advanced HIV disease: stop AIDS. Technical brief. Geneva: WHO; 2020. Available from: <https://apps.who.int/iris/handle/10665/332907>.

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delivery, and monitoring issued during the International AIDS Society (IAS) 2021 meeting.⁴ As part of its framework for a differentiated approach to HIV care and services, WHO strongly recommends offering a comprehensive package of interventions to everyone presenting with AHD that includes screening, treatment or prophylaxis for major opportunistic infections, rapid antiretroviral therapy (ART) initiation, and intensified adherence support interventions.^{3,4,5}

In its 2022 guidance for all supported countries, the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) included "Identification and Treatment of Advanced HIV Disease" (chapter 6.4.2) with "Approach to CD4 testing revised to allow identification and improve management of advanced HIV disease" (section 6.4.2.1) and "Identification and treatment of pediatric advanced disease" (section 6.4.2.2) as program priorities.⁵

Importance of CD4 cell counts to identify AHD

CD4 cell count testing is the only efficient way to assess patient immunological status and is critical to identify people with AHD who are eligible for the AHD package. Indeed, more than 50% of people with AHD are not yet at WHO clinical stage 3 or 4 and will be missed if using only clinical staging.⁶

The 2016 WHO consolidated antiretroviral (ARV) guidelines recommend starting ART regardless of CD4 cell count and advise that the use of CD4 cell count for ART response monitoring can be stopped in settings where routine viral load (VL) monitoring is available and people are stable on ART.⁷ VL provides information about viral replication and treatment effectiveness but not about patient immunological status. Though the guidelines clearly mention that CD4 cell count testing at baseline remains important for all PLHIV to identify those with AHD, baseline CD4 testing has decreased in recent years because of the priority given to VL monitoring.⁸ A consequence of this policy has been a decrease — or even absence — of funding support for CD4 testing in some countries, which might have led to underdiagnosed AHD at facilities and, possibly, increased HIV mortality. Knowing patient immunological status

⁴ World Health Organization. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach. Geneva: WHO; 2021. Available from: <https://www.who.int/publications/i/item/9789240031593>.

⁵ U.S. Department of State. PEPFAR 2022 Country and Regional Operational Plan (COP/ROP) guidance for all PEPFAR-supported countries. 2022. Available from: <https://www.state.gov/2022-country-operational-plan-guidance/>.

⁶ Hakim J, Musiime V, Szubert AJ, Mallewa J, Siika A, Agutu C, et al. Enhanced prophylaxis plus antiretroviral therapy for advanced HIV infection in Africa. *N Engl J Med* 2017; 377:233-45. DOI: 10.1056/NEJMoa1615822.

⁷ World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach—2nd ed. Geneva: WHO; 2016.

⁸ Zaniewski E, Ostinelli CHD, Chammartin F, Maxwell N, Davies M, Euvrard J, et al. Trends in CD4 and viral load testing 2005 to 2018: multi-cohort study of people living with HIV in Southern Africa. *Journal of the International AIDS Society*. 2020 Jul; 23(7): e25546. Available from: <http://onlinelibrary.wiley.com/doi/10.1002/jia2.25546/full>.

through CD4 cell count remains critical to propose the intervention and support, especially in the first few months after diagnosis and ART initiation, when AHD clients remain in danger with CD4 counts below 200 cell/mm³.⁹

Advanced HIV disease in Indonesia: Policies and real practices

Through national guidelines, standard operating procedures (SOP), and Ministry of Health (MOH) circular letters, the Government of Indonesia (GOI) has disseminated policies for HIV care and treatment that include some key components for the management of AHD clients. However, the National HIV Program has not yet created comprehensive policy and program interventions focused on AHD.

HIV care and treatment guidance in Indonesia includes the use of baseline CD4 for newly enrolled PLHIV, of cotrimoxazole (CTX) prophylaxis when CD4 <200 cells/mm³, tuberculosis preventive therapy (TPT) for latent tuberculosis (TB) infection, and Xpert-MTB/RIF to improve TB diagnosis, as well as the use of cryptococcal antigen (CrAg) test screening (when CD4 <200 CD4 cells/mm³) and fluconazole pre-emptive therapy for those found CrAg positive. The guidance also calls for rapid ART initiation in AHD clients. The guidance does not mention use of fluconazole prophylaxis to prevent cryptococcal disease for those who do not have access to CrAg testing. Other interventions that are neither mentioned nor available include the lateral flow lipoarabinomannan (LF-LAM) test for the diagnosis of TB among PLHIV with low CD4 counts and reinforced adherence support for AHD clients initiated on ART.

In practice, limited funding for CD4 testing is available from the GOI or the Global Fund in Indonesia, causing sites to find local solutions using their own funds, other stakeholder support, or direct client contributions. Consequently, baseline coverage of CD4 is low (as illustrated by the evaluation described below), as is AHD identification among newly enrolled PLHIV at public facilities. In addition, availability of opportunistic infection (OI) prophylaxis drugs is limited at HIV treatment sites as the medications are largely locally funded. When fluconazole is available, it is used only for candidiasis because of the absence of guidance for cryptococcal prophylaxis. While the guidance mentions CrAg testing, its use has not been implemented in the absence of funding, an organized supply chain, and appropriate training of health care providers.

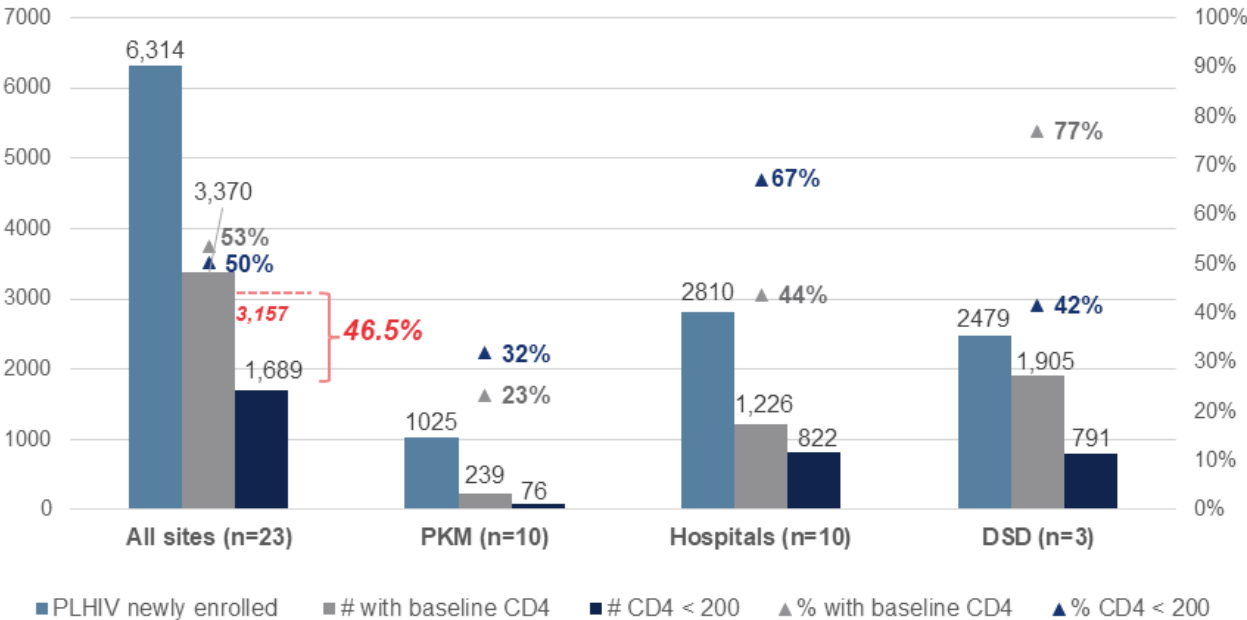
⁹ Ford N, Meintjes G, Vitoria M, Greened G, Chiller T. The evolving role of CD4 cell counts in HIV care. *Curr Opin HIV AIDS*. 2017; 12:123–128, DOI:10.1097/COH.0000000000000348.

Initial assessment of baseline CD4 test coverage among newly enrolled PLHIV in Jakarta

In collaboration with the Jakarta provincial health office (PHO) and district health offices (DHOs), the EpiC team conducted a retrospective review of data on baseline CD4 tests among newly enrolled PLHIV from January 2019 to May 2021 in 23 representative sites, including nine hospitals (one to two per district), 10 puskesmas (two per district), and four direct service delivery (DSD) sites (Angsamerah Fatamawati, Angsamerah Menteng, Globalindo, and Ruan Carlo).

Among 6,314 newly enrolled PLHIV, 3,370 (53%) had a baseline CD4, and 1,689 of them (50%) had CD4 counts below 200 cells/mm³ (Figure 1). Baseline CD4 coverage was much lower at the puskesmas (PKM) level (23%). As expected, higher rates of PLHIV with CD4<200 cells/mm³ were found at hospitals compared to PKM (67% vs 32%). DSD sites, supported by USAID and EpiC to conduct CD4 testing, had higher baseline CD4 coverage (77%). We estimate that, as of May 2021, only 53.5% of clients (1,689/3,157) with CD4<200 cells/mm³ had been identified, meaning that 46.5% of AHD clients had been missed.

Figure 1. Baseline CD4 coverage among newly enrolled PLHIV in Jakarta, Jan. 2019–May 2021 (n=23 sites)



EpiC AHD program activities (April 2021–Dec. 2021)

The Epic AHD program was initiated in quarter three of fiscal year 2021 (Q3 FY21) at the national (MOH, PHO), district (DHOs, PKM, hospitals, and DSD sites), and community (CSOs) levels. Activities included the following:

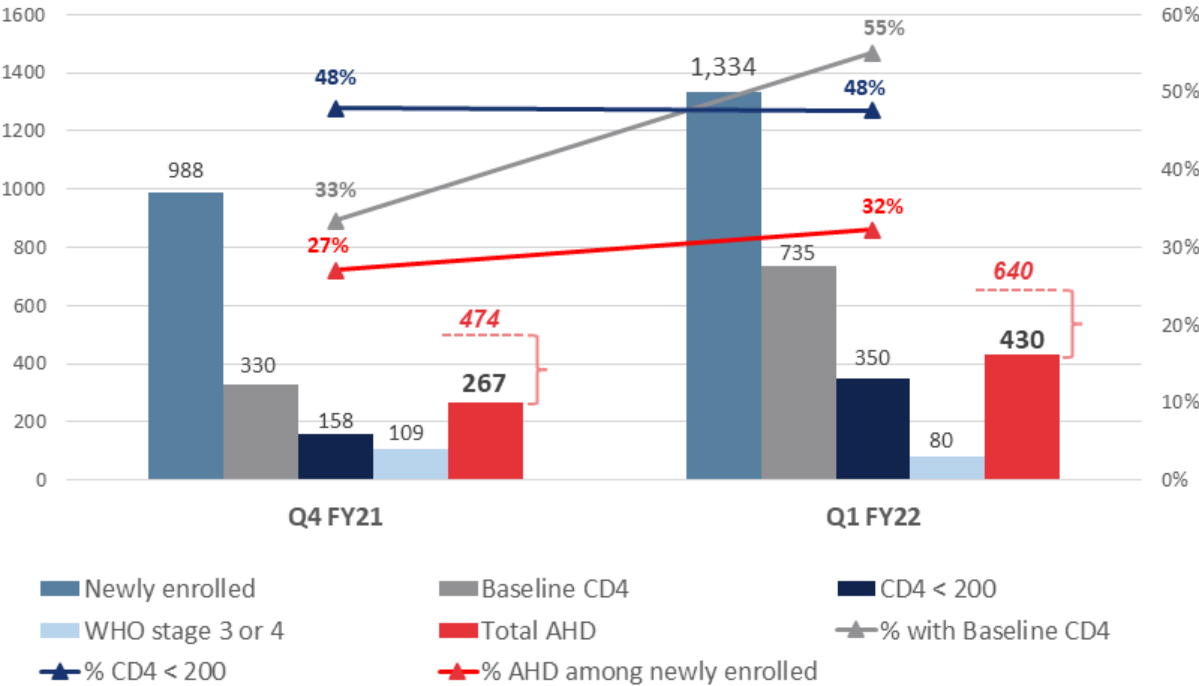
April 2021	<ul style="list-style-type: none"> ▪ Discussed the need to reinforce baseline CD4 and address AHD management with PHO and DHOs ▪ Conducted AHD orientation sessions for Jak-Mentor
May 2021	<ul style="list-style-type: none"> ▪ Evaluated baseline CD4 coverage at 23 sites in Jakarta and disseminated results to the PHO, DHOs, and clinical sites ▪ Developed an AHD site performance checklist
June 2021	<ul style="list-style-type: none"> ▪ Developed AHD SOPs with PHO/DHOs and mentors collecting and adapting MOH guidance for AHD management according to current MOH recommendations
July 2021	<ul style="list-style-type: none"> ▪ Developed AHD data collection and reporting tools, training modules, and information, education, and communication (IEC) materials for clients and health care workers (HCWs) including guidance, leaflets, and posters.
August 2021	<ul style="list-style-type: none"> ▪ Finalized AHD management guideline, leaflets, and technical posters
September 2021	<ul style="list-style-type: none"> ▪ Designed a CD4 laboratory network and referral system with PHO and DHO, including five referral laboratories and more than 120 facilities ▪ Provided the five laboratories with a total of 1,500 CD4 test kits to cover needs until January 2022 ▪ Conducted refresher trainings on baseline CD4 for HCWs, reporting and recording staff, and lab analysts ▪ Initiated rollout of CD4 baseline test support ▪ Organized and supported CD4 sample transportation from facilities to laboratories by hiring 12 JAK-TRANSPORTER drivers dedicated to CD4 specimen transport in close coordination with DHO and sites through the WhatsApp application
October 2021	<ul style="list-style-type: none"> ▪ Organized a national webinar for more than 200 HIV practitioners with speakers from the MOH, HIV expert panel, and EpiC program. During the webinar, the MOH officially endorsed the EpiC AHD program.
November 2021	<ul style="list-style-type: none"> ▪ Distributed AHD IEC materials ▪ Conducted regular monitoring of CD4 baseline test support
December 2021	<ul style="list-style-type: none"> ▪ Developed/finalized an AHD dashboard to visualize key indicators and facilitate the monitoring of AHD activities. ▪ Conducted training sessions for clinical mentors to build their mentorship capacities on AHD and CD4 acceleration at site levels

EpiC AHD program achievements (April 2021–Dec. 2021)

BASELINE CD4 ACCELERATION AND AHD IDENTIFICATION (FIGURES 2 AND 3)

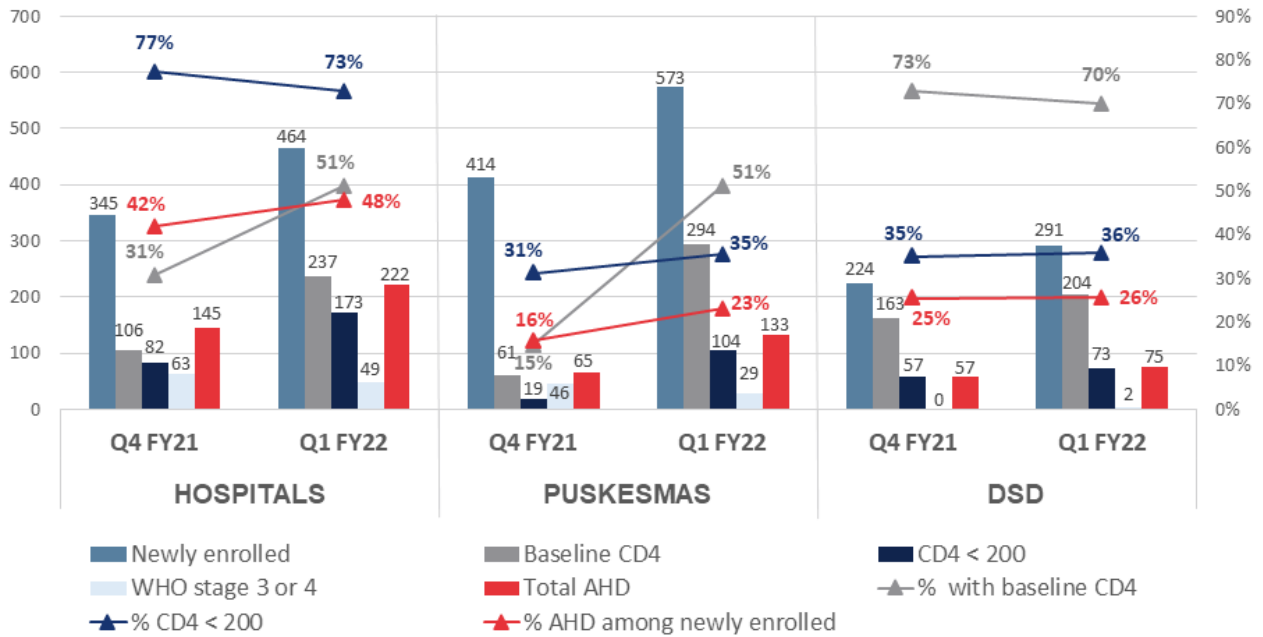
1. Increased baseline CD4 coverage among newly enrolled PLHIV (+22%) between Q4 FY21 (33%) and Q1 FY22 (55%), with an important increase at PKM (+36%) and hospital levels (+20%)
2. Increased proportion of newly enrolled PLHIV found to have AHD in Q1 FY22 (32%) compared to Q4 FY21 (27%), with a notable increase at the PKM level (+7%)
3. As expected, even with improvement of baseline CD4 coverage, the rates of newly enrolled PLHIV with CD4 <200 cells/mm³ remained stable — above 70% at hospital level and about 35% at PKM and DSD levels.

Figure 2. AHD cascade among newly enrolled PLHIV at PEPFAR sites in Jakarta (n=109 sites)



Source: MOH ARK 6.0, December 2021

Figure 3. AHD cascade among newly enrolled PLHIV at PEPFAR sites in Jakarta by quarter and type of site (n=109)

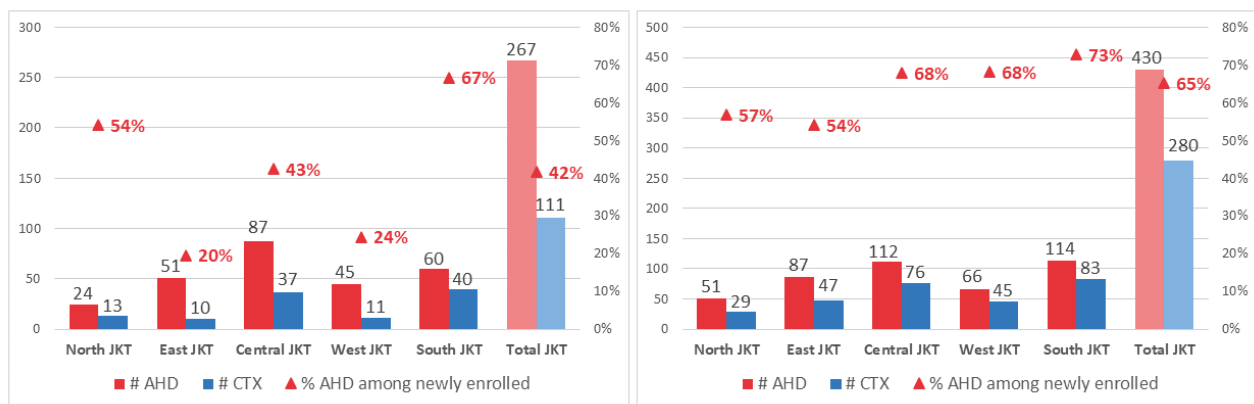


Source: MOH ARK 6.0, December 2021

COTRIMOXAZOLE PROPHYLAXIS COVERAGE AMONG PLHIV WITH IDENTIFIED AHD IN JAKARTA (FIGURE 4)

- 4. Increased CTX coverage (+23%) between Q4 FY21 and Q1 FY22, mainly in West Jakarta (+44%), East Jakarta (+34%), and Central Jakarta (+25%)

Figure 4. CTX coverage among AHD clients at PEPFAR sites in Jakarta by quarter and district (n=109 sites)

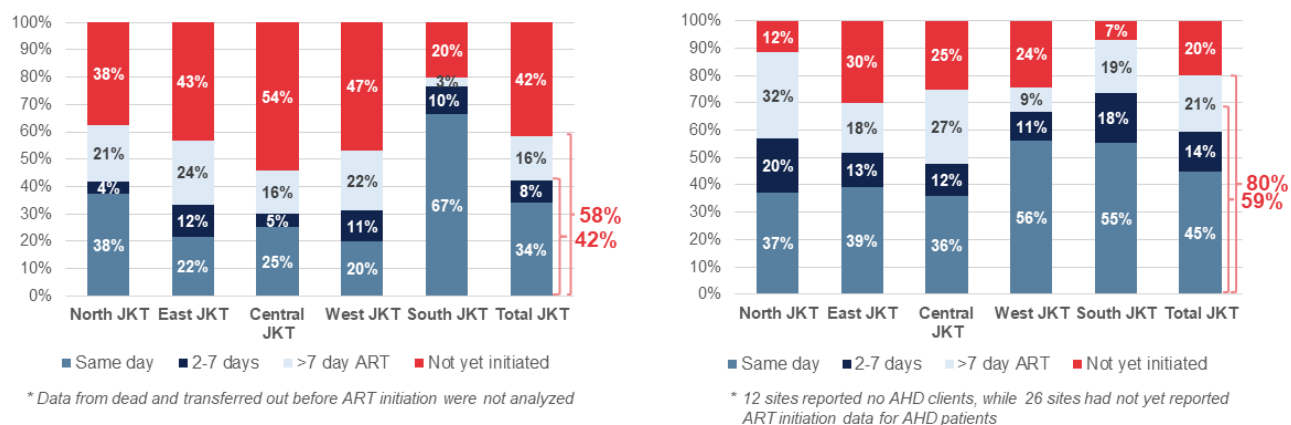


Source: MOH ARK 6.0, December 2021

RAPID ART INITIATION AMONG PLHIV WITH IDENTIFIED AHD IN JAKARTA (FIGURE 5)

5. Increased rapid ART initiation (within one to seven days) among PLHIV with AHD between Q4 FY21 and Q1 FY22 (+17%) both for same-day ART initiation (+11%) and initiation in two to seven days (+6%)
6. Increased percentage of PLHIV with AHD who initiated ART between Q4 FY21 and Q1 FY22 (+22%)

Figure 5. Rapid ART initiation among PLHIV with identified AHD at PEPFAR sites in Jakarta by quarter and district (n=109 sites)



Source: MOH ARK 6.0, December 2021

EpiC AHD program: Lessons learned and priorities for upcoming quarters

- **Baseline CD4 coverage and AHD identification:** Access to baseline CD4 remains limited, and EpiC — in close collaboration with USAID and its implementing partners — will work with the MOH and GFATM to improve forecasting and procurement processes. Introducing new Point of Care (POC) CD4 technologies (WHO-prequalified Omega Diagnostics VISITECT® CD4 AHD test) might help to reduce costs and improve implementation at remote sites.¹⁰
- **OI prophylaxis:** Working with the USAID GHSC-PSM project and GOI will be critical to maintain appropriate supply and drug availability of the key OI prophylaxes (CTX, TPT, and fluconazole) needed for AHD clients. These medications have been proven to save lives and represent a key intervention to reduce morbidity and mortality of PLHIV in Indonesia.

¹⁰ World Health Organization. Point-of-care CD4 tests to support the identification of individuals with advanced HIV Disease. WHO brief, April 2020. Available from: <https://apps.who.int/iris/handle/10665/331681>.

- *Improve cryptococcal meningitis (CM) diagnosis and treatment:* Improving CM prevention and treatment is critical as CM is one of the deadliest OIs for those with AHD. A key priority of the AHD program should be introducing CrAg test supplies and training HCWs about proper cryptococcosis management. The EpiC team has proposed an estimated budget, but registration, procurement, clinical algorithm, and training modules need to be discussed and developed.
- *Reinforce TB-HIV diagnosis and treatment:* TB is another leading cause of death among PLHIV with AHD. In line with the TB recovery program, the EpiC AHD team will work to improve TB screening, diagnosis, and treatment among AHD clients. In collaboration with PSM, the EpiC AHD team will also continue to advocate for the introduction of LF-LAM tests for those with suspected TB and low CD4 as the test has been proven to improve TB case finding and reduce mortality in this population.
- Interventions for AHD that might be implemented in the coming months include:
 - Address AHD in children and adolescents (in line with the recently issued Stop AIDS Strategy)
 - Extend the AHD program to Greater Jakarta
 - Further document AHD patient characteristics and management for more effective targeting of AHD interventions

EpiC is a global cooperative agreement dedicated to achieving and maintaining HIV epidemic control. It is led by FHI 360 with core partners Right to Care, Palladium International, Population Services International (PSI), and Gobe Group. For more information about EpiC, including the areas in which we offer technical assistance, click [here](#).