

GUIDELINES FOR MANAGING  
**ADVANCED HIV DISEASE AND RAPID  
 INITIATION OF ANTIRETROVIRAL THERAPY**

JULY 2017



**1 in 3 people  
 living with HIV  
 present to care  
 with advanced  
 HIV disease**

### What is advanced HIV disease?

The burden of morbidity and mortality associated with HIV infection has decreased over the past decade as access to antiretroviral therapy (ART) has increased. Nevertheless, around 1 in 3 people living with HIV (PLHIV) present to care with advanced HIV disease (figure 1); this proportion is higher in low- and middle-income settings. Additionally, a growing number of PLHIV are returning to care with advanced disease following a period of treatment interruption.

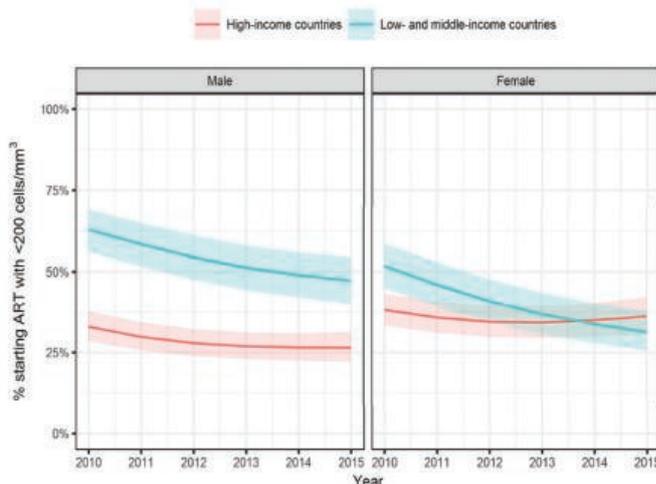
People with advanced HIV disease are at high risk of death, even after starting ART, with this risk increasing with decreasing CD4 cell count. The most common causes of death are tuberculosis (TB), severe bacterial infections, and cryptococcal meningitis.

WHO is releasing new guidelines recommending that people who present with advanced HIV disease should be provided with a defined package of care, which includes screening, treatment and prevention of major opportunistic infections, in order to reduce morbidity and mortality.



Patient with advanced HIV disease, Conakry, Guinea. N'gadi Ikram/MSF. 19 February, 2014

**Figure 1. Proportion of people with advanced HIV disease starting ART by sex and country income group, 2010–2015<sup>1</sup>**



### The WHO definition of advanced disease is as follows:

- For adults and adolescents, and children  $\geq 5$  years old, advanced HIV disease is defined as the presence of a CD4 cell count  $<200\text{ cells/mm}^3$  or a WHO clinical stage 3 or 4 event.
- All children  $< 5$  years old with HIV infection are considered as having advanced HIV disease<sup>2</sup>.

<sup>1</sup> This figure represents data from on 951 855 adults from 55 countries after imputation of missing data. The shaded areas represent 95% confidence intervals. Source: IeDEA/COHERE–WHO Collaboration.

<sup>2</sup> Most children with HIV present for care with advanced immunosuppression and have a high risk of disease progression and mortality regardless of their clinical and immune condition. Furthermore, varying age-dependent CD4 cell count definitions for advanced immunosuppression among children with HIV younger than five years make definitions based on CD4 cell count difficult to implement in programmatic settings.

## What does WHO recommend?

WHO guidelines recommend that a defined package of care interventions, which includes screening, treatment and prophylaxis for major opportunistic infections, rapid initiation of ART and intensified treatment adherence support, should be provided to patients presenting with advanced HIV disease to reduce associated morbidity and mortality. This package should be offered to all people presenting with advanced HIV disease including those who are re-engaging with care after a period of ART interruption.

Baseline CD4 cell count testing remains clinically important in order to identify those who have advanced HIV disease and who should be offered this package of care interventions.

## Components of the package of care interventions

Several large randomized trials have shown that providing a package of care interventions can reduce morbidity and mortality associated with advanced HIV disease. The individual components contained within the package of care interventions are already recommended by WHO, and are brought together in a standardized, simplified and evidence-informed package of HIV priority interventions.

### New recommendation

A package of interventions including screening, treatment and/or prophylaxis for major opportunistic infections, rapid ART initiation and intensified adherence support interventions should be offered to everyone presenting with advanced HIV disease (*strong recommendation, moderate-quality evidence*).

**Table 1: Components of package of care interventions for advanced HIV disease**

Areas for the package	Intervention	CD4 cell count	Adults and adolescents	Children
Screening and diagnosis	Sputum Xpert MTB/RIF as first test for TB diagnosis in symptomatic patients	any	yes	yes
	Urine LF-LAM for TB diagnosis in patients with symptoms and signs of TB	≤100 cells/mm <sup>3</sup> Or at any CD4 cell count value if seriously ill	yes	yes*
	Cryptococcal antigen (CrAg) screening	≤ 100 cells/mm <sup>3</sup>	yes	no
Prophylaxis and pre-emptive treatment	Co-trimoxazole prophylaxis <sup>§</sup>	≤350 cells/mm <sup>3</sup> or WHO clinical stage 3 or 4 event. Any CD4 cell count value in settings with high prevalence of malaria and/or severe bacterial infections	yes	yes**
	TB preventive treatment <sup>§</sup>	any	yes	yes <sup>#</sup>
	Fluconazole pre-emptive therapy for CrAg-positive patients without evidence of meningitis	< 100 cells/mm <sup>3</sup>	yes	Not applicable (Screening not advised)
	Rapid ART initiation	any	yes	yes
ART initiation	Defer ART initiation if clinical signs and symptoms are suggestive of TB or cryptococcal meningitis	any	yes	yes
Adapted adherence support	Tailored counselling to ensure optimal adherence to advance disease care package, including home visits if feasible	< 200 cells/mm <sup>3</sup>	yes	yes

<sup>#</sup> For children <12 months of age, only those with a history of TB contact should receive TB preventive treatment if the evaluation shows no active TB disease.

<sup>\*\*</sup> Priority should be given to all children less than 5 years old regardless of CD4 cell count or clinical stage, and those with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4 event and /or those with CD4 ≤ 350 cells/mm<sup>3</sup>)

<sup>§</sup> Co-trimoxazole, isoniazid and pyridoxine are available as a fixed-dose combination tablet.

Urine LF-LAM: lateral flow urine lipoarabinomannan assay.

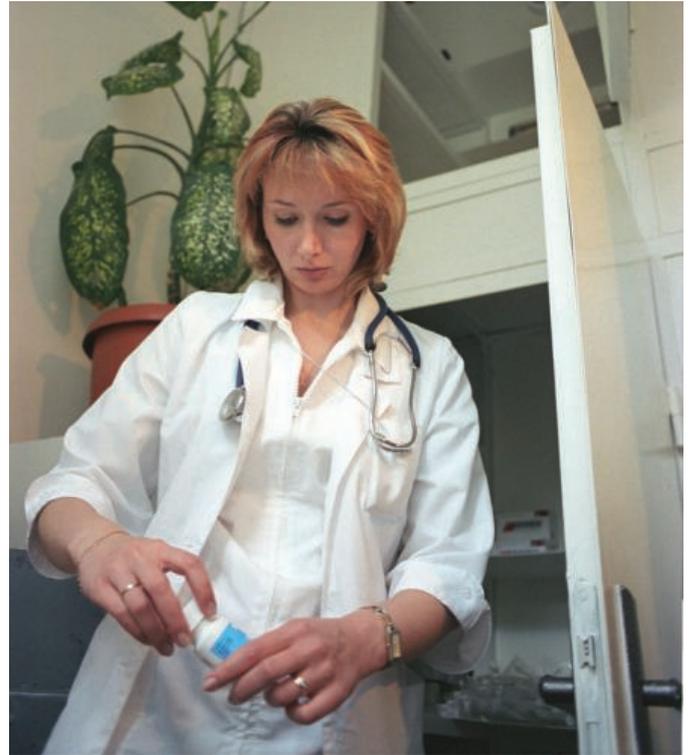
\* Limited data available for children.

### Implementation of the package of care interventions

The package of care for people with advanced HIV disease **should be offered at both hospitals and decentralized primary care clinics** according to the clinical status of PLHIV (ambulatory or requiring hospital admission), the clinical skills of the health-care workers and access to diagnostics at the facilities.

However, to increase access to the package, improving access at peripheral sites through mobile outreach or decentralization should be encouraged. This may be enabled by providing point-of-care diagnostic tests at the peripheral level where feasible (CD4 cell count, cryptococcal antigen testing, LF-LAM testing and Xpert® MTB/RIF) or through sample transport systems.

Where care has been decentralized, **clear referral criteria should be established** to ensure that people requiring further investigation or specialist management receive services in a timely manner. Likewise, referral mechanisms and optimal communication following discharge back to the peripheral clinic must be implemented to ensure appropriate follow-up (such as continuation of fluconazole, TB treatment or the timing of the switch to second-line ART for those receiving an ART regimen that is failing).



Where referrals are not feasible because of cost or distance constraints, advice should be sought from an experienced clinician and, where indicated, presumptive treatment started at the peripheral site. Referral and assessment should not result in unwarranted delays in starting ART and prophylaxis.

**Task shifting to nurses and other mid-level health care workers** for the clinical management of patients with advanced HIV disease should be supported with training, supervision, mentorship and appropriate patient care and referral pathways in place for those patients needing further investigations or management. Point of care diagnostic tests (e.g. CD4 cell count, cryptococcal antigen testing, LF-LAM testing and Xpert® MTB/RIF) or transport systems for laboratory samples can facilitate task shifting and the delivery of the package of interventions at peripheral sites.

## Rapid initiation of antiretroviral therapy

Linking people testing positive for HIV to ART services is a challenge in HIV programmes and historically substantial numbers of people have been lost to follow up in the period between HIV testing and initiation of ART. Recent attention has focused on how quickly ART should be started once HIV diagnosis is confirmed and on whether starting people on ART quickly, including on the same day of diagnosis can reduce loss to care before initiation of ART and improve clinical outcomes.

WHO has issued new guidelines on how soon ART should be offered to people who are ready to start treatment after a confirmed diagnosis of HIV.

### What does WHO recommend?

WHO now recommends that all PLHIV should be offered rapid initiation of ART, defined as within seven days of a positive HIV diagnosis, providing there are no contraindications. ART initiation should be offered on the same day for people who are ready to start.

This recommendation applies to all PLHIV at all age groups and is particularly important in people with very low CD4 cell counts who have an increased risk of death. However, previous WHO recommendations on the timing of ART initiation in the presence of TB and cryptococcal disease should be followed.

### New recommendations

**Rapid ART initiation should be offered to all people living with HIV following a confirmed HIV diagnosis and clinical assessment.** (Strong recommendation: high quality evidence for adults and adolescents; low-quality evidence for children)

Rapid initiation is defined as within seven days from the day of HIV diagnosis; people with advanced HIV disease should be given priority for assessment and initiation.

**ART initiation should be offered on the same day to people who are ready to start.** (Strong recommendation: high-quality evidence for adults and adolescents; low-quality evidence for children)

Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy is available from the WHO website at: <http://www.who.int/hiv/pub/guidelines/advanced-HIV-disease/en/>

## Evidence for rapid initiation of ART

A review of the available evidence found that the offer of rapid initiation, including same-day ART start, increases the number of people starting ART, reduces mortality, and may further reduce both mother-to-child transmission and transmission to HIV-negative partners. Rapid ART initiation was broadly found to be acceptable to PLHIV.

### Considerations for implementation of rapid and same-day start of ART

Not all PLHIV will be ready to start ART on the same day as diagnosis and they should not be coerced to start immediately, but they should be fully informed of the benefits of ART including the option of starting on the same day and supported to make an informed choice regarding when to start ART. **ART initiation should follow the overarching principles of providing people-centered care** which is focused around the health needs, preferences and expectations of people and communities. The decision to start ART ought to be a collaborative process between the health-care worker and PLHIV.

The **timing of counselling** should be adapted. Priority should be given to how to develop an immediate adherence plan and how to recognize ART side-effects. Further counselling to support treatment literacy, including the need for lifelong optimal adherence, how ART should be monitored, and options for future differentiation of HIV care should be covered in subsequent counselling sessions during the first months on ART.

Finally, particular consideration should be given to **children and their care givers, adolescents and people who inject drugs**, for whom there may be specific adherence challenges, and where the evidence for the acceptability of same day initiation is limited.



WHO / SEARO / Arifin Fitrianto: 15/10/2010: Indonesia  
Healthcare worker providing ART to a client

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POLICY BRIEF

HIV TREATMENT