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**NO TIME TO LOSE: DETECT,  
TREAT AND PREVENT AIDS.**



**MEDECINS SANS FRONTIERES  
DOCTORS WITHOUT BORDERS**

**AIDS related mortality remains high** - 770,000 deaths in 2018 - and has hardly declined in recent years. This global trend is reflected in countries where Médecins sans Frontières (MSF) works and continues to witness high ongoing mortality. To achieve the UNAIDS target of 500,000 deaths in 2020 requires a focus on and a drastic acceleration of measures to decrease mortality. For this it is necessary to plan, fund and implement a package of care to prevent, detect and treat Advanced HIV Disease (AHD) or AIDS, as outlined in the World Health Organisation's 2017 Guidelines for managing Advanced HIV Disease and rapid initiation of antiretroviral therapy.

This report, compiled by MSF, presents data from the AHD dashboard initiated by the HIV Advanced Disease Consortium (HIV-ADC). Findings from ongoing monitoring of the current status of AHD in terms of guidelines, funding and implementation in 15 countries where MSF works are presented: **the Central African Republic, the Democratic Republic of Congo, eSwatini, Guinea, India, Kenya, Lesotho, Malawi, Mozambique, Myanmar, Nigeria, South Africa, South Sudan, Uganda and Zimbabwe.** While an increasing number of countries are addressing AHD in their national guidelines, progress has been slow, and funding as well as implementation of a package of care for AHD remains extremely limited.

The WHO AHD guidelines outline a package of care for prevention, diagnosis and treatment of AHD. **Diagnostic tools** include 4 point of care tests: **CD4 count** for diagnosis of AHD, **GeneXpert MTB/RIF**, **Lateral Flow urine lipoarabinomanam assay (TB-LAM)** and **cryptococcal antigen screening (CrAG)**. Recommended treatment include **1st and 2nd line antiretroviral treatment (ART)**, **tuberculosis (TB) treatment**, **fluconazole**, **flucytosine and amphotericin B for cryptococcal meningitis**, **antibiotics for severe bacterial infections**, and **chemotherapy for Kaposi sarcoma**. **Prevention** consists of **cotrimoxazole** for severe bacterial infections, **TB preventive treatment**, and **fluconazole** for pre-emptive treatment of cryptococcal meningitis.

In MSF supported hospitals treating people with HIV, many present with AHD and mortality is high. The majority of patients have been exposed to ART and are resistant to first line antiretroviral drugs, requiring a rapid change of ART regimen. The use of point of care (POC) diagnostic tests has led to significant decreases in time between

presentation to care and start of appropriate treatment for TB and cryptococcal meningitis at primary and secondary level, with anticipated benefits on mortality. Access to point of care diagnostic tests and treatment for opportunistic infections is extremely limited, particularly at primary health care level where the majority of patients initially seek medical care.

Seven of the 15 countries have included AHD in their national guidelines, and 5 countries are in the process of updating their guidelines. However, even when AHD is mentioned in guidelines, key recommendations might be missing. Seven of the 15 countries do not recommend CD4 count for diagnosis of AHD; seven do not recommend TB-LAM and CrAg is only recommended in five. Four countries still recommend fluconazole alone for the treatment of cryptococcal meningitis, a suboptimal option associated with high mortality and whilst six recommend the WHO preferred option of amphotericin and flucytosine, this last drug is still not registered and available in any African country. Isoniazid preventive treatment remains the only recommended option for TB in 11/15 countries, even if there are more promising options such as 3 months of rifapentine-isoniazid (3HP).

Initially, unfavorable market conditions, with high prices and lack of registration of certain commodities, and limited commitment from funders, might have contributed to the slow adoption of WHO AHD guidelines by countries. Funding of commodities for AHD has been sporadic. However, there have been significant positive changes. Global advocacy efforts have resulted in reduction of prices of key diagnostics, treatment and prevention tools (e.g. flucytosine, liposomal amphotericin B, 3HP, GeneXpert). In addition, initiatives such as the UNITAID grant for AHD implemented by CHAI in seven countries in Africa, and increased attention to AHD in the Global Fund and PEPFAR guidance notes should further stimulate countries to address AHD in their national guidelines, implementation plans and requests for funding.

This report calls on countries, donors and implementers to have AHD high on their resource allocation, policy development and implementation agenda within the HIV/TB response. The level of commitment and focus to end AIDS deaths must translate into national level plans and actions by countries to detect, treat and prevent AIDS among people living with HIV. There is no TIME TO LOSE!



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# 1. INTRODUCTION AND BACKGROUND

**Three decades into the HIV epidemic**, nearly a million people living with HIV continue to die annually from preventable and treatable ailments. In 2018 approximately 770,000 people living with HIV including 100,000 children died from AIDS, only a slight decline from the 800,000 people who died from AIDS in 2017. Globally AIDS related illnesses are reported as the leading cause of death among women aged 15 – 49 years.<sup>1</sup> Similarly the number of AIDS deaths in some of the countries where MSF works has not significantly declined. In 2018, 71,000 deaths were reported in South Africa, 54,000 in Mozambique, 25,000 in Kenya, 17,000 in DRC, 13,000 in Malawi and 4,300 in Guinea.<sup>2</sup>

UNAIDS portends that meeting the global target of less than 500,000 AIDS deaths by 2020 will require a reduction of AIDS deaths by at least 135,000 annually in both 2019 and 2020.<sup>3</sup>

However, AIDS mortality numbers have plateaued over the last years, with a reduction of only 30,000 in 2018. Concerns arise on the ability to achieve these targets.<sup>4</sup>

Worldwide, an estimated 33% of people who test positive for HIV start treatment with an alarmingly low CD4 count (below 200 cells/mm<sup>3</sup>), an indicator of serious immunological failure and high risk of dying. At least one in three people living with HIV still present to care with Advanced HIV Disease (AHD).<sup>5</sup>

In 2017, the World Health Organization (WHO) developed Guidelines on Advanced HIV Disease giving guidance on the package of care needed for identification and prevention of HIV co-morbidities for people with AHD. AHD in adults is defined as when a person with HIV has a CD4 cell count below 200cell/mm<sup>3</sup> or WHO clinical stage 3 or 4 at the presentation of care and for all children less than five years.

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1 UNAIDS 2018; Women and HIV; A spotlight on adolescent girls and women  
2 UNAIDS fact sheets 2019  
3 HLM Targets  
4 UNAIDS Corrected mortality figures for 2017 reported as 800,000 deaths  
5 WHO Guidelines for Managing Advanced HIV Disease and Rapid Initiation of ART, <https://www.who.int/hiv/pub/guidelines/advanced-HIV-disease/en/>

In 2018, a coalition of NGOs and clinicians asked major donor agencies to support urgent measures to reduce high mortality from AIDS, in particular by allocating the necessary resources to enable earlier detection, prevention and treatment of people with advanced HIV disease. Members of the HIV Advanced Disease Consortium (HIV-ADC) include the African Society of Lab Medicine (ASLM), the Centers for Disease Control and Prevention (CDC), the Clinton Health Access Initiative (CHAI), the Global Action Fund for Fungal Infections (GAFFI), the Global Health Impact Group (GHIG), the International AIDS Society (IAS), ICAP at Columbia University, the International Diagnostics Center (IDC-dx), IRESSEF (Senegal), IS Global, Médecins sans Frontières (MSF), St. Georges University of London (SGUL), UNITAID, the World Health Organization (WHO), and various Health Ministries and HIV/AIDS programmes.<sup>6</sup>

In partnership with members of the AHD consortium, MSF has been monitoring progress on AHD in terms of national guidelines, funding and implementation through a dashboard targeting 32 countries. In this report we present data from the dashboard targeting fifteen countries where MSF is present and provides HIV and TB services: **The Central African Republic,**

<sup>6</sup> MSF joins new consortium to prevent AIDS-related deaths, <https://samumsf.org/en/news/msf-joins-new-consortium-prevent-aids-related-deaths>

**the Democratic Republic of Congo, eSwatini, Guinea, India, Kenya, Lesotho, Malawi, Mozambique, Myanmar, Nigeria, South Africa, South Sudan, Uganda and Zimbabwe.**

This report highlights where countries are in this moment with regards to adapting WHO guidelines on AHD, what is being implemented, what is currently being resourced or planned, and barriers to progress.

The Dashboard and Report aims to provide significant input into advocacy efforts ahead of key events in 2020 such as the PEPFAR Country Operational Planning (COP) and Regional Planning Meetings (RPM); Country applications to the Global Fund, other donor budget discussions and community awareness and collaborative advocacy and demand creation initiatives.

The findings show that two years after the WHO guidelines on AHD, as some countries - particularly those in Africa - are in the process of incorporating WHO recommendations into national guidelines, many are yet to do so. Funding and access to commodities for AHD remain extremely limited. There are significant gaps in implementation of the minimum package of care for AHD in all countries monitored. Many opportunities to reduce avoidable mortality are being missed.

## 1.1 WHY ADVANCED HIV DISEASE?

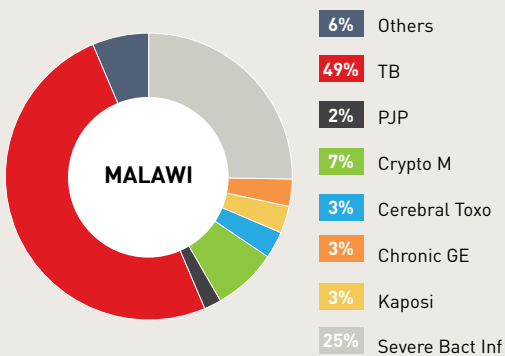
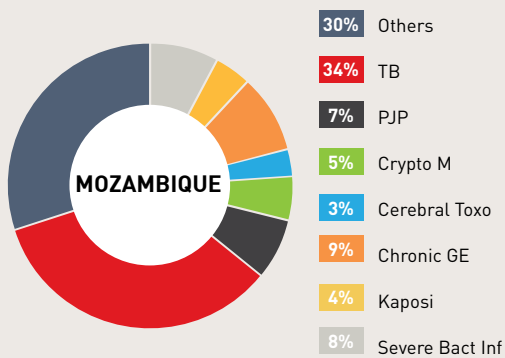
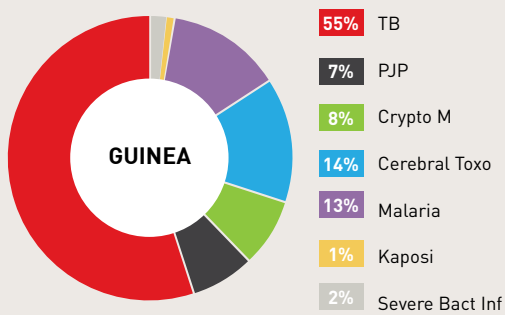
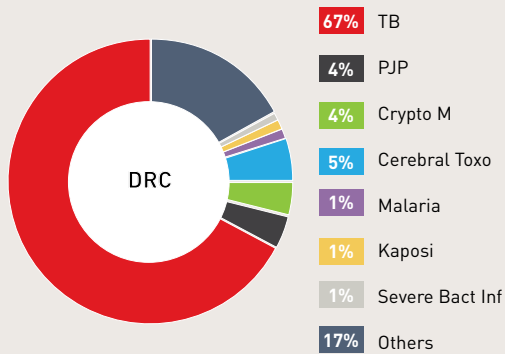
While ART coverage has improved in many contexts since the adoption of the WHO recommendations on 'test and treat', the number of deaths is hardly decreasing and almost a third of people entering care have AHD. In countries with low treatment coverage such as **CAR, DRC and Mozambique**, many people living with HIV continue to present with AHD because they access HIV testing and treatment too late. In addition, while some people still present late even in high ART coverage settings, there has been a shift in recent years: most people presenting to care with AHD are or have been

on ART. Their HIV progressed to AIDS either because they interrupted treatment or because of treatment failure.

In MSF supported hospitals providing care for AIDS patients the majority of patients treated in 2017 had already been on treatment: **71% in Kinshasa (DRC), 62% in Conakry (Guinea), 60% in Homa Bay (Kenya) and 67% in Nsanje (Malawi)**. A significant proportion of people with AHD have developed resistance to their ARV treatment. Among patients admitted with a CD4 <200 copies/mm<sup>3</sup> in MSF supported hospitals in Kenya and DRC, more than 70% had

**FIGURE 1**

# CAUSES OF DEATH IN 4 MSF SUPPORTED HOSPITALS



treatment failure with a viral load >1000 copies/ml and resistance to at least two classes of ARVs, highlighting the need for a rapid switch to 2<sup>nd</sup> or 3<sup>rd</sup> line regimens.<sup>7</sup>

Daily treatment for life is challenging and barriers to uninterrupted high adherence to ART include treatment fatigue, adverse reactions to drugs, late or lack of detection of treatment failure and initiation of 2<sup>nd</sup> or 3<sup>rd</sup> line ART, cost of transport and time off work, stigma, insufficient adherence support, and overburdened health systems struggling to provide adequate supportive care and models to promote retention in care. In addition, social drivers such as poverty, inequality, gender based violence (GBV), and unfavorable laws and policies contribute to people disengaging from care and treatment failure.

<sup>8</sup>HIV care is not a linear process but a circular one: many people disengage from and re-engage into care at some point in their life, and many struggle to maintain perfect adherence throughout their life. As a consequence, people continue to develop AHD.

## Opportunistic infections and the package of care for AHD

Opportunistic infections (OIs) are the leading causes of mortality amongst adults with AHD due to compromised immunity. The main opportunistic infections driving AHD mortality include tuberculosis (TB), cryptococcal meningitis (CM), severe bacterial infections (SBIs), pneumocystis pneumonia (PCP), toxoplasmosis and Kaposi sarcoma (KS).<sup>9</sup>

Worldwide, 10 million people developed tuberculosis in 2018, of whom 9% were people living with HIV. In the same year TB caused an estimated 251,000 deaths among HIV-positive people, accounting for one third of global AIDS related deaths. Although the number of TB deaths among HIV-positive people has fallen by 42% since 2000, from 534,000 in 2000 to 251,000 in 2018, these numbers are not reducing

7 Bossard et al. CROI 2019. <http://www.croiwebcasts.org/y/2019/7?link=nav&linkc=date>  
 8 Bukenya et al. AIDS Research and Therapy 2019. <https://aids-researchtherapy.biomedcentral.com/articles/10.1186/s12981-018-0214-y>  
 9 Fight is not over as AIDS deaths remain high. MSF 2019. <https://www.msf.org/high-number-aids-deaths-shows-fight-against-hiv-far-over>

fast enough to achieve TB targets for 2030.<sup>10 11</sup> Cryptococcal meningitis accounts for 15% to 20% of all AIDS related deaths, with an estimated 223,000 cases and 180,000 deaths in 2014.<sup>12</sup>

The WHO AHD guidelines outline a package of care for prevention, diagnosis and treatment of AHD. The **tools for diagnosis** include 4 point of care tests: **CD4 count** for diagnosis of AHD, **GeneXpert MTB/RIF** and **Lateral Flow urine lipoarabinomannan assay (TB-LAM)** for diagnosis of TB, and **cryptococcal antigen screening (CrAG)** for the diagnosis of cryptococcal meningitis. For **treatment** the guidelines recommend **rapid initiation of ART** among people living with HIV. Essential drugs for treatment of AHD include **1<sup>st</sup> and 2<sup>nd</sup> line ART, TB treatment, fluconazole, flucytosine and amphotericin B for treating cryptococcal meningitis, antibiotics for severe bacterial infections, and chemotherapy for Kaposi sarcoma.** **Prevention** consists of **cotrimoxazole** to prevent severe bacterial infections, **TB preventive treatment**, and **fluconazole** for pre-emptive treatment of cryptococcal meningitis. Additionally the guidelines provide for adapted adherence support for people living with HIV. Adherence to ARV's leads to viral suppression

which is necessary for successful treatment of people living with HIV.<sup>13</sup>

## Community awareness of AHD

The role and importance of community awareness on prevention and detection of AHD among people living with HIV is established. However, awareness of Advanced HIV Disease remains limited particularly at community level. People living with HIV and their communities often are unable to quickly detect danger signs and bring patients to the hospital early enough. Stigma remains one of the biggest barriers to retention and adherence to care, and in some contexts, such as in West and Central Africa, user fees and other costs to PLHIV prevent clients from accessing care early. Community awareness, particularly on the understanding of danger signs and prevention of AHD, is necessary to ensure peers or family members are empowered to access healthcare in time for prevention, diagnosis and rapid initiation of treatment. This includes referral to primary health care and post discharge support for adherence and retention. Additionally interventions for demand creation and community led advocacy interventions can be critical in ensuring development and implementation of responsive policies and programs.

10 [https://www.who.int/tb/publications/global\\_report/en/](https://www.who.int/tb/publications/global_report/en/)

11 Global Tuberculosis Report. WHO 2018. [https://www.who.int/tb/publications/global\\_report/en/](https://www.who.int/tb/publications/global_report/en/)

12 Guidelines for the diagnosis, prevention and management of cryptococcal disease in HIV-infected adults, adolescents and children. WHO 2018. <https://apps.who.int/iris/bitstream/handle/e/10665/260399/9789241550277-eng.pdf?sequence=1>

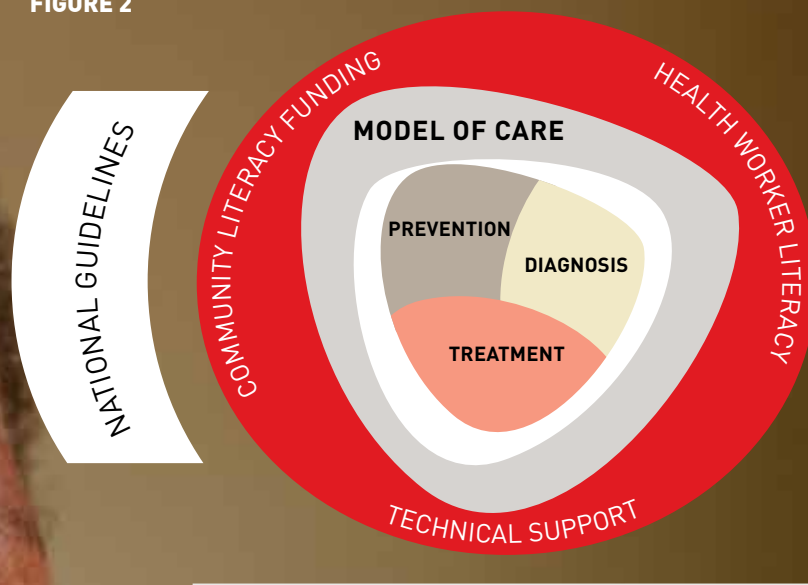
13 HIV/TB Guide for Hospital Level. MSF 2019. <https://samumf.org/en/resources/hiv/advanced-hiv-disease/msf-hivtb-guide-hospital-level#>

**TABLE 1** SUMMARY WHO PACKAGE OF CARE FOR AHD

Diagnosis	Prevention	ART initiation	Treatment of opportunistic infections	Adapted adherence support
<b>CD4 cell count</b>	Cotrimoxazole prophylaxis	Rapid ART initiation	<ul style="list-style-type: none"> <li>• TB treatment</li> <li>• All oral MDR TB treatment</li> </ul>	Tailored counseling to support adherence
<b>Xpert MTB/RIF as 1<sup>st</sup> test for TB</b>	TB preventive treatment: isoniazid (IPT) OR rifapentine-isoniazid (3HP) OR FDC of cotrimoxazole/INH/B6	Defer if symptoms of TB or cryptococcal meningitis	Cryptococcal meningitis:  Fluconazole, flucytosine, amphotericin B	Tracing of lost to follow-up
<b>TB-LAM if CD4 &lt;200</b>	Fluconazole pre-emptive therapy	Prompt switch to 2 <sup>nd</sup> line ART if treatment failure	Antibiotics for severe bacterial infections	Post-hospitalisation follow-up
<b>Cryptococcal antigen screening if CD4 &lt;200</b>				

\* Tailored counselling: considerations to be made e.g. for involvement of family support, community and/or home based care

FIGURE 2



### LITA'S EXPERIENCE:

Lita is a young woman living with HIV from Nsanje district in Malawi. Lita had been sick on and off and when her illness persisted she was taken to Nsanje District Hospital (NDH) for treatment. At the hospital, Lita was diagnosed HIV positive and because she was very ill, was immediately hospitalized and started on ARVs as narrated by her father James\*.

After she was discharged she went back to her marital home which was a long distance from Nsanje district Hospital. Unfortunately, she did not immediately get the transfer from the HIV management clinic at Nsanje district Hospital and experienced difficulties to get drug refills later running out of medication. As a result, Lita stopped taking ARV medication for two months from August to September 2019.

"Even before, I was having difficulties taking my medication everyday so somedays I would not take it" shares Lita from her hospital bed.

When her aunt Rose\* received a phone call that Lita is not well, she went to where Lita was staying and brought her straight to Nsanje district hospital. By then Lita was all alone her husband had left her. Lita and her husband had three children, two of whom had passed away, one in September 2019. Their HIV status was unknown.

On 16<sup>th</sup> October 2019 Lita was brought into Nsanje District hospital and because of her very ill status was quickly taken to the MSF supported Rapid Assessment Unit (RAU). Upon thorough assessment through point of care (POC) tests including CD4, VL, STI and OIs (TB, Meningitis), Lita was re-engaged into care and re-initiated on treatment.

The Rapid Assessment Unit (RAU), integrated as a unit of the emergency ward, is equipped with appropriate staff, commodities and diagnostic tools to ensure optimal diagnosis and efficient treatment initiation before the patients go to the hospital wards. This is critical for sick patients, who are often at very high risk of death the first 48 hours.

\*not real name



## 2. METHODOLOGY

MSF developed the Advanced HIV Disease (AHD) Dashboard to document progress on AHD in national guidelines, funding and implementation across 32 countries. The AHD Dashboard is a tool to track and monitor national policy and funding status, and further its translation into practice by focusing on factors that aid effective implementation. These include adoption of WHO Guidelines for managing advanced HIV disease at country level, resourcing for diagnostic and treatment products for advanced HIV, and provision of the AHD package of care at primary and secondary care level.<sup>14, 15</sup>

The progress of 15 of the 32 countries in the dashboard have been highlighted in this report. The countries highlighted are the **Central African Republic (CAR), the Democratic**

**Republic of Congo (DRC), eSwatini, Guinea, India, Kenya, Lesotho, Malawi, Mozambique, Myanmar, Nigeria, South Africa, South Sudan, Uganda and Zimbabwe.** These countries were selected based on their high HIV burden, AIDS related deaths, and morbidity and mortality due to TB and cryptococcal meningitis. They are also countries where MSF works to implement HIV/TB projects including for patients with advanced HIV disease.

From November 2018 to October 2019, we have tracked the progress of the above-mentioned countries by conducting a desktop review of each country's national policy documents, primarily national guidelines. The data was verified by MSF in-country offices. In addition, MSF in partnership with the CDC Foundation sent a mapping questionnaire to the 15 MSF country offices to be shared and completed with their Ministry of Health (MoH) counterparts in order to gain more detailed information on the status of implementation.

<sup>14</sup> Update of recommendations on first- and second-line antiretroviral regimens. WHO 2019. <https://www.who.int/hiv/pub/arv/arv-update-2019-policy/en/>

<sup>15</sup> WHO Guidelines for Managing Advanced HIV Disease and Rapid Initiation of ART, <https://www.who.int/hiv/pub/guidelines/advanced-HIV-disease/en/>



Key findings are reported on the status of AHD in policy and national guidelines, implementation, and funding. Indicators of progress were tracked in the following categories: 1. **Diagnostics:** CD4, HIV viral load, GeneXpert MTB/RIF, TB-LAM, and cryptococcal antigen (CrAg); 2. **Treatment:** antiretroviral therapy (ART), medicines to treat TB, cryptococcal meningitis and Kaposi Sarcoma; 3. **Prevention:** cotrimoxazole prophylaxis for severe bacterial infections, TB preventive therapy, and fluconazole for cryptococcal meningitis; 4. **Models of care:** HIV/TB integration, tracing of patients lost from care, and adaptation of services for AHD.

Some countries were still in the process of updating their national guidelines during the survey period. If guidelines were being updated at the time of the survey and the MoH or country mission staff provided information about their content, the status of the document was noted.

This report has several limitations. It only covers a limited number of countries, mostly from Africa. Four of the 15 countries presented benefit from the UNITAID/CHAI Advanced HIV disease project (**Malawi, Nigeria, South Africa, and Uganda**) which is likely to have a positive impact in regards to progress in their policy and implementation status and plans for AHD. This is however not representative of the realities of other countries in the survey. There is limited data on AHD in pediatrics and children under five years of age from what exists in policy to what is implemented. Countries had to varying levels limited information on the status of implementation and opportunities to discuss reasons for slow progress with country MoH were also limited.

This report is a work in progress on the monitoring of country adaptation and implementation of AHD packages of care and form a baseline from which subsequent updates and reports can be developed in the future.

**TABLE 2**  
**ADH POLICY STATUS DASHBOARD**

National Policy Documents	
Country	Indicator
	Include national guidelines on advanced HIV
CAR	Yes
DRC	In progress
eSwatini	Yes
Guinea	Yes
India	No
Kenya	Yes
Lesotho	Yes
Malawi	In progress
Mozambique	In progress
Myanmar	Yes
Nigeria	In progress
South Africa	Yes
South Sudan	No
Uganda	Yes
Zimbabwe	Yes



# 3. FINDINGS:

## KEY HIGHLIGHTS:

- Many National Guidelines **do not include AHD** as they were developed before the 2017 WHO AHD guidelines.
- Countries that have updated guidelines post 2016 and address AHD include **Guinea, Lesotho, India, Kenya, South Africa, Uganda and Zimbabwe.**
- Countries in process of reviewing national HIV and TB guidelines and making provisions now for AHD include **Malawi, Mozambique, DRC, eSwatini and Nigeria.**
- **Some guidelines do not provide** for all the components the WHO package of care for AHD.
- **Uganda has developed a national AHD implementation plan** with support from CHAI implementing the UNITAID grant on AHD.
- **Unfavorable markets with high pricing** for certain commodities contributed to countries slow progress in adoption of AHD package of care. Examples include **point of care CD4 machines, isoniazid-rifapentine for TB prevention, and flutocytosine for the treatment of cryptococcal meningitis.**

Country progress to adopt the WHO AHD guidelines released in 2017 has been slow. Many of the countries developed and released national HIV/AIDS consolidated guidelines in 2016, a year before the AHD guidelines were released and didn't provide guidance for management of patients with AHD. Five of the fifteen countries in this report updated their guidelines in 2018 and included guidance for the management of AHD: **Guinea, India, Kenya, Uganda, and Zimbabwe.** In 2019 **South Africa** released updated HIV guidelines making provisions for use of diagnostics and treatment options for the management of AHD, while Lesotho released an addendum to their national guidelines. **Uganda** also developed an AHD implementation plan which is currently operational. Six countries are finalizing new HIV guidelines with provisions for AHD: **Malawi, Mozambique, DRC, eSwatini, Uganda and Nigeria.**

A number of countries however have no plans yet to adopt the WHO guideline on AHD. **South Sudan** for example continues to have gaps in provision of basic diagnostics and treatment of OI's like TB. Only four of the fifteen countries, **DRC, Guinea, Malawi and Eswatini,** have recommendations for treatment of Kaposi Sarcoma (skin cancer) within their HIV package of care.

National guidelines are the foundation of implementation, prioritization, procurement and use of AHD package of care. Unfavorable market trends often characterized by high pricing of commodities for diagnostics, prevention and treatment of common opportunistic infections have been a barrier to the willingness of countries to include certain elements of the recommended package of care within national lists of essential diagnostics or treatment.<sup>16</sup> Additionally, lack of firm recommendations and direct financial support from donors such as PEPFAR and Global Fund to procure these commodities have had a bearing on the slow pace at which countries are adopting the WHO guidelines for AHD.

The influence of global market shaping strategies from the UNITAID grant for AHD implemented by CHAI, alongside advocacy by partner organizations in the AHD consortium for price reduction on key diagnostics and treatment options, as well as accelerated processes of country level registration of commodities by countries have resulted in some positive shifts in the last half of 2019.<sup>17</sup>

<sup>16</sup> De Luca et al. PHA 2014. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4533504/>

<sup>17</sup> Prioritizing Advanced HIV Disease and Overcoming Barriers to Access. Amole. IAS 2019. [http://programme.ias2019.org/PAGMaterial/PPT/2174\\_4275/CHAI%20presentation%20for%20AHD%20satellite%20at%20IAS%202019\\_final.pptx](http://programme.ias2019.org/PAGMaterial/PPT/2174_4275/CHAI%20presentation%20for%20AHD%20satellite%20at%20IAS%202019_final.pptx)

## ACCESS BARRIERS; EXPERIENCE OF ACCESS TO FLUCYTOSINE FOR TREATMENT OF CRYPTOCOCCAL MENINGITIS IN SOUTH AFRICA.

While updating guidelines is an essential first step, availability and affordability of the medicines required to implement them is a key challenge in many countries in sub-Saharan Africa. The WHO recommends a combination of flucytosine and amphotericin B for the treatment of cryptococcal meningitis – both of which are largely unavailable in the region. In South Africa, still no generic manufacturer has filed to register flucytosine with the South African Health Products Regulatory Authority (SAHPRA). MSF SA has established in 2018 a Flucytosine Access Program that distributes Flucytosine to 15 tertiary hospitals within South Africa. So far 400 courses have been distributed in that period. From January CHAI is going to take over the Access Program following the distribution on the MSF sites. MSF and other organizations are able to import under a “compassionate use” type mechanism authorizing use of unregistered medicines, Section 21, but this does not allow for appropriate scale up to meet the needs of the country.

Flucytosine needs to be registered to allow its inclusion in the national Essential Medicines List, incorporation into national guidelines and procurement under national tenders. Multiple generic companies produce this medicine, which should be urgently registered in high-burden HIV countries across the sub-Saharan African region.

Liposomal Amphotericin B (L-AMB), from Gilead, the preferred formulation of amphotericin, is not included in any guideline because of its high price. It is registered in South Africa, but is only available in the private market at \$200 per vial. Using approximately 3 vials per day for one week of induction treatment would cost \$4,200 USD to treat one person in South Africa – an excessive price that is far out of reach. Gilead did announce a price reduction to \$16.25 per vial for 116 LMICs (including South Africa) in September 2018<sup>18</sup> but as of today, this has yet to be implemented and the drug remains largely unavailable in the countries where it is most needed.

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18 Gilead Sciences Announces Steep Discounts for Ambisome to Treat Cryptococcal Meningitis in Low- and Middle-Income Countries. Gilead 2018. <https://www.gilead.com/news-and-press/company-statements/discount-for-ambisome>

**TABLE 3**

# DIAGNOSTICS DASHBOARD

■ Yes 
 ■ No 
 ■ Not applicable

Country	CD4			Viral Load		TB Screening -- GeneXpert (screening of patients clinically suspected of TB)
	Baseline	Routine	Diagnostic	Routine Monitoring	Switching Standard Operating Procedures	National guidelines recommend GeneXpert for TB screening?
Central African Republic (CAR)	Yes	Yes	No	Yes	Yes	Yes
Implementation:	Yes	Yes	Yes	Yes	Yes	Yes
Democratic Republic of Congo (DRC)	Yes	No	No	Yes	Yes	Yes
Implementation:	Yes	Yes	Yes	Yes	Yes	Yes
eSwatini	Yes	Yes	Yes	Yes	No	Yes
Implementation:	Yes	Yes	Yes	Not applicable	Not applicable	Yes
Guinea	Yes	Yes	No	Yes	Yes	Yes
Implementation:	Yes	Yes	Yes	Yes	Yes	Yes
India	Yes	Yes	No	Yes	Yes	Yes
Implementation:	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Kenya	Yes	Yes	Yes	Yes	Yes	Yes
Implementation:	Yes	Yes	Yes	Yes	Yes	Yes
Lesotho	Yes	Yes	Yes	Yes	Yes	Yes
Implementation:	Yes	Yes	Yes	Yes	Yes	Yes
Malawi	No	No	Yes	Yes	Yes	Yes
Implementation:	Yes	Yes	Yes	Yes	Yes	Yes
Mozambique	Yes	Yes	No	Yes	Yes	Yes
Implementation:	No	No	No	Yes	Yes	Yes
Myanmar	Yes	Yes	No	Yes	Yes	Yes
Implementation:	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Nigeria	Yes	Yes	Yes	Yes	Yes	Yes
Implementation:	Yes	Yes	Yes	Yes	Yes	Yes
South Africa	Yes	Yes	Yes	Yes	Yes	Yes
Implementation:	Yes	Yes	Yes	Yes	Yes	Yes
South Sudan	Yes	Yes	Yes	Yes	Yes	Yes
Implementation:	No	No	No	No	No	No
Uganda	Yes	Yes	Yes	Yes	Yes	Yes
Implementation:	Yes	Yes	Yes	Yes	Yes	Yes
Zimbabwe	Yes	Yes	No	Yes	Yes	Yes
Implementation:	Yes	Yes	Yes	Yes	Yes	Yes

■ Yes   
 ■ No   
 ■ Not applicable (N/A)   
 ■ Pilot

CD4 threshold:   
 ■ <100   
 ■ 100   
 ■ 200

Country	National guidelines for Cryptococcal meningitis screening (CrAg)						TB Screening: TB-LAM					
	CrAg Recommended	CD4 threshold	Reflex screening	Clinician initiated	Primary Healthcare (PHC)	In Hospital	TB-LAM recommended?	CD4 threshold	Reflex Screening	Clinician Initiated	Primary Healthcare (PHC)	In Hospital
Central African Republic (CAR)	Yes	N/A	No	No	No	No	No	N/A	No	No	No	No
Implementation:	No						No					
Democratic Republic of Congo (DRC)	No	N/A	No	No	No	No	Yes	N/A	No	No	No	No
Implementation:	No						No					
eSwatini	Yes	<100	Yes	No	Yes	Yes	Yes	<100	No	Yes	Yes	Yes
Implementation:	Yes						Yes					
Guinea	Yes	N/A	Yes	Yes	No	Yes	Yes	N/A	Yes	Yes	Yes	Yes
Implementation:	Yes						Yes					
India	No	N/A	No	No	No	No	No	N/A	N/A	N/A	N/A	N/A
Implementation:	N/A						N/A					
Kenya	Yes	No	Yes	Yes	Yes	Yes	No	N/A	N/A	N/A	N/A	N/A
Implementation:	Yes						Yes					
Lesotho	Yes	N/A	No	Yes	No	Yes	Yes	N/A	No	Yes	Yes	Yes
Implementation:	Yes						Yes					
Malawi	Yes	N/A	No	Yes	No	Yes	Yes	N/A	No	Yes	No	Yes
Implementation:	Yes						Yes					
Mozambique	Yes	N/A	No	Yes	No	Yes	Yes	N/A	No	Yes	Yes	Yes
Implementation:	No						No					
Myanmar	Yes	200	No	Yes	Yes	Yes	Yes	N/A	No	Yes	Yes	Yes
Implementation:	N/A						N/A					
Nigeria	Yes	200	Yes	Yes	Yes	Yes	Yes	200	No	Yes	No	Yes
Implementation:	No						Pilot					
South Africa	Yes	N/A	Yes	Yes	Yes	No	Yes	N/A	N/A	N/A	N/A	N/A
Implementation:	No						Yes					
South Sudan	Yes	N/A	No	Yes	No	Yes	No	N/A	No	No	No	No
Implementation:	No						No					
Uganda	Yes	N/A	Yes	Yes	Yes	Yes	Yes	N/A	No	Yes	Yes	Yes
Implementation:	No						Yes					
Zimbabwe	Yes	N/A	No	Yes	Yes	Yes	Yes	N/A	No	Yes	No	Yes
Implementation:	Yes						Yes					

# 3.1 DIAGNOSTICS: POLICY AND IMPLEMENTATION

## KEY HIGHLIGHTS:

- **Seven of the 15 countries** recommend CD4 testing for diagnosis of AHD: DRC, Eswatini, Kenya, Malawi, Nigeria, South Africa and Uganda.
- **Coverage of CD4 is limited.** Most countries only provide CD4 in selected sites and availability of reagents is sporadic.
- **Viral load testing for routine monitoring** is recommended in the 15 countries. Coverage and implementation is variable.
- **GeneXpert for diagnosis of TB** is recommended and available in all of the 15 countries. Implementation is limited as not POC.
- **TB LAM for diagnosis of TB is recommended in 8 of the 15 countries:** CAR, eSwatini, Guinea, Lesotho, Malawi, Myanmar, Mozambique, Nigeria and South Africa.
- **In Mozambique and Malawi,** TB LAM and CrAg is proposed for inclusion in the national treatment guidelines currently in development progress and Malawi is planning roll out of CrAg in 2020.
- **TB-LAM is not implemented** widely in any country even if recommended. Kenya finalised a pilot in 2019, while Malawi, Nigeria and South Africa will pilot TB-LAM to inform national scale up in 2020.
- **CrAg for screening of cryptococcal meningitis** is recommended in five of the 15 countries: Kenya, Mozambique, South Africa, South Sudan, Uganda and Zimbabwe.
- **CrAg is not widely implemented** in most of the countries except South Africa.
- **Point of care TB-LAM and CrAg tests** available in all MSF supported health facilities in any of the 15 countries.

## CD4 for the diagnosis of Advanced HIV Disease

The WHO guidelines define AHD as a CD4 below 200 cells/mm<sup>3</sup> or WHO clinical stage 3 or 4 and all children under five. This makes CD4 for diagnosis of AHD a critical step in the management of people with AIDS. With the evolution of guidelines to 'test and treat' all who are HIV positive, the use of CD4 to determine initiation to ART was completely stopped. The shift from CD4 to viral load testing to monitor progress on treatment resulted in many countries dropping investment in CD4 machines. However, CD4 remains a critical diagnostic test to detect people with AHD; it is the entry door to further diagnostic testing such as TB-LAM and CrAg. CD4 for diagnosis of AHD should be done at initiation of ART, in patients returning to care after interruption, and in patients with suspected clinical or virological failure.

Clinical staging for WHO III and IV is critical for diagnosing AHD particularly where access to CD4 is limited or nonexistent although staging alone has a poor accuracy for diagnosing AHD.

Seven of the fifteen have provisions in their guidelines for use of CD4 for diagnosis of AHD: **DRC, Eswatini, Kenya, Malawi, Nigeria, South Africa and Uganda.** However, coverage of CD4 is limited and availability of reagents for testing is very sporadic. **Scale up is happening in a number of countries making plans to address AHD in pilot programs as well as national scale up.** **Uganda** for example **revised AHD sites from 695 to 917,** has increased use of CD4 for diagnosis of AHD and centralized services to about 55 health facilities. However, a gap of CD4 reagents currently exists and the next consignment is only expected in April 2020, with a negative impact on access to CD4 testing.

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## Viral load, testing for TB and cryptococcal meningitis

Use of GeneXpert for the diagnosis of TB for patients with clinical signs of TB is recommended in the guidelines of the 15 countries. Similarly, guidance on viral load testing for routine monitoring of ART is recommended everywhere. Implementation gaps exist in coverage and availability of reagents.

TB LAM and CrAG for diagnosis of TB and cryptococcal meningitis respectively among people with CD4 <200 or with signs and symptoms are recommended by WHO because they allow for rapid detection of the two diseases and have been proven to reduce mortality. Use of these point of care diagnostic tests is limited in most of the countries featured in this report. **DRC** plans to make TB LAM available in high volume health facilities with support from PEPFAR<sup>19</sup> while **Uganda** reports irregular supply of TB LAM. **Kenya and South Sudan** do not

<sup>19</sup> [https://www.state.gov/wp-content/uploads/2019/09/DRC\\_COP19-Strategic-Directional-Summary\\_public.pdf](https://www.state.gov/wp-content/uploads/2019/09/DRC_COP19-Strategic-Directional-Summary_public.pdf)

recommend TB LAM in the national guidelines. In Mozambique, TB LAM and CrAG is proposed for inclusion in the national treatment guidelines currently in development progress.

Currently, TB-LAM and CrAG is not available in primary health care outside of pilot sites and MSF supported facilities, especially at primary health care.

As national HIV guideline updates progress the report finds various national plans to include these important diagnostic tools into national procurement plans. For example, Kenya just completed a pilot of TB-LAM and is currently reviewing data which will be used to determine national scale up. **Lesotho, Nigeria and South Africa** have updated guidelines and are in various levels of pilot and roll out on the use of TB-LAM with help from CHAI who are supporting pricing and supply opportunities. **Nigeria** is also finalizing registration of CrAG and plan to procure 12,738 tests in 2020.

### Time is Life!

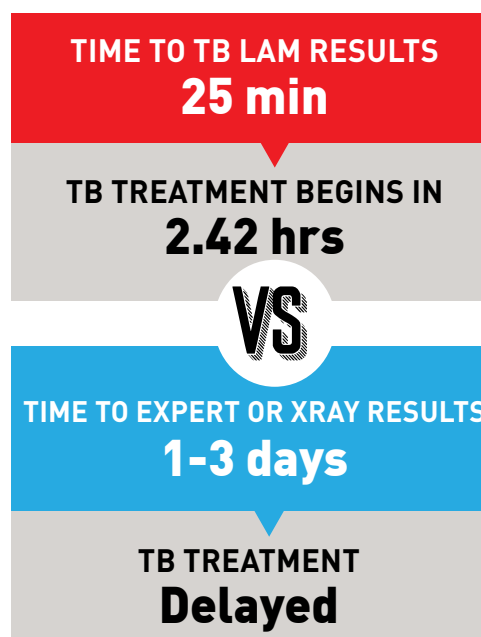
Time sensitive testing, diagnosis and initiation of treatment remains the biggest challenge to averting deaths of people with AIDS. In many countries where MSF provides HIV/TB services, up to a third of patients with AHD died within 48 hours admission to hospital. **In the MSF project in Nsanje, Malawi** diagnosis of patients with TB was much faster with TB LAM compared to GeneXpert or chest Xray. On average, turnaround time for TB LAM results was **25 minutes** compared to 2-3 days for GeneXpert and 1-3 days for chest Xray. The average time from TB LAM request (once a CD4 test has been done) to first dose of TB treatment was 2.42 hours.

Timely diagnosis with CD4, TB LAM and CrAg is critical and needed at secondary as well as at primary health care level, where most of the patients get to first because of proximity and cost implications. People need to be screened and managed at PHC level and community level in order to prevent and treat diseases associated with AHD early enough to avoid severe illness and death.

In MSF projects implementing AHD models of care, point of care CD4 allows for diagnosis of AHD within one hour of presentation. When rapidly followed by TBLAM and CrAG tests

this strategy has resulted in a reduction of time between presentation and initiation of treatment from 48 hours or more to 24 hours or less, thereby saving lives. Implementing the AHD package of care **in the MSF project in Nsanje, Malawi**, has led to a marked reduction in mortality at the health facility, from approximately 27% at the start to less than 15%.

FIGURE 3



**TABLE 4**

# AHD TREATMENT MANAGEMENT DASHBOARD

■ Yes   
 ■ No   
 ■ Not applicable   
 ■ In progress

Country	Cryptococcal meningitis management in national guidelines [Induction Phase]				Transition to DTG for ART Treatment
	One-week amphotericin B deoxycholate and flucytosine	Two weeks fluconazole + flucytosine	Two weeks amphotericin B deoxycholate + fluconazole	Non-recommended options (such as fluconazole only)	
Central African Republic (CAR)	Yes	No	No	No	In progress
Implementation:	Not applicable	Not applicable	Not applicable	Yes	No
Democratic Republic of Congo (DRC)	Yes	No	Yes	No	In progress
Implementation:	Not applicable	Not applicable	Not applicable	Yes	Yes
eSwatini	Yes	No	Yes	Yes	Yes
Implementation:	Not applicable	Not applicable	Not applicable	Yes	Yes
Guinea	No	No	Yes	No	In progress
Implementation:	Not applicable	Not applicable	Not applicable	Yes	No
India	No	No	No	Yes	No
Implementation:	Not applicable	Not applicable	Not applicable	Not applicable	No
Kenya	No	No	Yes	Yes	Yes
Implementation:	Not applicable	Not applicable	Not applicable	Yes	Yes
Lesotho	Yes	Yes	Yes	Yes	Yes
Implementation:	Not applicable	Not applicable	Not applicable	Yes	Yes
Malawi	Yes	Yes	Yes	Yes	In progress
Implementation:	Not applicable	Not applicable	Not applicable	Yes	Yes
Mozambique	Yes	Yes	Yes	No	In progress
Implementation:	Not applicable	Not applicable	Not applicable	Yes	Yes
Myanmar	No	No	Yes	Yes	Yes
Implementation:	Not applicable	Not applicable	Not applicable	Yes	Yes
Nigeria	Yes	No	Yes	Yes	Yes
Implementation:	Not applicable	Not applicable	Not applicable	Yes	Yes
South Africa	Yes	Yes	Yes	No	Yes
Implementation:	Not applicable	Not applicable	Not applicable	Yes	Yes
South Sudan	No	No	Yes	Yes	No
Implementation:	Not applicable	Not applicable	Not applicable	Yes	Yes
Uganda	Yes	No	Yes	Yes	Yes
Implementation:	Not applicable	Not applicable	Not applicable	Yes	Yes
Zimbabwe	No	No	Yes	Yes	Yes
Implementation:	Not applicable	Not applicable	Not applicable	Yes	Yes



■ Yes   
 ■ Yes for IPT only   
 ■ No   
 ■ Not applicable

Country	Kaposi sarcoma management in national guidelines				TB Prevention	
	Doxorubicin/Adriamycin, Bleomycin, Vincristine (ABV)	Liposomal doxorubicin	Paclitaxel (taxol)	Inferior regimens (such as BV or bleomycin alone)	isoniazid/cotrimoxazole/vitamin B6 (pyridoxine) (QTIB)	Isoniazid (INH or IPT)
Central African Republic (CAR)	■	■	■	■	■	■
Implementation:	■				■	■
Democratic Republic of Congo (DRC)	■	■	■	■	■	■
Implementation:	■				■	■
eSwatini	■	■	■	■	■	■
Implementation:	■				■	■
Guinea	■	■	■	■	■	■
Implementation:	■				■	■
India	■	■	■	■	■	■
Implementation:	■				■	
Kenya	■	■	■	■	■	■
Implementation:	■				■	■
Lesotho	■	■	■	■	■	■
Implementation:	■				■	■
Malawi	■	■	■	■	■	■
Implementation:	■				■	■
Mozambique	■	■	■	■	■	■
Implementation:	■				■	■
Myanmar	■	■	■	■	■	■
Implementation:	■				■	■
Nigeria	■	■	■	■	■	■
Implementation:	■				■	■
South Africa	■	■	■	■	■	■
Implementation:	■				■	■
South Sudan	■	■	■	■	■	■
Implementation:	■				■	■
Uganda	■	■	■	■	■	■
Implementation:	■				■	■
Zimbabwe	■	■	■	■	■	■
Implementation:	■				■	■

■ Yes   
 ■ Yes for IPT only   
 ■ No   
 ■ Not applicable

Country	TB Prevention		Cryptococcal Disease Prevention	Severe Bacterial Infections Prevention	Tracing of patients lost to follow up (LTFU)		
	3HP (3 months of weekly rifapentine-isoniazid)	1HP (1 month of daily HP)	Fluconazole	Cotrimoxazole	By phone	By community health workers	Home visits by car/Home-based care
Central African Republic (CAR)							
Implementation:							
Democratic Republic of Congo (DRC)							
Implementation:							
eSwatini							
Implementation:							
Guinea							
Implementation:							
India							
Implementation:							
Kenya							
Implementation:							
Lesotho							
Implementation:							
Malawi							
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Mozambique							
Implementation:							
Myanmar							
Implementation:							
Nigeria							
Implementation:							
South Africa							
Implementation:							
South Sudan							
Implementation:							
Uganda							
Implementation:							
Zimbabwe							
Implementation:							

## 3.2 PREVENTION AND TREATMENT: POLICY AND IMPLEMENTATION

### KEY HIGHLIGHTS:

- **All 15 countries are transitioning to a dolutegravir-based first line regimen** as per the WHO HIV treatment guidelines updates in 2019.
- All countries recommend and implement **cotrimoxazole prophylaxis**.
- **Isoniazid preventive therapy (IPT)** is the only recommended option for TB preventative therapy (TPT) in 11 of the 15 countries.
- The UNAIDS funded IMPACT4TB project plans to scale up isoniazid-rifapentine (3HP) to 400,000 people in 12 high-burden countries, including 5 of the 15 countries: **India, Kenya, Malawi, Mozambique, South Africa and Zimbabwe**.
- **Fluconazole is recommended for primary prophylaxis** in 8, pre-emptive treatment in 4, and secondary prophylaxis in all 15 countries.
- **Access to fluconazole is very limited**, with insufficient supply, in most settings.
- The preferred treatment for cryptococcal disease with amphotericin B and flucytosine is recommended in **9 of the 15 countries, but nationally available in none**.
- **Short-course Amphotericin B + Flucytosine** for induction phase treatment of cryptococcal meningitis is recommended in the HIV guidelines 2018 in Malawi.
- **Flucytosine is not registered in any African country** and remains unavailable outside of the South African flucytosine access programme and a few pilot and MSF sites.
- **Amphotericin B is available in hospitals in South Africa** and a limited number of hospitals elsewhere.
- **Guidelines for Kaposi sarcoma** often recommend sub-standard treatment regimens and access to chemotherapy remains extremely poor.

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**Access to ARV's:** Preventing AIDS begins with timely initiation of ART for people tested HIV positive. Beyond treatment initiation, support for adherence and retention to care is critical for ensuring viral suppression and a better quality of life. Access to first line ARV treatment remains a priority. However, persistent gaps in access to treatment exist in many of the countries covered in this report. Reduced donor funding and shifting priorities away from funding procurement of ARV's continue to put ART coverage at risk. This results in stock outs or disruptions in supply, more often of 2<sup>nd</sup> and 3<sup>rd</sup> line or pediatric ART, with direct implications on patients, such as treatment interruption and delays in switching to effective 2<sup>nd</sup> line. Where treatment coverage is poor or funding constrained, access to ARV's for those already on treatment is not assured. For those not already in care or newly diagnosed an even higher risk exists of being locked out from initiation targets.<sup>20</sup> From our analysis, all of the 15 countries are in different levels of progress to transition to dolutegravir-based regimens to adapt to the 2019 WHO guideline recommendations for first and second line ART. This has prompted countries to update their guidelines and operations.

**TB Preventive Treatment (TPT)** greatly reduces the risk of TB disease in people living with HIV. Isoniazid Preventative Therapy (IPT) is the recommended option for TPT in all of the 15 countries highlighted. Uptake and adherence to this regimen of at least 6 months is generally low. The promising three months of isoniazid-rifapentine regimen (3HP), a shorter and more optimized option for TB preventative therapy, is not yet available in any of the countries surveyed. Five of the fifteen countries will be implementing 3HP as pilot projects to inform national scale up in 2020, including **Malawi, Mozambique, South Africa, Zimbabwe and Kenya, alongside Tanzania and Ethiopia**. This will happen as part of the IMPACT4TB project supported by UNITAID.

National guidelines for TB treatment follow WHO recommendations and access to TB treatment is generally available, although there are repeated reports of stockouts.

<sup>20</sup> Burden sharing or burden shifting? How the HIV/TB response is being derailed. MSF 2019. <https://www.msf.org/burden-sharing-or-burden-shifting>



Only 9 of 15 countries included the WHO preferred treatment for cryptococcal meningitis, based on flucytosine and amphotericin B followed by fluconazole, in their national guidelines. However this treatment is not available in any country, with the exception of the South African flucytosine access programme. Flucytosine is not registered in any African country and is consequently not accessible in any of the countries surveyed. Access to amphotericin B, although registered, is also very limited, and many patients end up being treated with fluconazole alone, which is associated with higher mortality. Fluconazole itself, although cheap, is often not available at primary care and supply is erratic. In conclusion, very few patients with cryptococcal meningitis have access to diagnosis and optimal treatment.

The situation for Kaposi sarcoma is similar or worse. Five of the 15 countries recommended sub-standard chemotherapy regimens in their national guidelines, such as bleomycine-vincristine or bleomycine alone. Only two (Guinea and eSwatini) recommend optimal treatment with liposomal doxorubicin, and the cheaper but more toxic option of doxorubicin-bleomycine-vincristine. Access to chemotherapy is generally poor and often limited to a few central hospitals if available at all. In Kinshasa, DRC, the MSF treatment centre is the only site offering free treatment for Kaposi sarcoma.

# 4. MODELS OF CARE

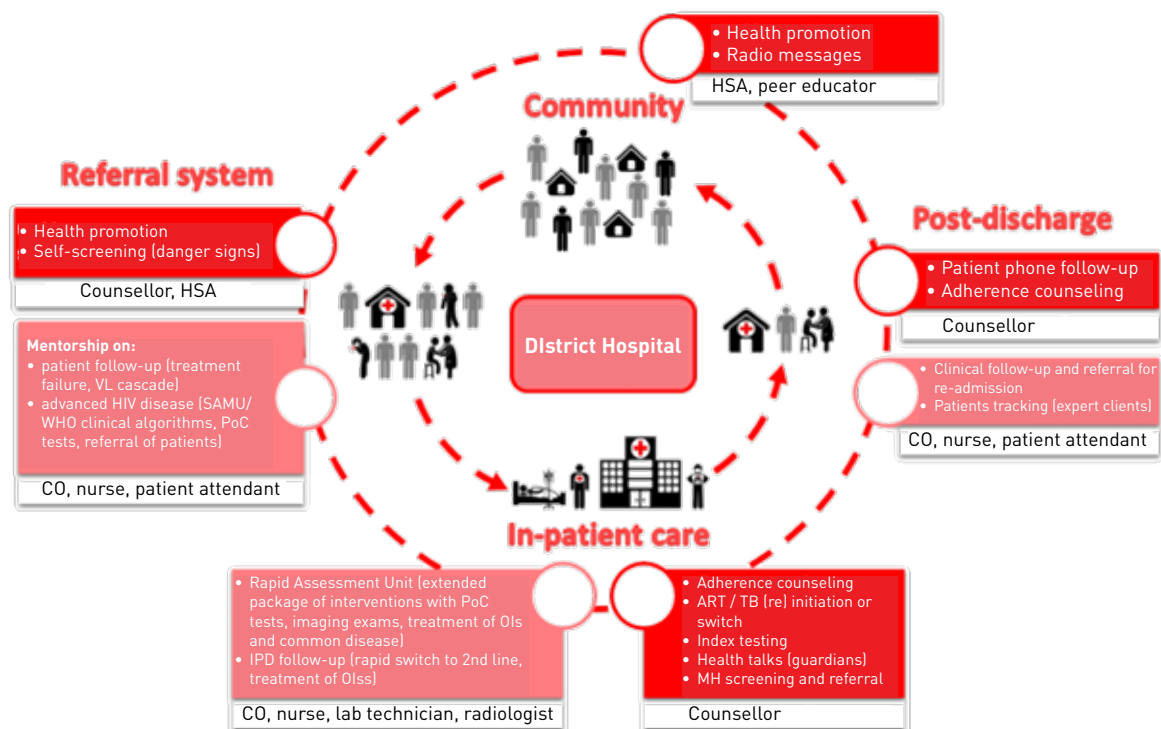
## 4.1 Primary care: Integration of AHD care, triage and referral system

While mortality is most visible in hospital settings, preventing deaths from AHD requires integrating the package of care for AHD at primary health care level. Detecting patients with severe immune suppression, TB and cryptococcal disease before they become severely ill is essential to decrease mortality from AHD. This requires setting up a functioning triage and referral system. Screening with CD4 allows identification of patients in need of preventive treatment for severe bacterial infections, TB and cryptococcal disease. For those who are already ill, earlier initiation of treatment or management of treatment failure greatly increases the likelihood of recovery. Equipping primary care clinics with point of care CD4, TB-LAM and CrAG, as well as ensuring a continuous supply of essential medicines for the prevention and treatment of major opportunistic infections is necessary to address AHD.

While triage was mentioned in a number of national guidelines this rarely included screening for AHD and integration of the full package of care for AHD at primary care is not widely implemented in any of the countries surveyed, although Malawi and Uganda have piloted AHD services in a number of sites and are now planning national roll out.



**FIGURE 4** Advanced HIV circle





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## 4.2 Hospital level: The Rapid Assessment Unit or Team

Addressing AHD at hospital level requires the capacity to rapidly diagnose HIV, TB, cryptococcal disease and other conditions associated with high mortality. A successful model is that of the rapid assessment team or unit, where dedicated staff ensure rapid diagnosis and initiation of treatment, either in the emergency room or in a separate rapid assessment unit (RAU). This requires equipping the emergency room or an adjacent mini-lab with point of care diagnostics

In 2018 MSF began implementing a Rapid Assessment Unit in Nsanje, Malawi and a Rapid Assessment Team in Beira and Maputo, Mozambique. A new RAU clinic has just been opened in Bangui, CAR, in September 2019. The units link integrated HIV/TB for critically ill patients with hospital emergency units. The units are equipped with mini laboratories which are able to rapidly diagnose AHD using POC CD4, TB-LAM, CrAG and a few basic tests. Health workers are also trained to quickly identify patients who are ill at triage and link them to the RAU for quick identification and treatment of stage III and IV illnesses.

## 4.3 Retention, interruption and re-engagement in care

Retention in HIV care and adherence to treatment remains one of the key challenges of the HIV response. Across the treatment cascade people living with HIV are likely to go through periods or events in which they disengage from care or fail to take their treatment as advised by health professionals. Experiences from patients attribute these situations to; treatment fatigue, adverse effects of treatment, limited literacy on treatment, all of which result in some people stopping treatment as soon as they feel better (in cases where initiation was started when a patient was sick), lack of transport money to go to the facility for frequent drug refills, conflicting priorities like going to work or running errands deemed more important. Adaptive adherence support is recommended within the WHO guidelines for AHD.

Interventions like the **welcome back service** being implemented by **MSF in South Africa** have proven effective in re-engaging people

living with HIV who had disengaged from HIV care and management. A training package for healthcare staff to address attitude and behavior towards patients who re-engage into care, or who come into the facility sick and need to be re-engaged back into treatment was implemented. Working with community groups and peer support staff health workers identify patients who have disengaged from care, rapidly diagnose for AHD, provide medical care needed including identifying treatment failure and a rapid switch to 2<sup>nd</sup> or 3<sup>rd</sup> line treatment if indicated. Additionally, psychosocial support for promoting adherence is also provided. For example, in **MSF in Beira, Mozambique**, post discharge interventions have included active follow up of patients once they are discharged from hospital including calling them on the 15<sup>th</sup>, 30<sup>th</sup> and 45<sup>th</sup> day post discharge from hospital to find out their progress in restarting ART and supporting any adherence challenges expressed.

Welcome Back Service is a series of activities carried out to support people living with HIV who have disengaged from health services and stopped the use of ARV's to re-engage back and be retained in care for their own health and wellbeing and that of their family and community.

MSF Khayelitsha, South Africa in collaboration with partners in the Provincial Government of Health, a patient advisory board and clinic staff developed the concept of the "Welcome back service". This was done to respond to the issue of patients developing treatment failure often caused by disengagement from HIV care and struggles of adherence to ART.

The package of interventions is designed to meet individualized care needs and address the barriers to successful engagement with treatment (re-engagement and improved adherence) that patients face. Addressing health worker attitudes through training has also proven effective. Welcome service was initially developed to support patients to re-engage with services, but was expanded to address the problem of struggling with engaging with services and adhering to treatment more broadly.



# 5. FUNDING

## Current and upcoming initiatives by donors and implementers:

- UNITAID initiative on AHD implemented by CHAI in seven countries: Malawi, Nigeria, South Africa, Tanzania, Uganda (with some support in Botswana and Lesotho)
- UNITAID initiative on piloting 3HP implemented by IMPAACT4TB in Tanzania, Ethiopia, Mozambique, Malawi, Kenya, South Africa and Zimbabwe
- Global Fund guidance to countries in the HIV guidance note
- PEPFAR COP guidance note includes attention to AHD package of care

Funding in all of the 15 countries is sporadic and not secure for most of the diagnostic tests needed for diagnosing AHD or for treating the two most common opportunistic infections. CD4 reagents for example are funded by both

PEPFAR and Global fund in some countries (e.g. Uganda, Kenya, Malawi and South Sudan). None of the countries have POC testing for CD4 funded within national Global Fund or PEPFAR resource allocations.

GeneXpert machines are present in all the 15 countries. Procurement was done with support to countries by UNITAID. Currently both Global Fund and PEPFAR provide some level of financial support for reagents, servicing and management of equipment. TB LAM is funded by PEPFAR only in a small number of AHD clinics in DRC and Uganda provided for in the COP19 plans.

Resource allocation for procurement and management of diagnostics and treatment options within the AHD package of care will determine whether countries have the capacity to make these tools available in country. Whether financing of these health products have domestic or international sources, the procurement mechanisms used should ensure WHO or SRA Quality Assurance standards are met.







## 6. CONCLUSION AND RECOMMENDATIONS

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In almost 24 months the world will be evaluating progress towards meeting targets on reducing AIDS mortality. UNAIDS predicts that to achieve these targets a reduction of almost 135,000 deaths in 2019 and 2020 respectively is required. Innovation to quickly identify, diagnose and treat people with advanced HIV disease must therefore be priority, not only for Governments of countries with high numbers of AIDS deaths but also for funders and program implementers.

Countries are currently at various levels of engagement with stakeholders to update HIV and TB treatment guidelines and align with the 2017 WHO guidelines on AHD; opportunities exist for ensuring guidance includes the minimum package of care for AHD at primary care and at hospital level.

Literacy and awareness of Advanced HIV Disease remains minimal for communities most affected and at risk. Ensuring that all people affected by HIV and TB can access effective prevention and treatment services requires their understanding of the danger signs in order to support peers or get individualised care in time. Additionally, communities have proven to play a critical role in demand creation which remains untapped for making diagnostics and treatment tools available particularly in primary healthcare.

Capacity building and training for health workers is also needed in order to quickly identify and

treat patients who are critically ill in a timely manner to save lives. This includes addressing health worker attitudes in order to be welcoming and understanding to patients re-engaging back into care.

Stronger commitment by main funders for HIV and TB for countries to prioritise AHD is necessary. The Global Fund has included AHD in the current HIV guidance note to countries as they plan to submit national applications for the period 2020-2022. PEPFAR have also in the last year given provisions within COP guidance on Advanced HIV Disease. These opportunities need to be tapped and utilised. UNITAID is currently supporting implementation of AHD initiatives as well as TB preventive treatment pilot initiatives in Africa.

The current progress in country adoption of WHO guidelines for AHD has been made possible by many stakeholders' advocacy and interventions, including market shaping mechanisms that have had a direct impact on reduced pricing for commodities, making them more accessible to countries. In order to stop deaths of people living with HIV from preventable and treatable diseases, this commitment needs to be replicated at country level by governments through their MOH prioritizing adequate resources needed to implement the minimum AHD package of care at primary care and hospital level.

# WE RECOMMEND:

1. Governments, international agencies, donors and implementing organizations must **keep Advanced HIV Disease high on their agenda in national HIV and TB responses and increase investments to ensure a minimum package of care for AHD as provided for in the WHO guidelines. Specifically:**

## FOR ACCESS:

- **Ensure adequate resources and implementation plans** for access to HIV testing and first line ARVs including rapid initiation of people newly diagnosed with HIV; support for adherence and retention as a critical first step towards viral suppression and good quality of life for people living with HIV.
- **Develop and/or intensify implementation of guidelines** specifically to make the minimum package of care for AHD as recommended by WHO available to all who need it.
- **Intensify market shaping interventions** that address barriers to access for AHD commodities including pricing and registration as this has an impact on national implementation plans.

## FOR SERVICE DELIVERY:

- **Increase funding for POC diagnostic tools** such as CD4, TB LAM and CrAg for quick diagnosis of AHD, TB and cryptococcal meningitis and timely initiation to treatment
- **Increased funding for the prevention** (CTX, TPT, fluconazole) and treatment of opportunistic infections, including TB and cryptococcal disease.
- **Invest in interventions to support** identification of people living with HIV who have treatment failure and rapidly switch them to 2<sup>nd</sup> and 3<sup>rd</sup> line.
- **Allocate additional resources** toward interventions that support adherence and retention to HIV/AIDS management and care.

## FOR NATIONAL SCALE UP AND IMPLEMENTATION:

- **Implement a package of care for AHD** at primary care for early detection of AHD, prevention and treatment of opportunistic infections, and rapid referral to hospital for severely ill.
- **Provide specific support to boost clinical capacity** at referral level to take care of patients with ADH.
- **Draw critical lessons from pilot projects** and link to models of care bringing diagnostics & prevention closer to patients that is responsive to their needs.

2. Intensify investments in **community-based and community-led programs and patient-centred care** proven to be key in reducing mortality including community awareness and literacy on AHD for demand creation and advocacy.
3. International Agencies and governments must map out and respond to **challenges and gaps** that continue to result in intermittent or no supply of key diagnostics and treatment for preventing and treating AHD.

# BASIC INFORMATION

## ON AHD FOR PLHIV AND COMMUNITY

### WHAT IS ADVANCED HIV DISEASE?

WE TALK ABOUT ADVANCED HIV DISEASE (AHD) WHEN:



A PATIENT'S CD4 DROPS BELOW 200 COPIES.



PATIENT HAS A SEVERE ILLNESS SUCH AS TB, A SEVERE INFECTION OF BRAIN, LUNG ETC.



ALL HIV INFECTED CHILDREN BELOW 5 YRS ARE CONSIDERED AHD PATIENTS.

### AHD DEVELOPS WHEN:

- People living with HIV are not diagnosed early and/or do not start ART before their immune system becomes weak.
- ART is stopped or fails, has been interrupted or not taken regularly or a specific regimen is no longer effective for a patient
  - Some AHD patients need to be hospitalized immediately.
  - Others can get the care they need at PHC level.
  - Some AHD patients may still feel well but need close follow-up.



### WHAT HEALTHCARE PROVIDERS CAN DO

- Adopt a **patient-friendly approach** and welcome PLHIV who missed appointments or stopped ART
- At every patient's visit, check for **danger signs/clinical symptoms** of OIs
- **Screen for specific package of AHD tests:** CD4, VL, Xpert MTB/Rif, TB-LAM, CrAg etc.
- **When needed, refer patient to hospital for specialized care**
  - Ensure patients are on an effective regimen (DTG, ART 1<sup>st</sup>/2<sup>nd</sup> line etc.)
  - Treat OIs (TB, Crypto etc) or provide focused prophylaxis (CTX, TPT, Fluconazole etc.)
- **Follow up closely post-discharge patients;** plan early tracing in case of missed appointments
- Sensitize PLHIV and communities on **danger signs** and about the importance of treatment



### WHAT PLHIV CAN DO

- Regularly **self-check for danger signs** and **go to health facility** if you are not feeling well.
- Your body needs **ARVs** every day to fight HIV, and **prophylaxis** or other treatment for OIs.
- If you miss doses or appointments, **don't give up your treatment.** You can always go back to the facility and make a plan to avoid the same in the future.
- **Ask for your lab tests** (VL, CD4) and explanations of results.
- **Ask for support from your healthcare provider** to help you to continue with lifelong treatment.



### DANGER SIGNS

- Respiratory rate >30
- Heart rate >120
- Systolic BP <90
- Temperature >39°C
- Saturation <90%
- Moderate/Severe dehydration
- **Altered mental state:** confusion, strange behaviour, reduced level of consciousness
- Unable to walk unaided
- Diarrhea/vomiting
- Loss of weight **Any other neurological problem:**
  - sever headache
  - seizure
  - paralysis
  - difficulty talking
  - cranial nerve problems
  - rapid deterioration in vision

PREVENT, IDENTIFY AND TREAT ADH **NOW**

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