20-tool checklist for diagnosing, treating and preventing AIDS

Diagnostic and treatment checklist for the management of HIV and advanced HIV disease in outpatient settings

More than 770,000 people died from HIV/AIDS in 2018. To more robustly and successfully confront disease progression and the key causes of death (tuberculosis [TB], cryptococcal disease) in people living with HIV (PLHIV), Médecins Sans Frontières (MSF) offers this checklist of 20 essential diagnostic and treatment tools, including cost information. This package of care,* together with models of care empowering PLHIV and facilitating treatment adherence, are needed at the primary health care level to assist MSF teams, civil society and governments in their efforts to control HIV and AIDS.

Diagnostics

1. HIV rapid diagnostic test (RDT)
2. Early infant diagnosis (EID) nucleic acid amplification test (NAAT)
3. Routine viral load (VL)
4. CD4 cell count
5. Xpert MTB/RIF (Ultra) NAAT
6. TB lipoarabinomannan (LAM) tests
7. Cryptococcal antigen (CrAg) RDT

Medicines

8. Pre-exposure prophylaxis: TDF/3TC or TDF/FTC
9. First-line adult antiretroviral (ARV) therapy
10. First-line paediatric ARVs
11. Second-line adult ARVs
12. Second-line paediatric ARVs
13. TB medicines
14. TB prophylaxis therapy (TPT) for adults
15. TB prophylaxis therapy (TPT) for children
16. Cotrimoxazole
17. Fluconazole
18. Flucytosine
19. Amphotericin B deoxylate or liposomal
20. Other opportunistic infection and cancer treatments (e.g. KS, CMV)

For more information, please see these MSF reports:

- *No time to lose: Detect, treat, and prevent AIDS*. November 2019. https://msfaccess.org/no-time-lose-detect-treat-and-prevent-aids
- *From guidelines to reality: Accelerating access to prevention and treatment of paediatric HIV.* December 2019. https://msfaccess.org/guidelines-reality-accelerating-access-prevention-and-treatment-paediatric-hiv
- *Stopping senseless deaths*: *Overcoming access barriers to affordable, lifesaving diagnostics and treatments for HIV and opportunistic infections*. July 2018. https://msfaccess.org/stopping-senseless-deaths
- *Time for $5: GeneXpert diagnostic tests.* December 2019. https://msfaccess.org/time-for-5

**Patient-centered and differentiated models of care, as well as other forms of support for people living with HIV or affected by TB, should also be explored, along with other enabling policies as part of the package of care.*

DIAGNOSTICS				
Diagnostic	**Recommendation**	**Forecasting**	**Cost (ex works list price for low- and middle-income countries)**	**Indicator**
1. HIV rapid diagnostic test (RDT)	Entry point to treatment and care	Consider historic demand, coverage of "first 90" in the UNAIDS 90/90/90 targets where 90% of PLHIV know their status Mix of testing strategies	RDT US$1 OraQuick HIV self-test (OraSure) US$2	% of people who know their status
2. Early infant diagnosis (EID) nucleic acid amplification test (NAAT)	What's needed: Virologic EID for children <18 months old, strategic mix of point-of-care (POC) and centralized testing. Note POC has certain advantages with respect to fast turnaround time (TAT) and linkage to care, especially for higher-risk groups. For example, in the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) POC EID project, a combination of POC strategies were used to increase access to testing, expand case finding, decrease result TAT and optimize platform utilization. These strategies included stand-alone sites, multiple entry points, Hub and Spoke networks and integrated testing sites. Rationale: POC EID, as opposed to conventional EID, significantly reduces TAT from sample collection to caregivers receiving results (0 vs 56 days); increases percentage of caregivers receiving results within WHO-recommended 30 days (98% vs 18%); and increases percentage of HIV-infected infants initiated on antiretroviral therapy (ART) within 60 days (93% vs 43%).[1] POC EID has also been shown to be cost-effective compared to conventional EID.[2]	Consider historic demand and add additional need according to updated guidelines (e.g. addition of 9-month test).	Cartridge: US$20 (Abbott Alere q (/m-PIMA) HIV-1/2 Detect) or US$14.90 (Cepheid Xpert HIV Qual)	% of HIV+ children receiving an EID Of those, % who have a POC EID (POC EID/total EID)

Diagnostic	Recommendation	Forecasting	Cost (ex works list price for low- and middle-income countries)	Indicator
3. Routine viral load (VL)	What's needed: Routine VL monitoring at 6 and 12 months and then annually thereafter, and in people with symptoms of clinical failure or adherence difficulties. Note POC VL has certain advantages with respect to fast TAT and linkage to care, especially for higher-risk groups. Rationale: "POC VL testing significantly improved HIV viral suppression and retention in care in South Africa, partly by ensuring rapid receipt of VL results to PLHIV and their providers. Increasing access to POC VL testing could help to achieve the 90-90-90 targets."[3]	Number of PLHIV on ART (annual VL) Number of new enrollments 10-15% repeats, number of people >6 months on ART	Contingent on the technology: Lab-based: US$10 (e.g., Roche, Abbott, Hologic) POC cartridge: USD$20 (Abbott m-PIMA HIV-1/2 VL) or US$14.90 (Cepheid Xpert HIV VL)	% PLHIV started on ART >6 months ago with a VL result within the last year % PLHIV started on ART >6 months ago with a VL <1000 copies/mL % PLHIV with repeat VL >1000 copies/mL switched to second-line therapy
4. CD4 cell count	What's needed: Baseline for all new initiations or PLHIV returning to care; targeted CD4 for people who are clinically sick or have a detectable VL (>1000 copies/mL). CD4 results should be available within 7 days of testing. Rationale: CD4 is essential for diagnosing (especially asymptomatic) advanced HIV disease (AHD) as clinical staging/symptom screening on its own misses half of people with AHD at entry and re-entry into care, according to the REALITY study.[4]	Annual CD4 need is based on cumulative number of newly enrolled PLHIV, number of people on ART monitored with 6-month CD4 in lieu of VL, number of people on ART with unsuppressed VL/clinically unstable/with new opportunistic conditions (10-15% of annual VL)	CD4 test: US$4-8 (e.g. rapid POC Omega Visitect AHD, benchtop Abbott PIMA, or benchtop BD FACSPresto more suitable for hospital and central labs)	% of PLHIV initiating ART with baseline CD4 % of PLHIV monitored with CD4 6 monthly where there is no access to VL % of PLHIV with unsuppressed VL or clinically unstable who get CD4 test

Diagnostic	Recommendation	Forecasting	Cost (ex works list price for low- and middle-income countries)	Indicator
5. Xpert MTB/RIF (Ultra) NAAT	What's needed: Initial TB test for all symptomatic patients Rationale: WHO considers undiagnosed TB as a main killer of PLHIV	See MSF adaptation of WHO Global Laboratory Initiative (GLI) tool for testing sputum and extrapulmonary TB clinical samples[5]	Cartridge: US$9.98	Number of PLHIV with TB symptoms at presentation screened with MTB/RIF Number of PLHIV with TB symptoms
6. TB lipoarabinomannan (LAM) test	What's needed: According to WHO 2019 recommendations, TB-LAM is recommended for use at all levels of care, including at hospital level for all HIV+ inpatients with TB symptoms or seriously ill irrespective of their CD4 count. If CD4 <200 cells/mm^3, TB-LAM is recommended even in the absence of TB symptoms. For outpatients this is less than 100 cells/mm^3.[6] Rationale: POC urinary TB-LAM testing increases the diagnosis of TB, particularly at lower CD4 cell counts, and shortens the time to TB treatment with a subsequent reduction of deaths.	60% of people with CD4 <100 who likely would be evaluated for TB based on signs or symptoms or danger signs, 30% people with CD4 <200[7]	Abbott Determine POC TB LAM LFA: US$3.50/test	% of HIV+ inpatients tested with TB-LAM Number of PLHIV with CD4 <200 at presentation screened with POC TB-LAM
7. CrAg RDT	What's needed: For diagnosis of cryptococcal meningitis (CM) in symptomatic patients (those with headache), WHO recommends CrAg screening in all PLHIV with CD4 <200 cells/mm^3. Rationale: CM remains the second-leading AIDS-related killer, second to TB. Prevention and early diagnosis and treatment is paramount to reducing CM-related mortality.	Number of PLHIV with baseline CD4 <200 (30%)	POC CrAg LFA (IMMY=US$2.00, Biosynex=US$2.40) Cost of lumbar puncture	Number of PLHIV with baseline CD4 <200 with CrAg tested

TREATMENTS				
Treatment	**Recommendation**	**Forecasting**	**Cost**	**Indicator**
8. Pre-exposure prophylaxis (TDF/3TC or TDF/FTC)	Pre-exposure prophylaxis (TDF/3TC or TDF/FTC) provision to key populations and those at high risk of HIV	Estimates of sex workers, men who have sex with men and intravenous drug users in need Estimates of population assessed as high risk	US$41 per person per year (TDF/3TC) US$55 per person per year (TDF/FTC)	
9. First-line adult ARVs	Dolutegravir (DTG) combined with TDF and 3TC is the WHO-recommended first-line regimen	Refer to national DTG transition plan, i.e. whether all new initiations or switching entire cohort to DTG ARV estimated needs tool[8]	US$64 per person per year (TDF/3TC/DTG)	Number of HIV-positive adults initiated or switched to DTG
10. First-line paediatric ARVs (LPV/r pellets and granules; DTG for >20kg)	**a. Lopinavir/ritonavir (LPV/r)-based ARV regimens** (initiation on/switching to): What's needed: Stable supply of paediatric formulations of LPV/r (granules and pellets) for children <20 kg Rationale: LPV/r is recommended as part of first-line ARV regimens for HIV+ children for whom there is not yet an appropriate approved DTG formulation. NOTE: Tentative FDA approval of LPV/r/ABC/3TC 4-in-1 (40/10/30/15 mg) from Cipla/DNDi is expected in April 2020; countries wishing to introduce the 4-in-1 should make their transition plans with this timeline for the new formulation in mind. **b. DTG-based ARV regimens** (initiation on/switching to, if >20kg):	**a. LPV/r-based ARV regimens** (initiation on/switching to): All children <20 kg newly diagnosed, or currently on an EFV- or NVP-based regimen ARV estimated needs tool[8] **b. DTG-based ARV regimens** (initiation on/switching to): All children 20 kg and up, newly diagnosed, or currently on an EFV- or	**a. LPV/r-based ARV regimens** (initiation on/switching to): LPV/r pellets: US$19.20 per bottle of 120 capsules (Cipla) LPV/r granules: US$18.25 per carton of 120 sachets (Mylan) LPV/r syrup US$30.82 per	**a. LPV/r-based ARV regimens** (initiation on/switching to): Number of children initiated on or switched to LPV/r regimens (disaggregated by formulation) **b. DTG-based ARV regimens** (initiation on/switching to): Number of children initiated on or switched to DTG

	What's needed: DTG is recommended as the preferred first-line ARV for all HIV+ children and can be given as 50-mg (adult) film-coated tablets for children 20 kg and up.	LPV/r- or NVP-based regimen ARV estimated needs tool[8]	package of 5x60mL bottles (Abbvie) 4-in-1: Price expected to be $1 per day in a fixed-dose combination ($15 per bottle of 120 capsules) Cipla/DNDi) **b. DTG-based ARV regimens** (initiation on/switching to): US$43 per person per year (DTG 50-mg tabs)	regimens (disaggregated by formulation)
11. Second-line adult ARVs	Required for people failing first-line ART according to national guidance	Number of patients with two sequential VL >1000 copies/mL (or as per national guidelines) ARV estimated needs tool[8]	AZT/3TC + ATV/r: US$218 per person per year AZT/3TC + LPV/r: US$279 per person per year	% of adult patients failing first line switched to second-line regimen
12. Second-line paediatric ARVs	Required for people failing first-line ART according to national guidance	Number of patients with two sequential VL >1000 copies/mL (or as per national guidelines) ARV estimated needs tool[8]	WHO preferred: AZT/3TC + LPV/r: US$159-513 per person per year (depending on	% of paediatric patients failing first line switched to second-line regimen

			formulation of LPV/r) >20 kg: AZT/3TC + DTG: US$89 per person per year	
Treatment	**Recommendation**	**Forecasting**	**Cost**	**Indicator**
13. TB medicines	What's needed: Drug-sensitive TB (DS-TB) drugs, including DS-TB fixed-dose combinations (FDCs) for adults and children; drug-resistant TB (DR-TB) drugs* for adults and DR-TB paediatric formulations Rationale: TB is the leading killer of PLHIV. FDCs of TB medicines to treat DS-TB in adults and children are essential for HIV programs. As for DR-TB, WHO strongly recommends all-oral regimens, including a regimen of 9-12 months duration.[9,10] **DR-TB drugs: bedaquiline (BDQ), linezolid (LZD), older generation fluoroquinolones (moxifloxacin, levofloxacin), delamanid (DLM), and pretomanid (Pa) for adults; BDQ and DLM paediatric formulations* *BDQ can be used for DR-TB treatment in children 6 years and older; DLM for children 3 and older with no drug-drug interactions with key ARVs*		DS-TB FDCs adults DS-TB FDCs children DR-TB paediatric formulations (available through the Global Drug Facility) BDQ† DLM† Pa (BPaL)† †*For prices, refer to the Global Drug Facility[11] and MSF's "DR-TB Drugs Under the Microscope" report[12]*	

Treatment	Recommendation	Forecasting	Cost	Indicator
14. TB preventative therapy (TPT) for adults	What's needed: TPT for all PLHIV who do not have active TB disease: • Cotrimoxazole/isoniazid/pyridoxine/vitamin B6 (CTX/INH/B6) • Rifapentine/isoniazid (3HP) once weekly for 12 weeks for all PLHIV who do not have active TB disease • Rifapentine/isoniazid (1HP) daily for one month for PLHIV stable on ART who do not have active TB disease NOTE: 1HP will likely be recommended by WHO in updated latent TB infection management guidelines to be released in first quarter 2020, so should be considered in country planning processes	All PLHIV should receive TB prophylaxis	US$5.97-11.94 per person per year for 3-6 months of CTX/INH/B6 (Cipla) US$15 per person 3HP course (Sanofi) US$25.50 per person 1HP course (Sanofi)	All PLHIV *without* symptoms of TB receive TB prophylaxis regardless of the Mantoux tuberculin skin test (TST) result
15. TB preventative therapy (TPT) for children	What's needed: 3HR or 6INH (if 3HR is not available) Rationale: 3HR (3 months of isoniazid and rifampin) is recommended by the WHO, as a regimen-shortening option for children <15 years old in high-TB-burden areas. The FDC of 3HR is available in both dispersible and tablet form. NOTE: 3HP can be offered to children 3 years or older.	All HIV+ children who have not already received TPT and do not have signs of active TB disease All children <5 years old who are household contacts of a confirmed TB case and do not have signs of active TB (WHO now recommends expansion of TPT to all household contacts of confirmed TB, regardless of age, in high-TB-burden areas)	Average of US$8.40 per child for 3HR	Number of children initiated on 3HR

Treatment	Recommendation	Forecasting	Cost	Indicator
16. Cotrimoxazole	What's needed: Cotrimoxazole (CTX) as preventive therapy in all PLHIV where severe bacterial infections and malaria are prevalent, or for PLHIV with stage 3 or 4 disease or CD4 <350 cells/mm^3. The duration of CTX prophylaxis is dependent on national guidelines and may be life-long or until viral suppression. Rationale: To prevent severe bacterial infections, *Pneumocystis* pneumonia (PCP) and toxoplasmosis in PLHIV. NOTE: Depending on national guidelines, CTX is recommended for all DS-TB and DR-TB HIV co-infected individuals regardless of CD4 count for the duration of TB treatment.	Dependent on national guidelines and protocols	CTX 800/160 mg (adult tablet) - US$40.38 per 1000 tablets/US$14.75 per person/year CTX 400/80 mg (paediatric tablet) - US$21.72 per 1000 tablets/US$7.92 per person/year	Number of PLHIV with CD4 <350 cells/mm^3, PLHIV with stage 3 or 4 disease
17. Fluconazole for treatment and prevention of cryptococcal disease	What's needed: Fluconazole if CrAg positive without meningitis; as part of some treatment regimens or after treatment of meningitis to prevent recurrence. It should also be available for primary prevention in high-prevalence countries for PLHIV with CD4 <100 cells/mm^3. Rationale: This is a preventive therapy for cryptococcal meningitis (CM), thereby preventing development of CM among PLHIV. Also, fluconazole is part of WHO-recommended CM treatment. Every facility treating PLHIV should have access to fluconazole.	Prevalence of cryptococcal antigenaemia in patients with CD4 <200 cells/mm^3. Global prevalence estimated 6%	<US$25 per year	Number of PLHIV CD4 <200 cells/mm^3 and serum CrAg-positive started on fluconazole prophylaxis
18. & 19. Amphotericin B (deoxycholate or liposomal formulation) and	What's needed: Amphotericin B deoxycholate (AmphoB) or the WHO-preferred liposomal amphotericin B (L-AMB), where available, and flucytosine (5-FC) for induction treatment, as part of WHO-preferred regimen.		AmphoB: US$7.62 per vial L-AMB: US$16.25 per vial from Gilead (pricing for 116 low- and middle-income	

flucytosine for CM treatment	Rationale: Mortality due to CM is reduced with the combination of amphotericin B and 5-FC followed by fluconazole. The 2018 WHO cryptococcal disease guidelines[13] recommend a 1-week induction phase of intravenous treatment with conventional amphotericin B (AmphoB) or L-AMB and oral 5-FC, followed by a week of oral fluconazole. The ideal regimen for CM recommends use of L-AMB. Choice of L-AMB versus deoxylate should be made based on costs and availability. All-oral regimens for treatment (5-FC plus fluconazole) may be a more feasible option for treatment where referral to higher-level facilities is not possible.		countries as of September 2018). 5-FC 500-mg tablets: US$110 per bottle of 100	
20. Other opportunistic infection and cancer treatments (e.g. KS, CMV) as appropriate for the health care context	**Kaposi sarcoma (KS) treatment:** Guidance on use of pegylated liposomal doxorubicin (PLD) versus other chemotherapeutic agents (paclitaxel, bleomycin, etc) is not clear at the moment. Also, major production issues with PLD limit access. **Cytomegalovirus (CMV) treatment:** Valganciclovir can be given for 3 weeks in the induction phase and then a minimum of 3 months intensive phase.	KS treatment: Depending on local prevalence; estimated 2.4% incidence in Latin America among ART-naïve PLHIV, global estimates are 0.1% and 2% incidence among ART-naïve PLHIV and PLHIV <1 year on ART, respectively.[14] CMV treatment: Depending on local prevalence of CMV retinopathy in screening programs; the highest prevalence of CMV retinitis among PLHIV is in Asia (14%) and seems to be low	KS treatment: 2mg/mL (20 mg) vial of PLD: US$140-173. 2mg/mL (50 mg) vial of PLD: US$181-350. CMV treatment: US$200 per pack of 60 tabs of 450-mg tablets or $200 per month per patient.	KS treatment: variable by country CMV treatment: number of PLHIV receiving CMV treatment; number of PLHIV CD4 <200.

		in Africa; in 73% of cases of CMV retinitis globally, CD4 count at diagnosis was <50 cells/µL.[15]		

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