EDUCATIONAL FUND

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Q&A: Vindi Singh, WHO, Switzerland

18 February 2020

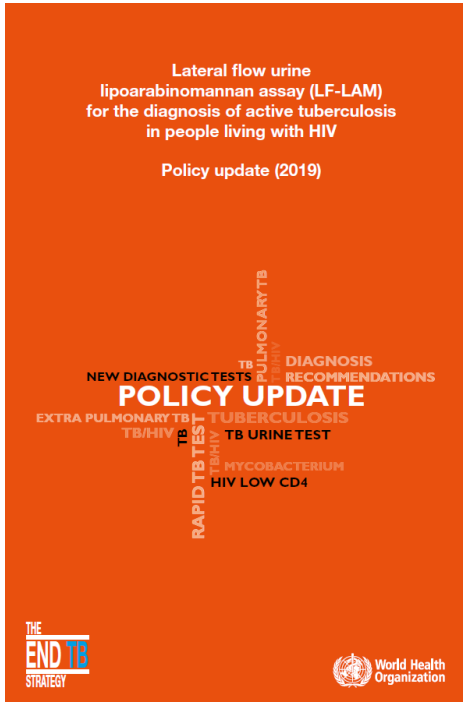
Outline

WHO guideline recommendation updates for diagnosis and management of RR-TB/HIV co-infection:

- TB LF-LAM (lipoarabinomannan) guideline updates
- Molecular assays guideline updates
- DR-TB cascade of care
- DR-TB treatment guideline updates

TB lateral flow urine lipoarabinomannan (TB LF-LAM) policy updates

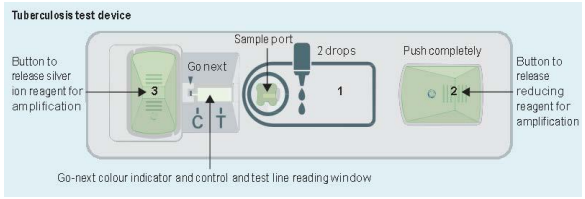
WHO LF-LAM Policy Update 2019: to Diagnose Active TB in PLHIV



- All recommendations apply to **Alere Determine™ TB LAM Ag test** (Abbott)

Abbott website

- **Fujifilm SILVAMP TB LAM** (FujiLAM) has better sensitivity (biobanked urine samples: Broger, T et al. 2019. *Lancet Infect Dis*, *8*, 852–886.)
- GDG will assess clinical data end 2020, after which test will enter guidelines (could expand recommendations)



Broger et al.

- **Further R&D** being undertaken on even more accurate LF-LAM tests with 2-3 year timeline

LF-LAM in inpatient settings

WHO STRONGLY RECOMMENDS using LF-LAM to ASSIST in the diagnosis of active TB in HIV-positive adults, adolescents and children:

No CD4 required

- with **signs and symptoms of TB** (pulmonary and/or extra-pulmonary) (strong recommendation; moderate certainty in the evidence about the intervention effects) or
- with advanced HIV disease or who are **seriously ill** (strong recommendation; moderate certainty in the evidence about the intervention effects) or
- irrespective of signs and symptoms of TB and with a ***CD4 cell count <200 cells/mm3*** (strong recommendation; moderate certainty in the evidence about the intervention effects)

CD4 required

LF-LAM in outpatient settings

WHO SUGGESTS using LF-LAM to ASSIST in the diagnosis of active TB in HIV-positive adults, adolescents and children:

No CD4 required

- with **signs and symptoms of TB** (pulmonary and/or extra-pulmonary) or **seriously ill** (conditional recommendation; low certainty in the evidence about test accuracy) – ***as with in-patients*** - and
- irrespective of signs and symptoms of TB and with a ***CD4 cell count <100 cells/mm3*** (conditional recommendation; very low certainty in the evidence about test accuracy)

CD4 required

Use of LF-LAM: key messages

Might not be available if no access to GeneXpert or person can't produce sputum

LF-LAM = rule-in test to screen for active TB
→Still requires molecular test for RR/MDR testing!
→Should treat if LAM positive (no need for positive Xpert MTB/RIF for confirmation)

LF-LAM = NOT a rule-out test
→ additional testing needed to rule-out TB!

Recommendation against LF-LAM

WHO RECOMMENDS AGAINST using LF-LAM to assist in diagnosis of active TB in HIV-positive adults, adolescents and children:

- without assessing TB symptoms (strong recommendation; very low certainty in the evidence about test accuracy)
- without TB symptoms and unknown CD4 cell count or without TB symptoms and CD4 cell count ≥200 cells/mm3 (strong recommendation; very low certainty in the evidence about test accuracy) and
- without TB symptoms and with a CD4 cell count of 100–200 cells/mm3 (conditional recommendation; very low certainty in the evidence about test accuracy)

LF-LAM testing can rapidly identify PLHIV with TB most at risk of death (1)

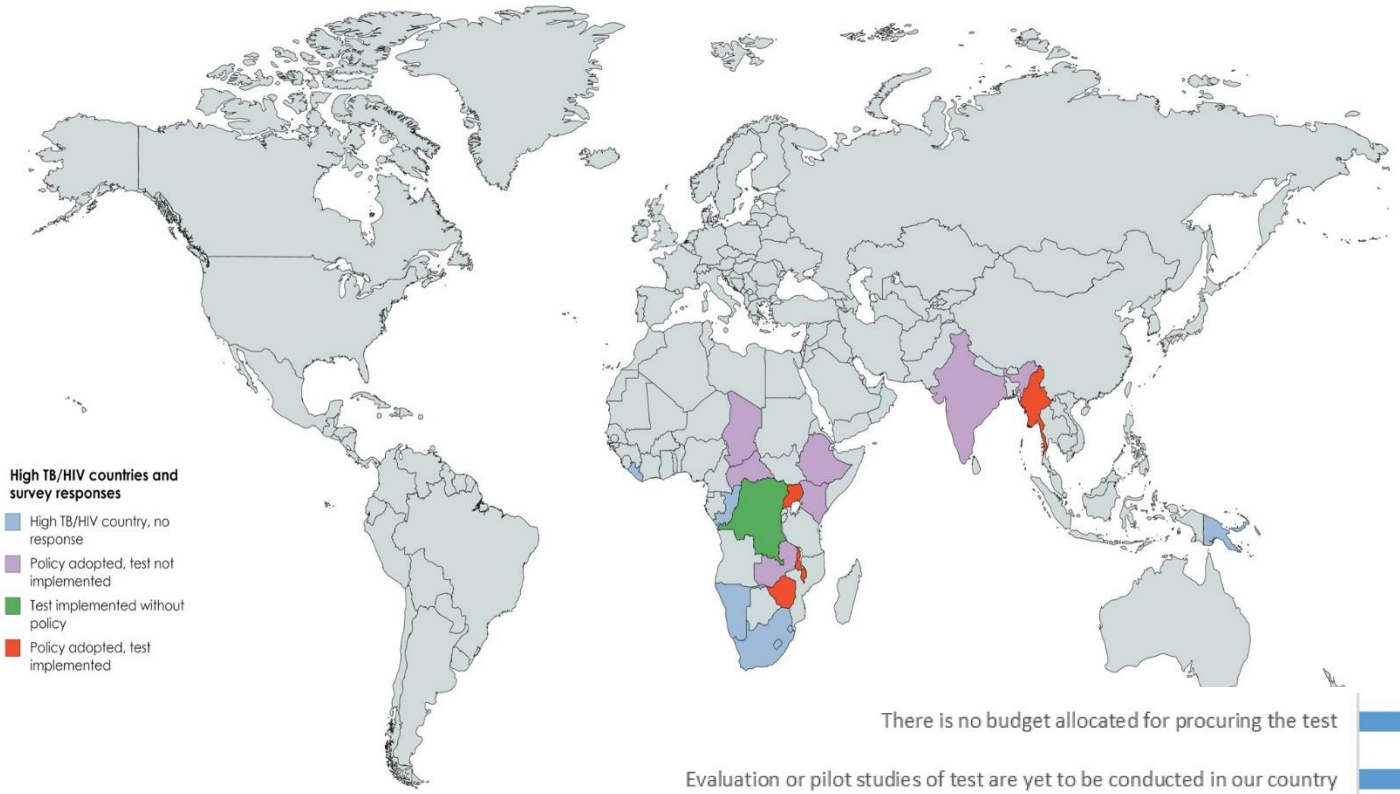
- **LF-LAM testing can help to decrease TB-related death:**
- Sample type = urine = easy to collect
- Test = quick (25 mins) and simple (add urine to LF test) = point of care; USD3.50 (GDF)
- Systematic review and meta-analysis: patients with HIV-TB and detectable urinary LAM have increased mortality risk compared to those patients without (Gupta-Wright et al. BMC Medicine (2016) 14:53)
- LF-LAM:
  - provides major incremental diagnostic yield with very high specificity when used in combination with sputum testing
  - has important utility among those without respiratory TB symptoms and/or unable to produce sputum
  - rapidly identifies individuals with a poor prognosis (Lawn et al. BMC Medicine (2017) 15:67)

LF-LAM testing can rapidly identify PLHIV with TB most at risk of death (2)

- LAM-guided initiation of anti-TB treatment in HIV-positive inpatients with suspected TB associated with reduced 8-week mortality
- Implementation of LAM testing likely to offer greatest benefit in hospitals where diagnostic resources are most scarce and where patients present with severe illness, advanced immunosuppression, and an inability to self-expectorate sputum (Peter et al. Lancet (2016) 381:1187)

LF-LAM use remains low in high TB/HIV burden countries

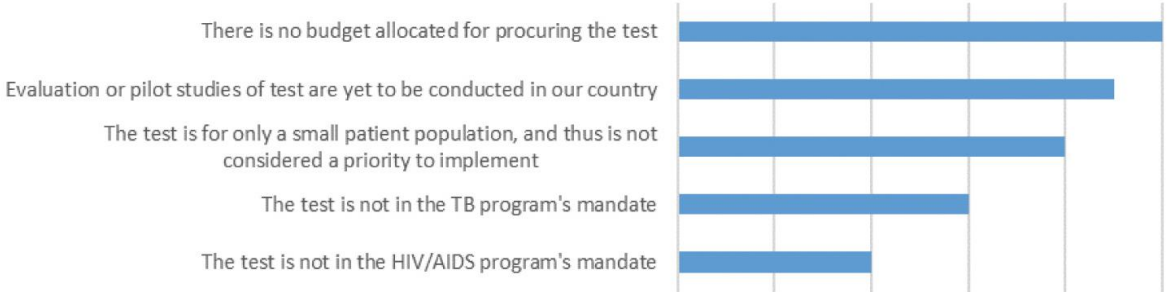
Based on prior WHO guidelines (symptoms, CD4<100)



Survey: 31 highest TB/HIV burden countries

- Response: 24 countries (77%)
- Adopted: 11/24 (46%)
- Routinely used: 5/24 (21%)
- Planning: 15/24 (63%)

Confusion about whether TB or HIV programme mandate



Singhroy, D. N., et al. (2020). Adoption and uptake of the lateral flow urine LAM test in countries with high tuberculosis and HIV / AIDS burden : current landscape and barriers. Gates Open Research, 4, 24. https://doi.org/https://doi.org/10.12688/gatesopenres.13112.1

TAKE ACTION – SAVE LIVES!
TAG's Activist Guide to TB LAM Test

TAG LF-LAM dashboard of countries with high burdens of TB and HIV:

- **13/30 (43%)** incorporated LAM testing into national **guidelines**
- Only **7/30 (23%)** are **implementing** testing (DRC, Kenya, Malawi, Myanmar, South Africa, Uganda, Zimbabwe)

Communities should demand access to LAM testing by:

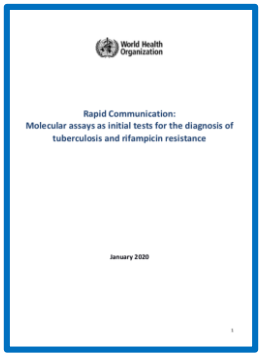
- Working with your **government** to incorporate LAM testing into **Global Fund and PEPFAR** Country Operational Plans (on TB and/or HIV programme budget)
- Asking National TB and HIV Programmes to introduce LF-LAM testing as per WHO guidelines, **including training of health care workers**
- If required, ask Abbott (manufacturer) and NRA to **register** test in country
- **Generate demand** by building **awareness** in TB/HIV-affected communities
- **Encourage donors** to support roll-out

UPDATED Feb 2020

TAG. An Activist's Guide to the LAM Test

https://www.treatmentactiongroup.org/publication/an-activists-guide-to-the-tb-lam-test/

WHO Rapid Communication: Molecular Assays


World Health Organization

Rapid Communication:
Molecular assays as initial tests for the diagnosis of tuberculosis and rifampicin resistance

January 2020

Overall conclusions

- Evidence reviewed supports continued **use of Xpert MTB/RIF and Xpert Ultra as initial diagnostic tests for pulmonary TB** in patients of **all ages**
- Also supports use of Xpert MTB/RIF and Xpert Ultra in diagnostic work-up of:
  - all patients with **extra-pulmonary TB**
  - **children with TB** (specifically gastric specimens, nasopharyngeal specimens and stool specimens)
- Both assays also show high accuracy in simultaneous detection of **rifampicin resistance**
- The performance of **Truenat MTB, MTB Plus and MTB-RIF Dx assays show comparable accuracy** with Xpert MTB/RIF and Xpert Ultra for
  - TB detection (Truenat MTB and Truenat MTB Plus)
  - Sequential rifampicin resistance detection (Truenat MTB-Rif Dx)
- Truenat MTB and MTB Plus assays also show comparable accuracy to the TB-LAMP® assay (Eiken Chemical Company Ltd (Tokyo, Japan) as replacement tests for sputum smear microscopy
- The data for **Truenat MTB-Rif Dx show similar accuracy to WHO-approved commercial line probe assays**:
  - GenoType MTBDRplus ®VER 1 and 2 (Hain Lifescience, Germany)
  - Nipro NTM+MDRTB detection kit 2® (Nipro, Japan).

Drug-resistant TB cascade of care

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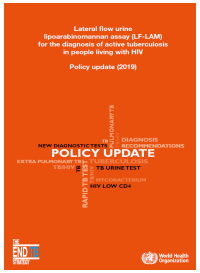

Algorithms for LF-LAM use

INPATIENT SETTING

Population: All hospitalized patients, including adults, adolescents and children living with HIV

- Assess for TB signs or symptoms †
- Assess if seriously ill †
- Assess for AHD *
- Perform CD4 testing (advisable)

Not CD4 count based

CD4 count based

Chest x-ray

Positive for TB signs or symptoms

No TB signs and symptoms with any of following:
- Positive for AHD and/or seriously ill † or
- CD4 < 200

- No TB signs and symptoms AND
- CD4 above 200 or Unknown CD4

Perform Xpert MTB/RIF (Ultra) and Urine LAM if available

Negative

Perform Urine LAM

Clinical Management

TPT, ART, Bactrim

Positive

Xpert Positive LAM Positive

Xpert Positive LAM Negative

Xpert Negative or N/A LAM Positive

Xpert Negative or N/A LAM Negative

CD4<200

Perform Xpert if available

Xpert Positive

Xpert Negative or N/A

TB Treatment

TB Treatment

Treat for TB, Perform workup to exclude DR-TB

Clinical Management

Apply AHD* package of care

TB Treatment

Treat for TB, Perform workup to exclude DR-TB

DS-TB or DR-TB Tx

DS-TB or DR-TB Tx

DS-TB or DR-TB Tx

TB is not ruled out

CRAG, TPT, ART, Bactrim

DS-TB or DR-TB Tx

*AHD – Advanced HIV Disease - For adults and adolescents, and children older than five years, advanced HIV disease is defined as CD4 cell count <200 cells/mm3 or WHO stage 3 or 4 event. All children younger than five years old are considered as having advanced HIV disease.

† WHO TB symptom screen includes presence of fever, weight loss, or any cough. "Seriously ill" is defined based on 4 danger signs : respiratory rate> 30/min, temperature>39°C, heart rate>120/min and unable to walk unaided. PLHIV with TB may also present with signs or symptoms of extrapulmonary TB including lymphadenopathy, meningitis, or other atypical presentations warranting evaluation.

Color codes: clinician/nurse action item | results | final outcomes

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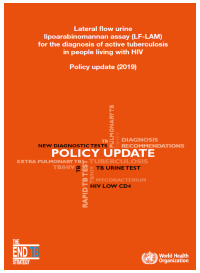

Algorithms for LF-LAM use

CLINIC / OUTPATIENT SETTING

Chest x-ray

- Assess for TB signs and symptoms†
- Assess if seriously ill†
- Assess for Advanced HIV Disease (AHD)
- Perform CD4 testing (advisable)

Applies to all of the following **populations of adults, adolescents, and children**
- All newly diagnosed HIV patients that are ART naïve
- HIV patients returning to care following an interruption of treatment
- HIV patients receiving an ART regimen that is failing
- Patients presenting at clinic and unwell

Positive for TB Signs and Symptoms and/or seriously ill†

Perform urine AlereLAM AND Xpert if available (and culture/DST if available)

Collect specimens before treatment, although Xpert may be negative

- Xpert Positive LAM Positive → TB Treatment
- Xpert Positive LAM Negative → TB Treatment
- Xpert Negative or N/A LAM Positive → Treat for TB, Perform workup to exclude DR-TB
- Xpert Negative or N/A LAM Negative → Clinical Management

TB is not ruled out

without TB symptoms AND not seriously ill

CD4 assessment if available

- CD4 < 100 or Stage 3 / 4 → Perform urine AlereLAM
  - Positive → Perform Xpert if available
    - Xpert Positive → TB Treatment
    - Xpert Negative or N/A LAM Positive → Treat for TB, Perform workup to exclude DR-TB
  - Negative → Apply AHD* package of care
- CD4 100-200 → Apply AHD* package of care
- Unknown CD4 / CD4>200 → Do not perform urine AlereLAM → Clinical Management

without assessing TB symptoms

Do not perform urine AlereLAM → Clinical Management

TPT, ART, Bactrim, DSD model of care

*AHD – Advanced HIV Disease - For adults and adolescents, and children older than five years, advanced HIV disease is defined as CD4 cell count <200 cells/mm3 or WHO stage 3 or 4 event. All children younger than five years old are considered as having advanced HIV disease.

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Color codes: clinician/nurse action item; results; final outcomes

Use of LF-LAM: key messages

LF-LAM = rule-in test to screen for active TB
→Still requires molecular test for RR/MDR testing!
→Should treat if LAM+ (no need for positive Xpert MTB/RIF for confirmation)

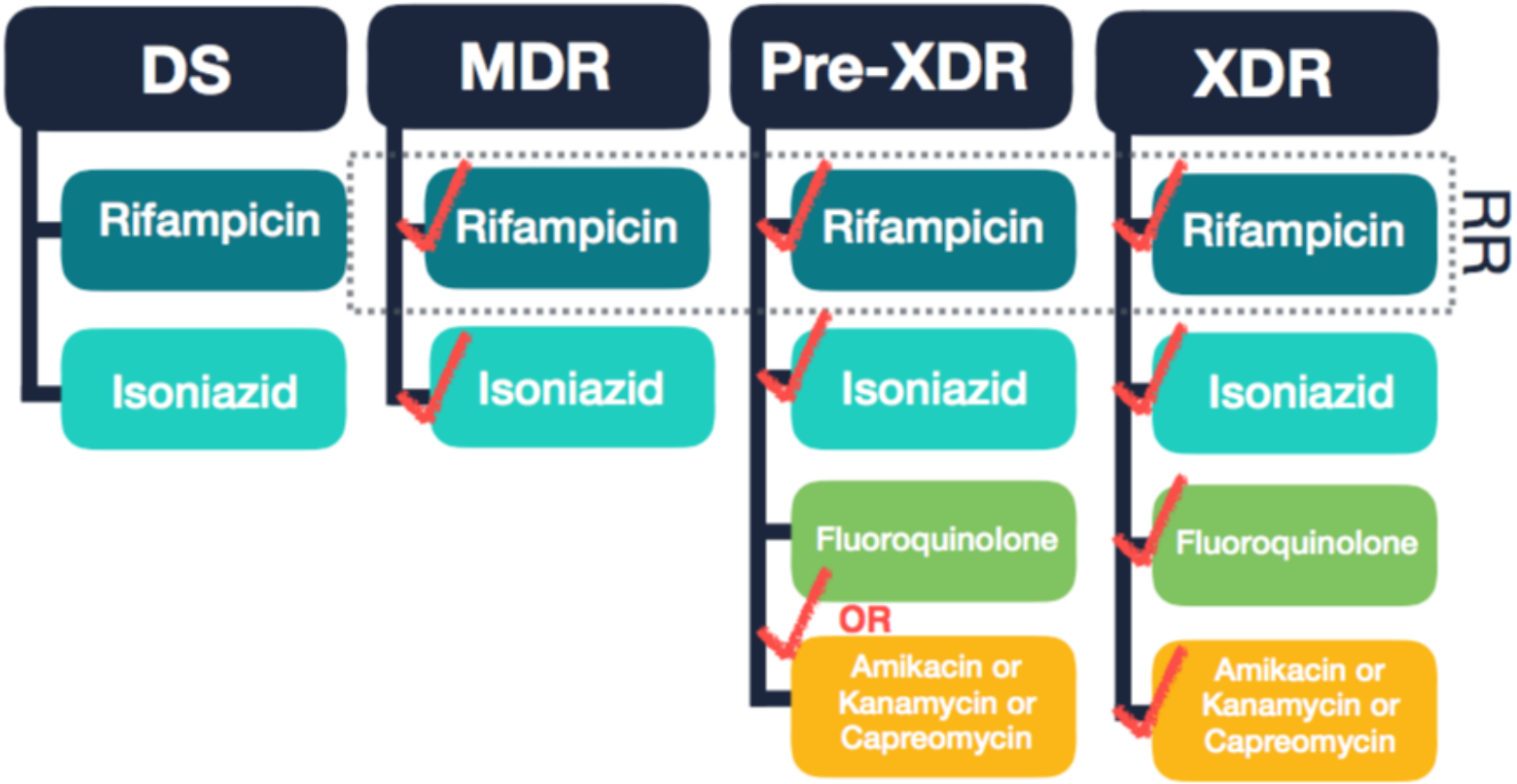
LF-LAM = NOT a rule-out test
→ additional testing needed to rule-out TB!

Might not be available if no access to GeneXpert or person can't produce sputum

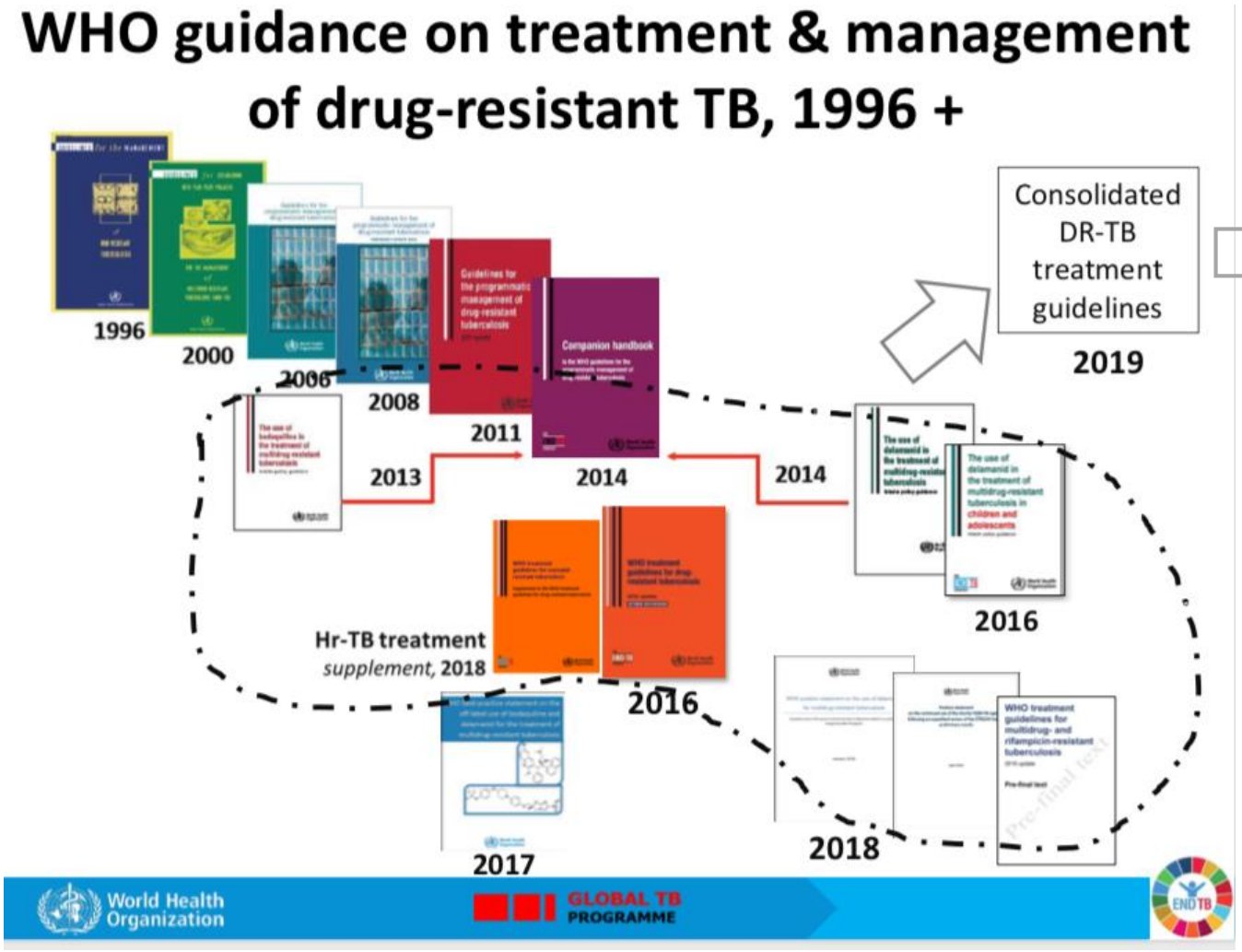
LF-LAM is a screening test and a diagnostic test

Drug-resistant TB policy updates

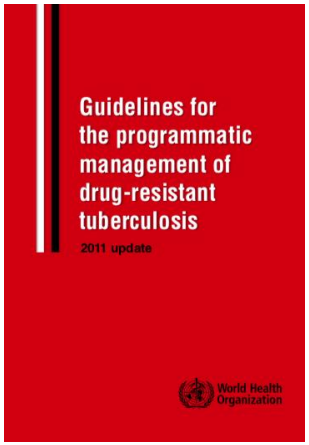
Definitions



Timeline of WHO guideline updates



WHO DR-TB guidelines Pre-2016



Treatment

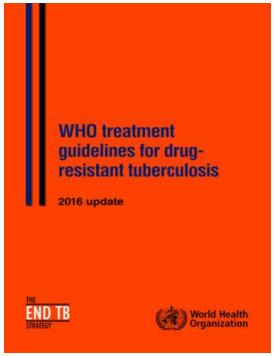
8 (Cm/Lfx/Pto/Cs/PAS/Z) – 12 (Lfx/Pto/Cs/PAS)

- Use of shorter treatment regimens: no recommendation
- 'Conventional' DR-TB regimen of 4 drugs + PZA:
  - Injectable agent (Cm, Km, Am)
  - Later generation quinolone (Lfx, Mfx)
  - Eto/Pto
  - Cs, plus PZA
- Treatment duration: at least 20 months
- Bedaquiline and delamanid: use for quinolone resistance and/or needed to construct an effective regimen, 6 month duration

Table 3. Groups of second-line anti-tuberculosis agents referred to in these guidelines

Group name	Anti-tuberculosis agent	Abbreviation
Second-line parenteral agent (injectable anti-tuberculosis drugs)	kanamycin amikacin capreomycin	Km Amk Cm
Fluoroquinolones	levofloxacin moxifloxacin gatifloxacin ofloxacin	Lfx Mfx Gfx Ofx
Oral bacteriostatic second-line anti-tuberculosis drugs	ethionamide prothionamide cycloserine terizidone *p*-aminosalicylic acid	Eto Pto Cs Trd PAS
Group 5 drugs	clofazimine linezolid amoxicillin/clavulanate thioacetazone clarithromycin imipenem	Cfz Lzd Amx/Clv Thz Clr Ipm

WHO DR-TB guideline updates 2016-2018



Treatment

- Use of shorter treatment regimens: 9-11 month standardized 7-drug regimen for MDR-TB may be used
- Longer DR-TB regimen of 4 drugs + PZA:
  - 1 from Group A (quinolones)
  - 1 from Group B (Injectable agents)
  - At least 2 from Group C + PZA
- Treatment duration: at least 20 months
- Bedaquiline and delamanid: Group D2, use if an effective 5 drug regimen can't be constructed with Groups A, B, C
- Paediatrics: avoid injectable, BDQ > 18 years, DLM > 6 years
- Elective lung resection as adjunct to treatment

4-6 Km-Mfx-Pto-Cfz-Z-$H_{high\text{-}dose}$-E / 5 Mfx-Cfz-Z-E

8 (~~Cm~~/~~Lfx~~/Pto/Cs/PAS/Z) – 12 (Lfx/Pto/Cs/PAS)

BDQ and/or DLM

Table 6. Medicines recommended for the treatment of rifampicin-resistant and multidrug-resistant TB[1]

A. Fluoroquinolones[2]		Levofloxacin Moxifloxacin Gatifloxacin	Lfx Mfx Gfx
B. Second-line injectable agents		Amikacin Capreomycin Kanamycin (Streptomycin)[3]	Am Cm Km (S)
C. Other core second-line agents[2]		Ethionamide / Prothionamide Cycloserine / Terizidone Linezolid Clofazimine	Eto / Pto Cs / Trd Lzd Cfz
D. Add-on agents (not part of the core MDR-TB regimen)	**D1**	Pyrazinamide Ethambutol High-dose isoniazid	Z E H^h
	D2	Bedaquiline Delamanid	Bdq Dlm
	D3	*p*-aminosalicylic acid Imipenem-cilastatin[4] Meropenem[4] Amoxicillin-clavulanate[4] (Thioacetazone)[5]	PAS Ipm Mpm Amx-Clv (T)

WHO DR-TB guideline updates end 2018-end 2019

Treatment

1. Use of shorter treatment regimens: 9-11 month standardized 7-drug regimen for MDR-TB may be used *with Am*
2. Longer DR-TB regimen of 4-5 effective drugs
   - All 3 from Group A
   - 1 or 2 from Group B
   - Group C if needed
3. Modified fully oral regimens Group A/B
   - Treatment duration: 18-20 months
   - Bedaquiline: Group A drug
   - Delamanid: Group C, use if an effective 5 drug regimen cannot be constructed with Groups A and B
   - Pediatrics: BDQ > 6 years, DLM > 3 years

~~Am~~

4-6 ~~Km~~-Mfx-Pto-Cfz-Z-$H_{high\text{-}dose}$-E / 5 Mfx-Cfz-Z-E

9 (BDQ/Lfx/Lzd/Cfz/Cs)

6 (BDQ/Lfx/Lzd/Cfz/Cs) / 12 (Lfx/Lzd/Cfz/Cs)

Table 2.1. Grouping of medicines recommended for use in longer MDR-TB regimens[1]

Groups & steps	Medicine	
Group A: Include all three medicines	levofloxacin *OR* moxifloxacin	Lfx Mfx
	bedaquiline[2,3]	Bdq
	linezolid[4]	Lzd
Group B: Add one or both medicines	clofazimine	Cfz
	cycloserine *OR* terizidone	Cs Trd
Group C: Add to complete the regimen and when medicines from Groups A and B cannot be used	ethambutol	E
	delamanid[3,5]	Dlm
	pyrazinamide[6]	Z
	imipenem–cilastatin *OR* meropenem[7]	Ipm–Cln Mpm
	amikacin (*OR* streptomycin)[8]	Am (S)
	ethionamide *OR* prothionamide[9]	Eto Pto
	p-aminosalicylic acid[9]	PAS

DR-TB/HIV co-infection

All people living with HIV and RR/ MDR-TB are considered to have advanced HIV and are at high risk of mortality, especially if not on ART

- The short and longer regimens should be given to people with HIV based on their DST and risk factors
- HIV status alone does not mandate any changes in regimen design
- PLHIV may need ART changed since bedaquiline cannot be given with efavirenz
  - ART options include **dolutegravir**, nevirapine, or lopinavir/ritonavir depending on the viral load
  - AZT also causes toxicity to the bone marrow and substitution may be considered in persons on linezolid
- All persons newly diagnosed with RR-TB who are HIV-positive:
  - CD4 count and viral load tested at RR-TB treatment initiation and after 6 months
  - repeat viral load can be tested at 2 months if the baseline is detectable

DR-TB/HIV co-infection

- For persons not yet on ART, HIV treatment should be initiated 2-8 weeks after starting RR-TB therapy
  - If CD4 count < 50, ART should be started within two weeks of TB/DR-TB treatment
  - If CNS involvement, ART should be started 4-8 weeks post TB treatment given risk of intracranial IRIS
- Co-trimoxazole therapy should be given regardless of CD4 count
- Identification and management of other co-morbid opportunistic infections is required for persons with RR-TB and HIV
- Additional counseling support will be needed to help people with RR-TB and HIV be successful in their treatment

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TABLE 6: GUIDANCE FOR MODIFICATION OF ART REGIMENS FOR ADULTS DURING TREATMENT FOR RR-TB

CURRENT ART REGIMEN	PROPOSED ART REGIMEN	
	VL < 400	VL > 400
TDF or ABC/ XTC/ EFV	1. Persons should remain on ABC if they have a contraindication to TDF. 2. TDF*/ XTC and Dolutegravir (if available) Or 3. TDF*/ XTC and LPV/ rit (or ATZ/ rit) † Or (as last resort) 4. TDF*/ FTC/ NVP	AZT, 3TC and DTG
TDF or ABC/ XTC/ NVP	Keep on same ART	Review previous VL and history. If history of treatment interruptions/ poor ART adherence or person is clinically unwell/CD4<50 switch NVP to LPV/rit (or ATZ/rit).If no change is made address adherence and repeat VL in 2 months – if VL remains > 400change AZT, 3TC and DTG
TDF or ABC or AZT/ XTC and LPV/ rit (or Dolutegravir)	Change AZT to TDF* Keep rest of regimen unchanged	Review and address reason for increased VL. Refer to guidance on genotyping if VL remains elevated.
XTC = FTC or 3TC		

South African Department of Health, Management of RR-TB Policy Guidelines, April 2019

EDUCATIONAL FUND

World Health Organization

1 month

Joint Statement: Accelerating action to end tuberculosis

WHO Director-General with the WHO Civil Society Task Force on TB

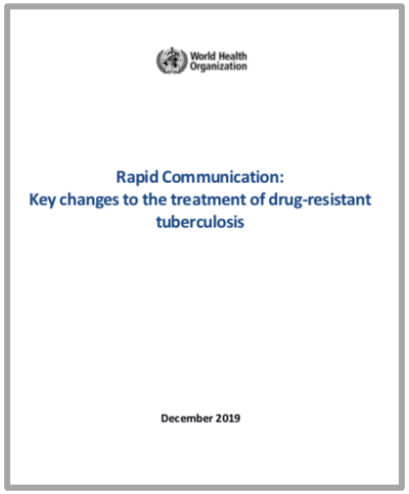
The World Health Organization (WHO) Director-General Dr Tedros Adhanom Ghebreyesus met with members of the WHO Civil Society Task Force on Tuberculosis (TB) in June 2019, on the sidelines of the annual meeting of the WHO Strategic and Technical Advisory Group on TB. There was frank and constructive dialogue in the

2. **Transition to an all-oral regimen to treat people with drug-resistant TB by World TB Day 2020.**

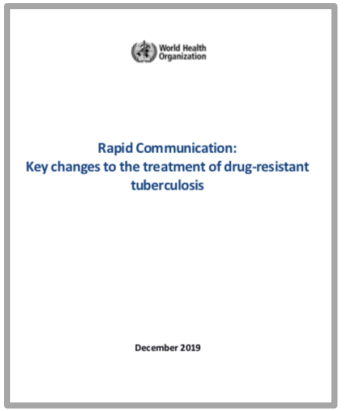
   In 2018, WHO issued new consolidated guidelines for the treatment of people with multidrug-resistant TB (MDR-TB) that could lead to major improvements in treatment outcomes and quality-of-life for patients. A fully oral regimen is strongly recommended as a preferred option for MDR-TB treatment. WHO and the Civil Society Taskforce strongly recommend that all countries transition to an all-oral regimen for drug-resistant TB by World TB Day 2020.

WHO Rapid Communication December 2019

- Public call for IPD data on BDQ extension, combination BDQ-DLM use, use of BDQ in pregnancy, and use of all oral BDQ based shorter 9-12 month regimens
- Added this data to IPD dataset used for GL update March 2019 – 13,000 patient records from 55 studies in 40 countries
- WHO Guideline Development Group meeting 12-14 November 2019
- Second Rapid Communication for DR-TB released



WHO Rapid Communication: Data


World Health Organization

Rapid Communication:
Key changes to the treatment of drug-resistant tuberculosis

December 2019

- Shorter, all oral BDQ based regimens
  - 4000 individuals treated in South Africa in 2017
  - Final outcomes and follow up data
  - Precedes announcement of all oral regimen in 2018
- Nix-TB trial data
  - 100+ records of XDR/MDR TI/NR MDR
- endTB observational cohort data
  - 1000 records: 1/3 with BDQ extension > 6 months, 100 received BDQ + DLM in combination
- Public call for data
  - 200 records from MSF projects in India and Uzbekistan
  - 100 records from NTP in Belarus
  - 100 records of pregnant women treated with BDQ based regimen in KZN, South Africa between 2013-2017

WHO Rapid Communication: Analysis of Results

Shorter BDQ based regimens*

- Compared to standardized 2016 WHO regimen with injectable
- No previous exposure to key second line drugs
- Confirmed quinolone susceptibility
- Excluded patients with severe disease and severe EPTB
- High **HIV co-infection rate of 71%**
- Significantly better treatment success
- Considerable reduction in lost to follow up

**Data was not available on other modifications – notably linezolid*

'South Africa' regimen with data available for analysis:
4-6 BDQ[6]-Lfx[Mfx]-Eto-E-Z-Hh-Cfz / 5 Lfx[Mfx]-Cfz-Z-E

WHO Rapid Communication: Analysis of Results

BPaL regimen: 6-9 BDQ-Pa-Lzd[1200 mg]

- 108 participants from Nix study – single arm open label study
- Excluded patients expected to die within 3 months of starting treatment
- BPaL compared at GDG with matched records in IPD – data on all oral regimens with Group A/B drugs not yet available
- High rates of treatment success with XDR in RSA (89% with favourable outcomes)*
- Study limitations (small numbers, high rate of adverse events) precludes programmatic implementation of regimen
- BPaL may be used under OR conditions
- Critical need for careful informed consent and clinical monitoring

WHO Rapid Communication: Summary

- Nearly all patients can be treated with all oral regimens, either shorter or longer depending on resistance pattern, severity of TB disease, location of TB disease, SLD exposure history
- Access to rapid DST testing to rule out FQ resistance is essential
- Further modifications to shorter all oral BDQ based regimen under OR conditions are possible, especially in regions with high probability of resistance to other drugs in regimen
- BPaL may be used for XDR-TB under OR (no previous exposure to BDQ or Lzd)
- 2020 guidelines expected in May-June 2020

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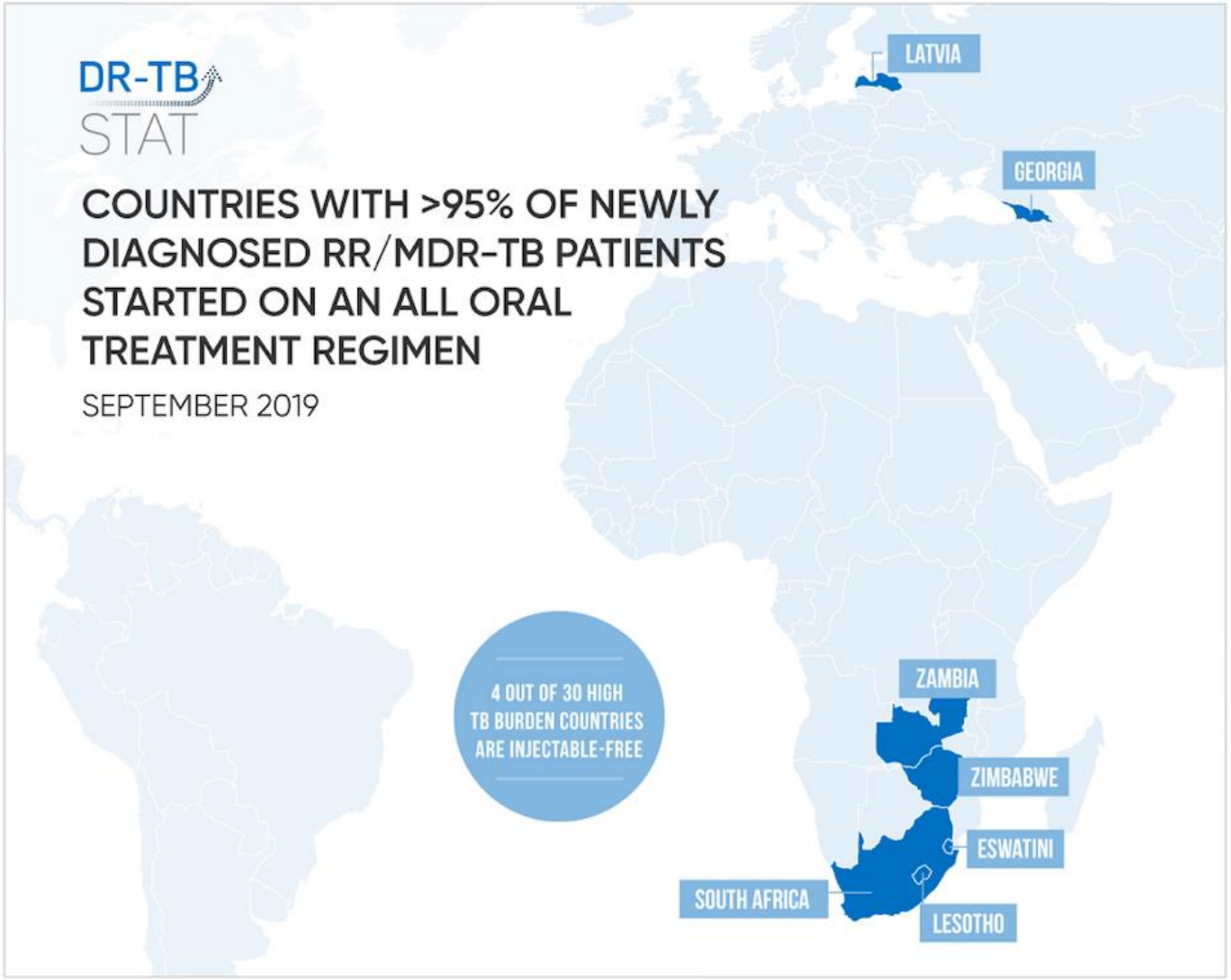
Future of RR/MDR-TB treatment: shorter, fully oral regimens

Regimens being studied in trials-timeline (http://www.resisttb.org/?page_id=1602)

Trial Name	Regimens tested	Study Population	Results expected	Registry URL
Nix ZeNix	6/9Pa-Bdq-Lzd (dose-ranging)	XDR, difficult-to-treat RR-TB	2019 2021	NCT02333799 NCT03086486
endTB	9Bdq-Lzd-Mfx-Z 9Bdq-Cfz-Lzd-Lfx-Z 9Bdq-Dlm-Lzd-Lfx-Z 9Dlm-Cfz-Lzd-Lfx-Z 9Dlm-Cfz-Mfx-Z	FQ-S RR-TB	2022	NCT02754765
endTB-Q	6/9Bdq-Dlm-Cfz-Lzd	FQ-R RR-TB	2022	NCT03896685
STREAM	4-6Km-H_{HD}-Pto/9-11M/Lfx-Cfz-Z-E 16wH-Pto/ 40wBdq-Cfz-E-Lfx-Z	FQ- & SLI-S RR-TB	Nunn et al., 2019; 2022	NCT02409290
MDR-END	9-12 Dlm-Lzd-Lfx-Z	FQ-S RR-TB	2021	NCT02619994
TB-PRACTECAL	6 Bdq-Pa-Mfx-Lzd 6 Bdq-Pa-Cfz 6 Bdq-Pa-Lzd	RR-TB	2019/2021	NCT02589782
SimpliciTB	Pa-Bdq-Mfx-Z	FQ-S RR-TB	2022	NCT03338621
BEAT-Tuberculosis	6Bdq-Lzd-Del-(Cfz)-(Lfx)	RR-TB, including XDR	2023	NCT04062201

EDUCATIONAL FUND



EDUCATIONAL FUND

WHO suggested LAM research priorities

- Develop simple, more accurate tests based on LAM detection, with potential use for HIV-negative populations;
- Evaluate use of LF-LAM in PLHIV, without signs and symptoms of TB;
- Evaluate use of LF-LAM in children and adolescents with HIV;
- Evaluate combination of parallel use of LF-LAM and rapid qualitative CD4 cell count systems;
- Implementation research on acceptance, scale-up and impact of LF-LAM in routine clinical settings;
- Qualitative research on user perspectives of LF-LAM for feasibility, accessibility, equity issues;
- Implementation research on LF-LAM integrated into HIV care packages;
- Evaluate performance of LF-LAM as HIV epidemic evolves and more people on treatment with viral load suppression are hospitalized;
- Evaluate cost–effectiveness of LF-LAM;
- Evaluate other rapid LAM-based tests such as FujiLAM.

Red = including HIV/TB co-infection

Summary: LAM

- LF-LAM is a rapid rule-in test to assist in the diagnosis of TB/DR-TB for both inpatients and outpatients with:
  - Signs and symptoms of PTB or EPTB
  - Advanced HIV disease
  - Seriously ill
  - Inpatient only: CD4 count < 200 irrespective of signs and symptoms of TB
  - Outpatient only: CD4 count < 100 irrespective of signs and symptoms of TB
- A positive LF-LAM test should prompt TB treatment initiation while doing additional tests
  - Xpert MTB/RIF or other molecular test should be done for all presumptive TB and positive LAM results
- LAM provides major incremental diagnostic yield and can reduce mortality via quicker diagnosis and treatment

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Summary: DR-TB/HIV co-infection

- TB/DR-TB is the leading cause of death for HIV co-infected individuals
- Nearly all DR-TB/HIV patients can be treated with all oral regimens, either shorter or longer depending on resistance pattern, severity of TB disease, location of TB disease, SLD exposure history
- Drug-drug interactions, overlapping toxicities, pill burden are manageable but require close clinical management and strong patient support strategies
- Newer drugs and regimens are promising for improved treatment outcomes in PLHIV with DR-TB co-infection

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WEBINAR

DIFFERENTIATED SERVICE DELIVERY

Tuesday 24 March

3:00pm Zurich, 4:00pm Johannesburg,
10:00am New York

Register here

LEVERAGING DIFFERENTIATED ART DELIVERY MODELS FOR STABLE CLIENTS TO SCALE UP TB PREVENTIVE THERAPY

For more information on differentiated service delivery, including the latest best practices, normative and clinical guidelines and tools to support country implementation, visit www.differentiatedservicedelivery.org


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