EVALUATION OF XPERT® MTB/XDR TEST FOR SUSCEPTIBILITY TESTING OF *MYCOBACTERIUM TUBERCULOSIS* TO FIRST AND SECOND LINE DRUGS, AND STATUS OF ROLL-OUT IN UGANDA

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Presentation outline

- Background
- Rationale
- Main and Specific Objectives
- Results and findings
- Discussion
- Conclusions and the way forward
- Status of uptake and roll-out in Uganda

Background

- TB remains an important cause of global morbidity and mortality.
- Drug-resistant TB (DR-TB) is one of the key challenges to TB control
- Treatment for DR-TB is longer and more expensive
- Huge gaps remain in diagnosis and treatment initiation

Rationale

- There is an urgent need for rapid and accurate DST methods for the core 1st and 2nd TB drugs.
- Several technical and operational challenges still exist with the current DST methods.
- However, the effective management of DS-TB and DR-TB relies upon early diagnosis including universal DST and effective treatment of resistant TB strains.
- There are higher benefits for fast molecular DST followed by the fast initiation of appropriate treatment.

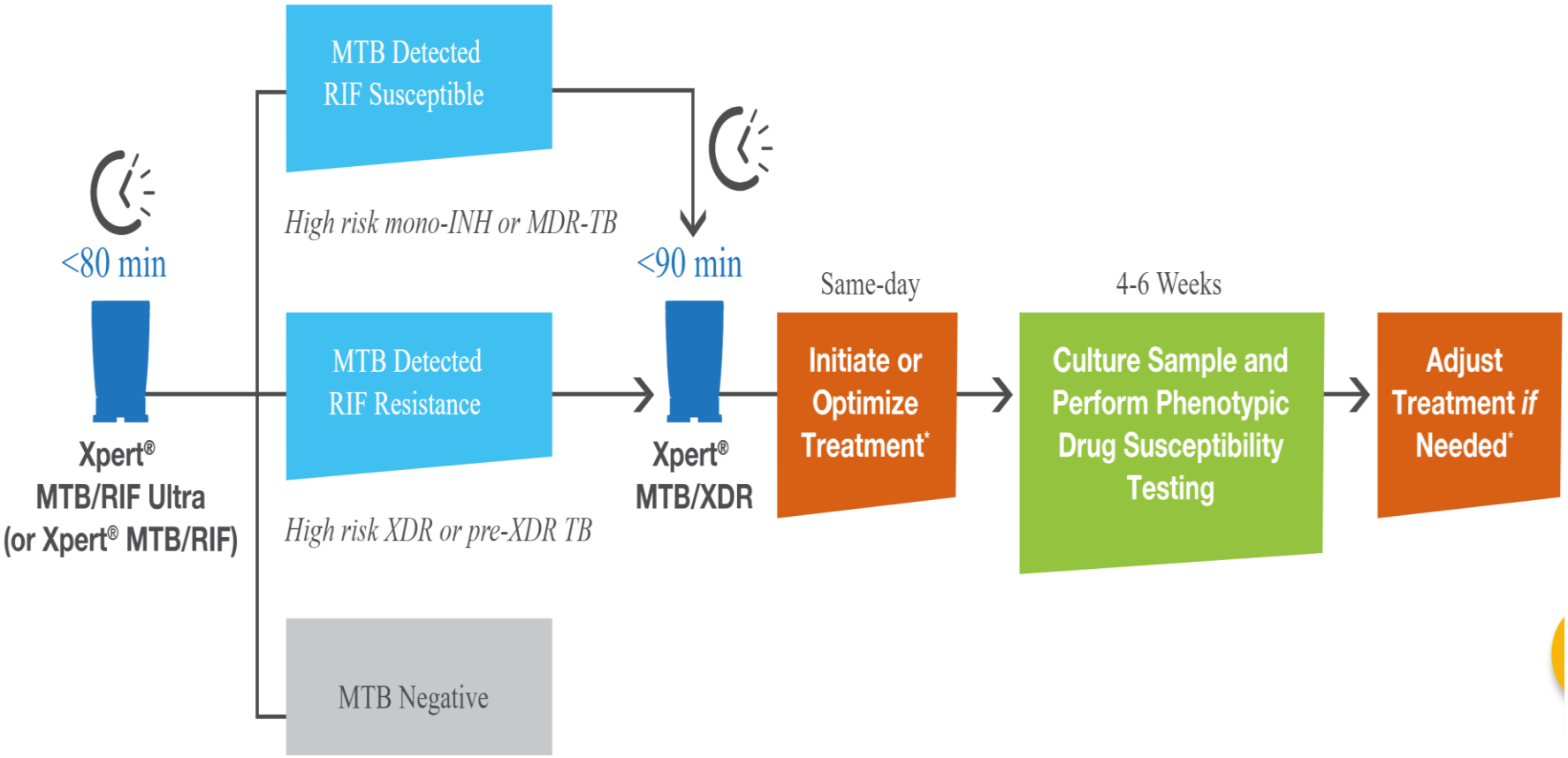
Xpert XDR Machine

Xpert XDR test, Detects resistance to second line drugs in 2hrs. Endorsed by WHO in 2021

10 color used in TB research lab at Makerere University

10 color used at the TB clinic lab at Mulago Hospital, Uganda

Schematic implementation strategy for Xpert® MTB/XDR test



Main Objective

- To validate the performance of the Xpert® MTB/XDR test for susceptibility testing of MTB among presumptive XDR-TB patients.

- The test performance indicators were compared with current standard drug susceptibility test methods including the MGIT 960 liquid culture drug susceptibility (DST) systems, Line probe Assay (LPA), and Whole genome sequencing (where possible).

Specific Objectives

- Assess the sensitivity and specificity of the Xpert® MTB/XDR test in previously-stored sputum samples compared to the **pDST method** as a gold standard.

- Assess sensitivity and specificity of Xpert® MTB/XDR test in previously-stored sputum samples compared **genotypic DST** (MTBDRplus and MTBDRsl) method as a gold standard.

Secondary objectives

- To evaluate factors for lab uptake
  - Training needs
  - Recording and Reporting Needs
  - Error rates
  - The proportion of results interpretable
  - TAT
  - Workflow

Methods

- Blinded, laboratory–based cross-sectional study to determine the performance of the Xpert® MTB/XDR test in; a) stored sputum samples.

- Patient's MTB+ samples/culture isolates with RR-TB and/or with higher suspicion index for INH-R and/or 2nd line FQ and injectable agents were included in the study.

- Approved by MAKSBS REC and UNCST.
- The study was done between September 2021 and April 2022

Results and Findings

Diagnostic accuracy of Xpert® MTB/XDR test using pDST as a reference comparator

Drug (n)		R	S	Sensitivity n(%; 95% CI)	Specificity n(%; 95%CI)	PPV % (95%CI)	NPV % (95%CI)
INH (99)	R	58	4	58 (**89.2**; 79.1-95.5)	30 (**88.2**; 72.5-96.6)	**93.5** (84.2-98.2)	**81.1** (**64.8-92.0**)
	S	7	30				
FQ (100)	R	4	0	4 (**80.0**; 28.3-99.4)	95 (**100**; 96.2-100)	100 (39.7-100)	**99.0** (**94.3-99.9**)
	S	1	95				
IAs (100)	R	----	----	N/A	100 (**100**; 96.3- 100)	N/A	**100** (**96.3-100**)
	S	**----**	**100**				

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Diagnostic accuracy of Xpert® MTB/XDR test using Hain MDR*plus* and MTBDR*sl* as a reference comparator

Drug (n)		R	S	Sensitivity n(%; 95%CI)	Specificity n(%; 95%CI)	PPV % (95%CI)	NPV % (95%CI)
INH (98*)	R	50	12	50 (**96.1**; 86.7-99.5)	34 (**74.0**; 58.8-85.7)	**80.6** (68.6-89.5)	**94.4** (81.3-99.3)
	S	2	34				
FQ (100)	R	3	1	3 (**100**; 29.2-100)	96 (**99.0**; 94.3-99.9)	**75** (19.4-99.3)	**100** (96.2-100)
	S	0	96				
IAs (98)	R	---	---	N/A	96 (**100**; 96.2-100)	N/A	**98.0** (92.8-99.7)
	S	1	96				

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Additional factors for uptake

- **Training needs:** None for those with previous Xpert experience and 1 day for those without.

- **Recording and Reporting Needs:** No difference from that required for Ultra
- **Error rates:** 4/100 (4%)
- **The proportion of results interpretable:** None
- **Test TAT:** 1:45 minutes
- **Workflow**: similar to that of Ultra

Discussion

- There is high sensitivity and specificity of Xpert XDR cartridge for INH, FQ, and Injectable using pDST as RS
- Better diagnostic accuracy is seen when LPA is used as RS.
- Better test attributes in terms of training, TAT, error rates, and workflow have been recorded
- The differences in diagnostic accuracy with different RS methods (pDST vs gDST) is well documented

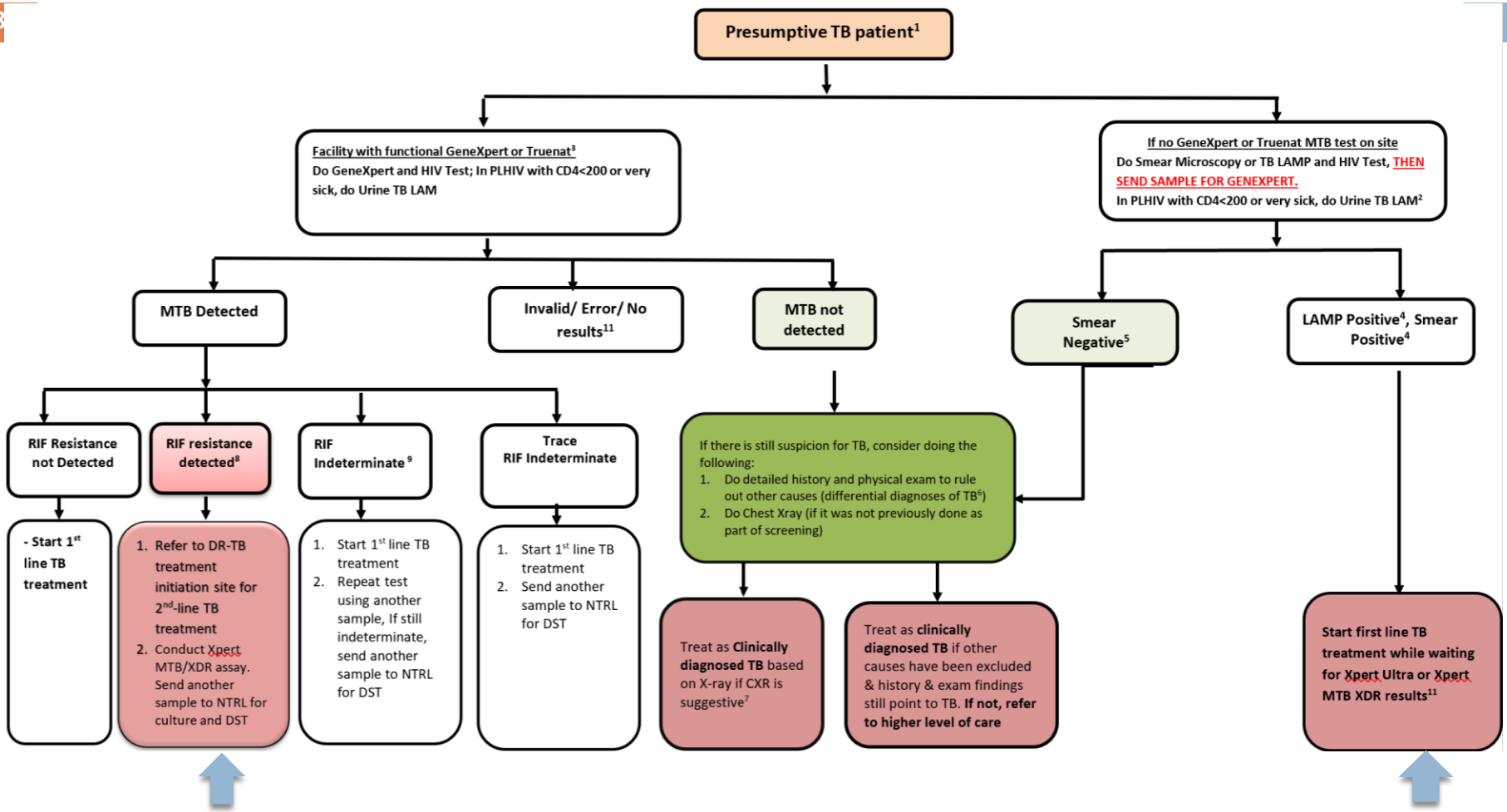
Conclusions and wayforward

- Xpert XDR test is a reliable, rapid accurate, and easy-to-use DST method for INH, FQ, and IA.
- The country should consider that; all new Xpert machine procurements should be 10-color for easy integration
- DR-TB treatment centers should be prioritized to have 10-color machines for Xpert Ultra and XDR
- The manufacturer should plan to swap 6-color with 10-color Xpert machines to ensure better access to XDR test in all Xpert sites.

Status of uptake and roll-out in Uganda

- Our network studies have accepted the validation results and switched to Xpert XDR for patient screening in Clinical trials.
- Uganda considered uptake and roll-out of XDR TB and revised the diagnostic algorithm.
- All DR-TB treatment centers have 10 color machines, and all RR-TB are tested for INH and FQ using Xpert.
- Currently 22 DR-TB treatment initiation sites but there is plan to continuously decentralize DR-TB management.

ALGORITHM FOR SCREENING, DIAGNOSIS AND MANAGEMENT OF TUBERCULOSIS IN UGANDA



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