Confirmation of RIF-resistance using a 2nd Xpert MTB/RIF test: Analysis of routinely collected data in MSF-supported sites in Mozambique, Zimbabwe and Kenya

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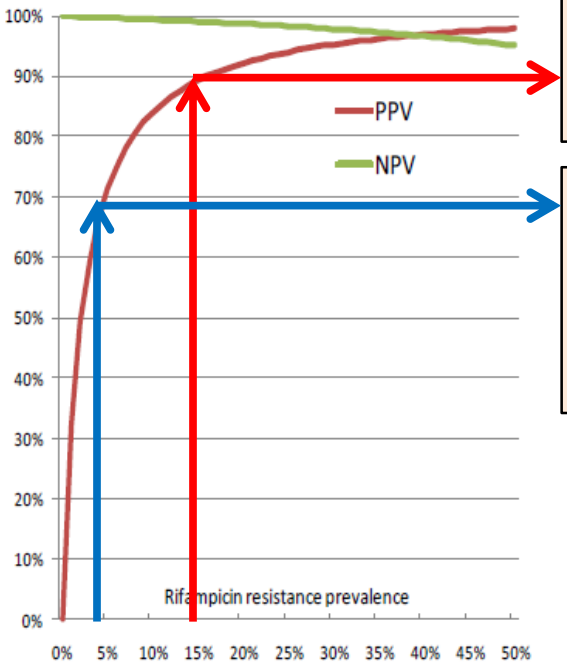
CONFIRMATION OF RIF-RESISTANCE

- In settings or patient groups with a **low prevalence/risk of MDR-TB**, the WHO recommends that Xpert **RIF-resistant results be confirmed** with the Line Probe Assay (**LPA**) or phenotypic drug susceptibility testing (**DST**) before initiating patients on treatment.

Rifampicin resistance prevalence	PPV	NPV	True positive*	False negative*	False positive*	True negative*
1%	32.4%	99.9%	9.5	0.5	19.8	970.2
2%	49.2%	99.9%	19	1	19.6	960.4
3%	59.5%	99.8%	28.5	1.5	19.4	950.6
4%	66.4%	99.8%	38	2	19.2	940.8
5%	71.4%	99.7%	47.5	2.5	19	931
6%	75.2%	99.7%	57	3	18.8	921.2
7%	78.1%	99.6%	66.5	3.5	18.6	911.4
8%	80.5%	99.6%	76	4	18.4	901.6
9%	82.4%	99.5%	85.5	4.5	18.2	891.8
10%	84.1%	99.4%	95	5	18	882
11%	85.4%	99.4%	104.5	5.5	17.8	872.2
12%	86.6%	99.3%	114	6	17.6	862.4
13%	87.7%	99.2%	123.5	6.5	17.4	852.6
14%	88.5%	99.2%	133	7	17.2	842.8
15%	89.3%	99.1%	142.5	7.5	17	833
20%	92.2%	98.7%	190	10	16	784
25%	94.1%	98.3%	237.5	12.5	15	735

* Sensitivity (95%) and specificity (98%) for Xpert MTB/RIF rifampicin resistance, compared with reference method (culture)

WHO, 2011

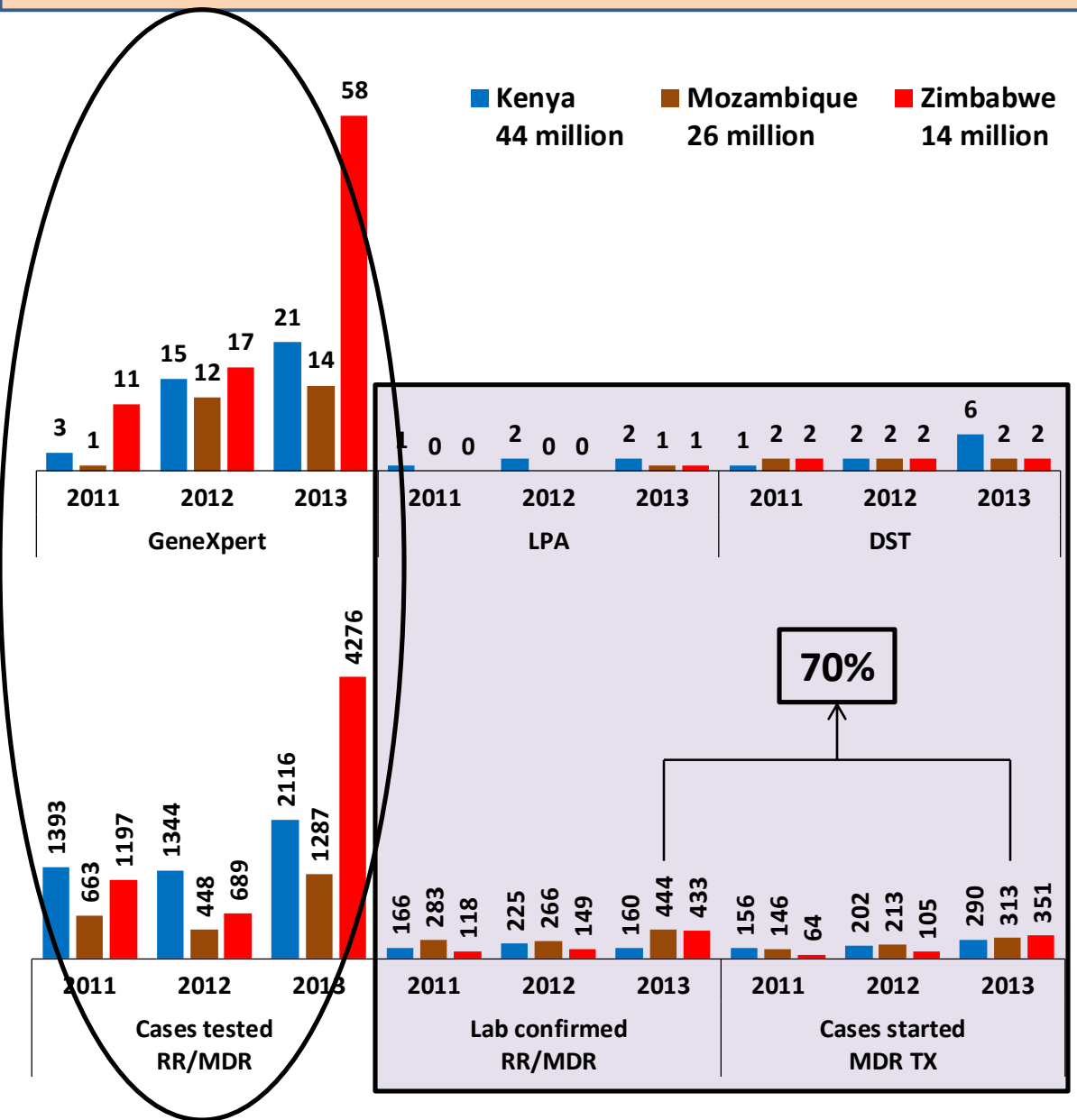


When the prevalence of RIF-resistance is >15%, the PPV of Xpert is high (>90%).

When the prevalence of RIF-resistance <15% the PPV is adversely affected:
84% when prevalence is 10%
71% when prevalence is 5%

- However, **LPA** is not routinely available in resource-limited settings and is validated only for smear-positive samples. **Phenotypic DST** is generally available only at central or regional laboratories with **long turn-around times** (TAT) of results.

NEED TO STRENGTHEN DIAGNOSTIC CAPACITY

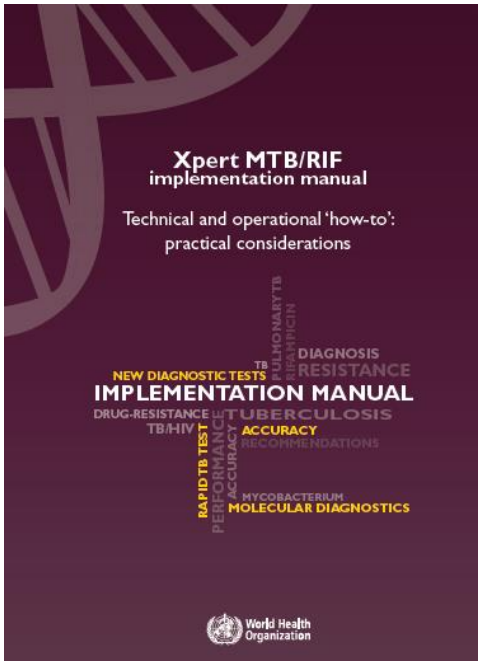


The rapid expansion of GeneXpert has lead to an increase of cases tested and diagnosed with RR.

Despite progress in the detection of MDR/RR-TB cases, a major diagnostic gap remains: **55% of reported TB patients estimated to have MDR-TB were not detected in 2013.**

(WHO Global TB Report, 2014)

UPDATED WHO XPERT IMPLEMENTATION MANUAL (2014)

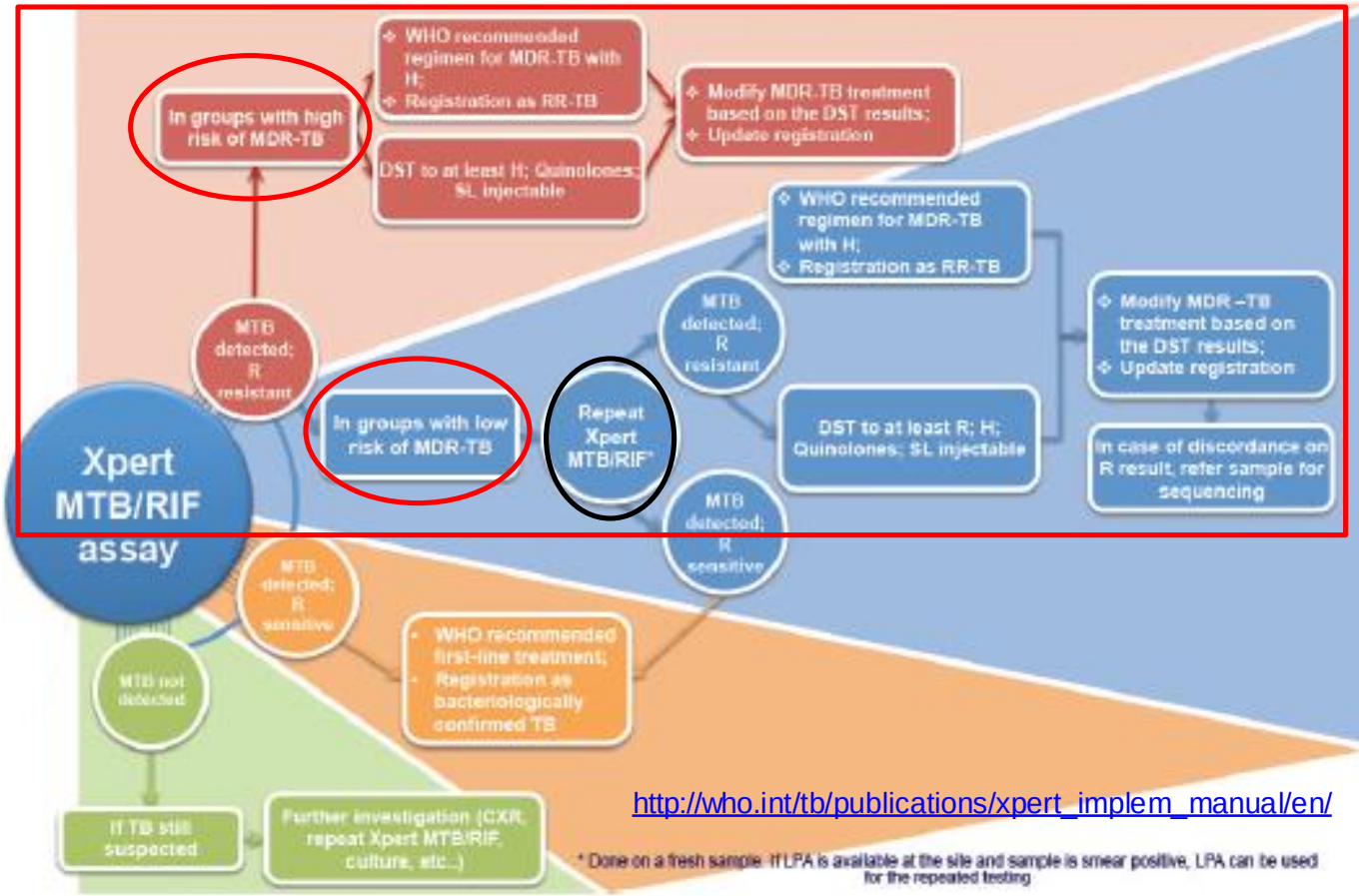


When Xpert shows RIF-resistance:

Perform risk assessment :

Groups with high risk (retreatment cases, etc) ➔initiateTx

Groups with low risk (new cases, etc) ➔ **repeat Xpert**



http://who.int/tb/publications/xpert_implem_manual/en/

STUDY DESCRIPTION

Study objectives

- To assess the added value of performing a 2nd Xpert test on a 2nd sputum sample to confirm rifampicin resistance.
- To determine the concordance between two Xpert RIF-resistant results and DST

Methods

We analysed the confirmatory test results and TAT among 253 patients from TB programmes in Mozambique (Maputo and Tete), Zimbabwe (Buhera) and Kenya (Kibera), who tested RIF-positive on Xpert between June 2011 and Oct 2014. Additional sputum samples were collected for confirmatory testing using a second Xpert test and/or DST for first line.

PRELIMINARY RESULTS

	MOZAMBIQUE	ZIMBABWE	KENYA	TOTAL
1ST Xpert RIF+	**150**	**78**	**25**	**253**
DST done, n (%)	21 **(14%)**	31 **(38%)**	13 **(52%)**	65 **(25%)**
TAT, months, mean (range)	**4** (3-7)	**3** (2-5)	**2** (2-6)	**3** (2-5)
DST confirming RIF+, n (%)	17 **(81%)**	30 **(97%)**	10 **(77%)**	57 **(88%)**
2nd Xpert done, n (%)	66 **(44%)**	78 **(100%)**	25 **(100%)**	169 **(68%)**
TAT, days, mean (range)	**6** (1-30)	**6** (1-21)	**2** (1-5)	**4** (1-19)
2nd Xpert RIF+, n, (%)	54 **(82%)**	75 **(96%)**	21 **(84%)**	150 **(89%)**

65 DST

92% concordance

52 double RIF+

48 DST RIF+

4 DST RIF-

13 single RIF+

10 DST RIF+

3 DST RIF-

77% concordance

CONCLUSIONS AND RECOMMENDATIONS

- Confirmation with LPA/DST was extremely low (25%) with long TAT

- There is an urgent need to strengthen diagnostic capacity to confirm DR-TB, including referral networks for transport of samples and rapid result-delivery.

- Performing a second GeneXpert shortened the time for RIF-resistance confirmation

- Although repeating Xpert increases costs, it provides a practical alternative to decide on earlier treatment initiation while awaiting DST confirmation.

- The concordance between DST with double Xpert RIF-resistant results was high (92%)

- Discordant results between Xpert and DST are common (10-13%). There is growing evidence that phenotypic DST may miss clinically relevant mutations. In these cases resolution with DNA sequencing is recommended.

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THANK YOU