Feasibility and impact of using Xpert MTB/RIF: Results from demonstration studies

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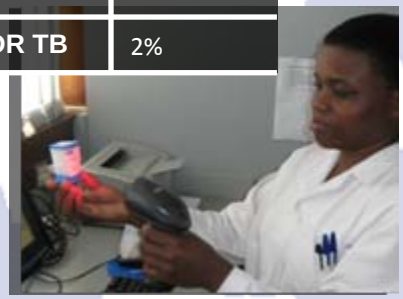
Multi-center implementation studies

- **9** district, sub-district and microscopy centers in **6 countries**
- **Diverse** laboratories (temperature, staff background) & populations
- **7000** TB or MDR-TB suspected patients screened

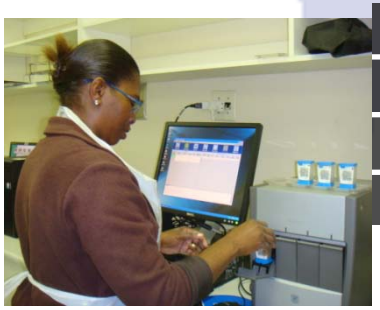
Lima	Peru
HIV	3%
TB (C+)	17%
MDR TB	8%

Kampala	Uganda
HIV	100%
TB (C+)	42%
MDR TB	2%



Baku	Azerbaijan
HIV	6%
TB (C+)	47%
MDR TB	22%

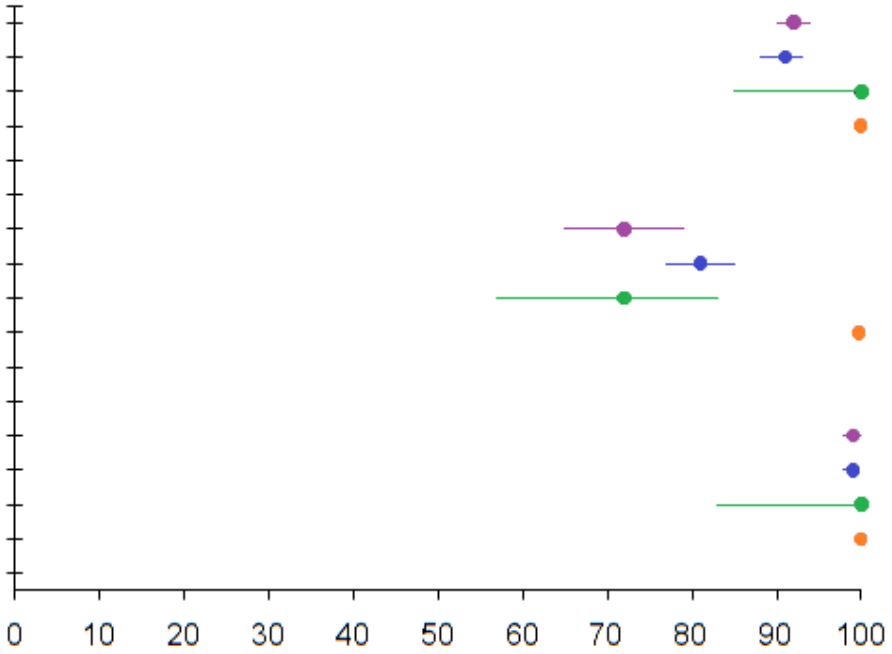
Vellore	India
HIV	<1%
TB (C+)	10%
MDR TB	7%



Cape Town	South Africa
HIV	77% (K), 30% (P)
TB (C+)	26%
MDR TB	4%

Manila	Philippines
HIV	<1%
TB (C+)	20%
MDR TB	54%

Sensitivity and specificity in comparison with published Xpert evaluation results



Sensitivity in culture +	
92.2% (675/732)	90.0 – 93.9
90.7% (641/707)	88.3 – 92.6
100.0% (29/29)	85.4 – 100.0
99.9%	99.7 – 99.9
Sensitivity in smear-,culture +	
72.5% (124/171)	65.4 – 78.7
81.2% (263/324)	76.6 – 85.1
71.5% (38/53)	57.4 – 82.8
99.7%	99.4 – 99.9
Specificity in smear-,culture -	
99.2% (604/609)	98.1 – 99.7
98.5% (1938/1968)	97.8 – 98.9
100.0% (25/25)	83.4 – 100.0
99.9% (7567/7568)	99.9 – 100.0

- Boehme et al. 2010 (Evaluation)
- Demonstration studies
- Helb et al. 2010
- Naidoo 2010

Rifampicin resistance detection

1. Good performance for RIF resistance (95% RIF sensitivity; 98% RIF specificity)
2. Suboptimal PPV in low MDR-TB prevalence settings
3. Further optimization ongoing

Planned assay adjustments based on root cause analysis

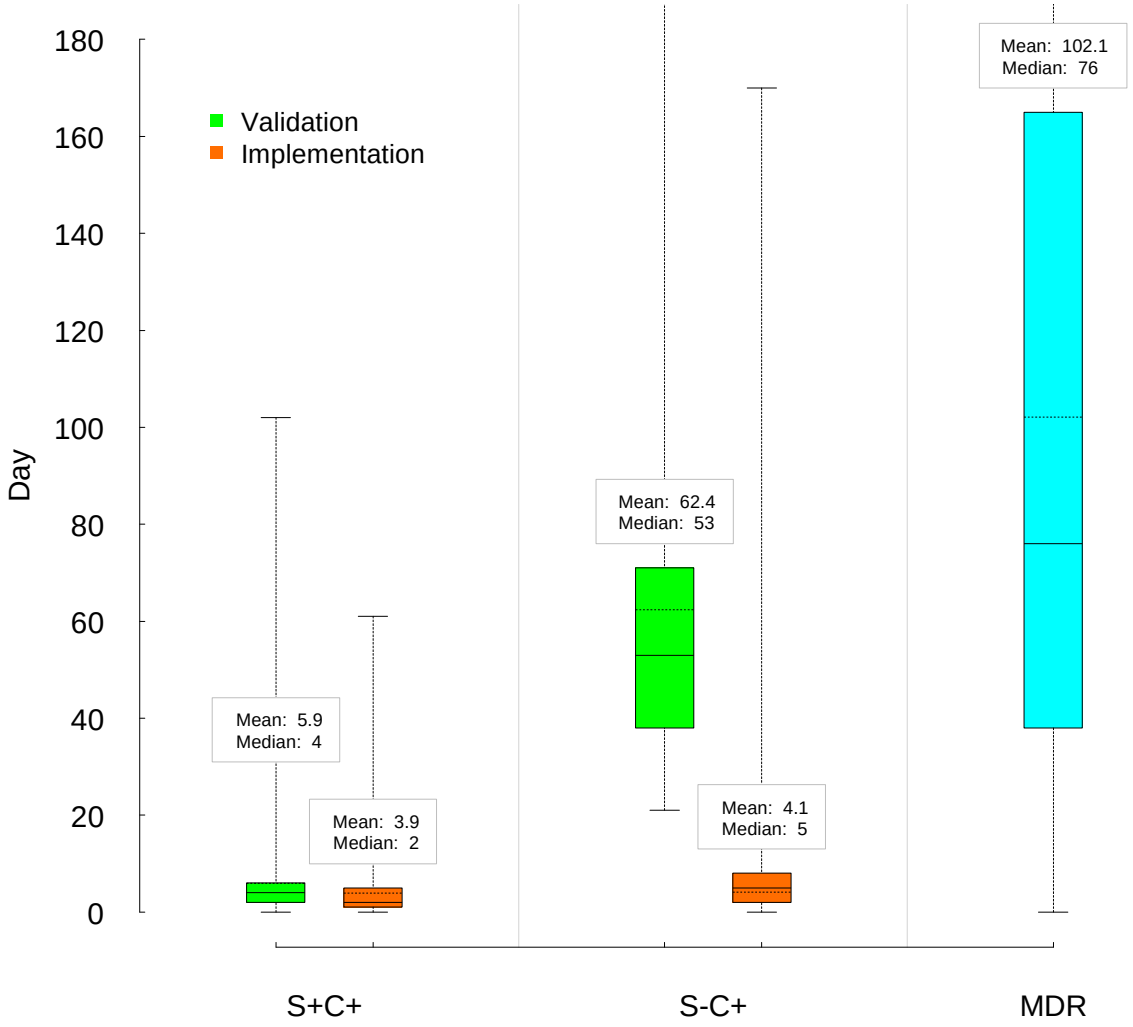
- Causes of probe delays identified:
  1. Scale up of manufacturing process of beads;
  2. Annealing temperature requirements of Probe B

- Solutions identified:
  1. Improved bead reconstitution (software change implemented Oct 10);
  2. Probe B adjustment to increase robustness;

- Analytical validation: Complete resolution of probe delays and improved accuracy of Rif resistance detection

- Implementation of modifications as part of development cycle: Q4 2010 – Q2 2011

Time to treatment



- Validation → Tx based on routine tests.
- Implementation → Tx based on Xpert MTB/RIF.
- MDR → conventional DST (or LPA in SA).

Operational performance & Implementation issues (1)

Variable	Performance / outcome
Indeterminate rate	2.5% and 0.3% after repetition. Culture indeterminate rate 4.7%.
Biosafety requirements	Same as smear microscopy*.
DNA contamination events	None observed.
Training needs	2 days for non-experienced lab techs.
User appraisal	Less difficult than microscopy; user friendly; user-independent read-out.

*Banada PP., et al. Containment of bioaerosol infection risk by the Xpert MTB/RIF assay and its applicability to point-of-care settings. J Clin Microbiol 2010; 48 (10): 3551-7




Operational performance & Implementation issues (2)

Variable	Performance / outcome
Preventive maintenance	Annual calibration (logistics and costs)
Operating and short term storage temperature	High lab temperature = no effect on performance.
Storage	2-28°C; require substantial storage space.
Electrical supply and back-up power	power outage reported; uninterruptable power supply with UPS (400 VA) for 20 min. Serial car batteries tested.
Waste management	As for sputum containers; additional waste compared to smear microscopy.




Conclusions

- Implementation in intended settings of use successful
- Trainings needs minimal
- Consistently high sensitivity and specificity for TB detection
- Good performance for Rifampicin resistance, confirmatory testing to be considered in low MDR prevalence areas
- Impact for patients shown to be significant

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Thank you