“Diagnostic fit” of 1st and 2nd line LPA improves time to detection of M(X)DR-TB.

Marinus Barnard

“Game Changers”

2008

Line probe assay endorsed by WHO STAG

UNITAID/GLI/GDF/FIND announce MDR Dx plans

2010

Expert Committee Recommendations

1. **Xpert MTB/RIF should be used as the initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB (strong recommendation)**

2. **Xpert MTB/RIF may be used as a follow-on test to microscopy where MDR and/or HIV is of lesser concern, especially in smear-negative specimens (conditional recommendation, recognising major resource implications)**

Advantages/disadvantages

	Xpert MTB/RIF	MTBDRplus
Turn-around-time	2 hours	48 hours
Sensitivity	Smear positive an negative specimens	Smear positive specimens only
DST	rifampicin	isoniazid and rifampicin
Pharmacogenetics	No	Yes
Throughput		
Risk of cross-contamination	No	Yes
Technical expertise	Low	High
Infrastructure	Low	High

Diagnostic performance of Genotype® MTBDR*plus* Version 2 line probe assay is equivalent to the Xpert®MTB/RIF assay

		Culture positive			Performance % (95% CI)			
	Total	Positive for *M. tuberculosis* complex	Negative for *M. tuberculosis* complex	Total	Sensitivity	Specificity	PPV	NPV
Xpert®MTB/RIF								
MTB+	**42**	**37**	**0**	**37**	**71.2**	**100**	**100**	**51.6**
MTB-	**233**	**15**	**16**	**31**				
Total	**275**	**52**	**16**	**68**				
Genotype® MTBDRplus (v2.0) LPA & GenoLyse® kit								
MTB+	**48**	**38**	**0**	**38**	**73.1**	**100**	**100**	**53.3**
MTB-	**227**	**14**	**16**	**30**				
Total	**275**	**52**	**16**	**68**				

Barnard M, Gey van Pittius NC, van Helden PD, Bosman M, Coetzee G, Warren RM. 2012 Diagnostic performance of Genotype MTBDR*plus* Version 2 line probe assay is equivalent to the Xpert(R)MTB/RIF assay. J. Clin Microbiol.

Diagnostic performance of Genotype® MTBDR*plus* Version 2 line probe assay is equivalent to the Xpert®MTB/RIF assay

	RIF susceptibility			INH susceptibility	
	S	R	Total	S	R
Xpert®MTB/RIF					
S	**33**	**0**	**33**		
R	**0**	**3**	**3**		
MTB-	**12**	**3**	**15**		
Total	**45**	**6**	**51**		
Genotype® MTBDRplus (v2.0) LPA & GenoLyse®					
S	**34**	**0**	**34**	**34**	**0**
R	**0**	**3**	**3**	**0**	**3**
MTB-	**11**	**3**	**14**	**11**	**3**
Total	**45**	**6**	**51**	**45**	**6**

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Take Home Message

Complement the Xpert®MTB/RIF screening assay

Validate RIF susceptibility on smear positive and smear negative specimens

Provide information on INH susceptibility

Provide pharmacogenetic information which may be critical in guiding appropriate treatment

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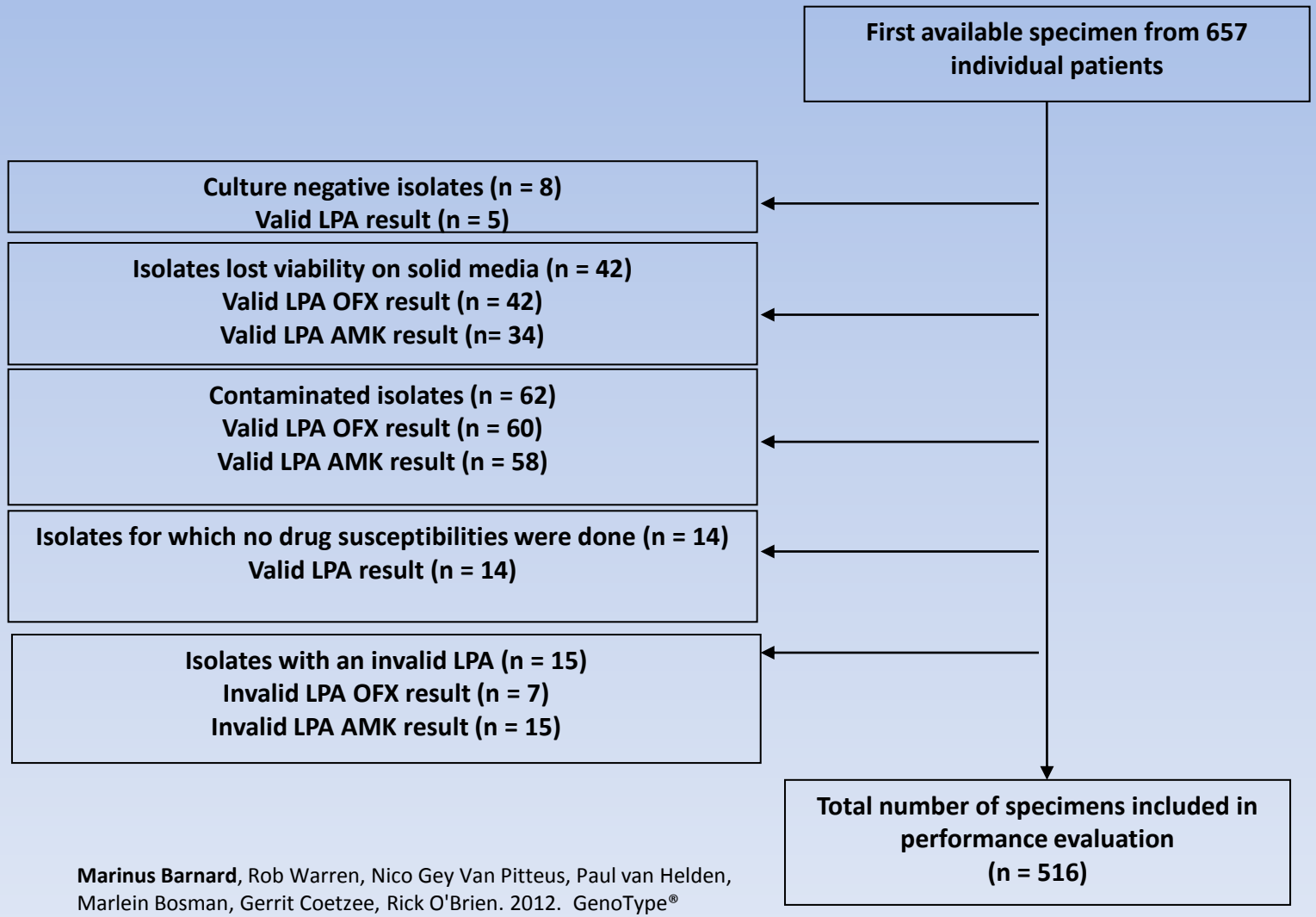
GenoType® MTBDR*sl* Line Probe Assay shortens time to diagnosis of XDR-TB in a high-throughput diagnostic laboratory.



Marinus Barnard, Rob Warren, Nico Gey Van Pitteus, Paul van Helden, Marlein Bosman, Gerrit Coetzee, Rick O'Brien. 2012. GenoType® MTBDR*sl* Line Probe Assay shortens time to diagnosis of XDR-TB in a high-throughput diagnostic laboratory. AJRCCM (in press)

GenoType® MTBDR*sl* Line Probe Assay shortens time to diagnosis of XDR-TB in a high-throughput diagnostic laboratory.

	OFX % (95% CI)	AMK % (95% CI)	XDR-TB % (95% CI)
Sensitivity	90.7 (80.1 – 96.0)	100 (91.8 – 100)	92.3% (75.9 – 97.9)
Specificity	98.1 (96.3 – 99.0)	99.4 (98.2 – 99.8)	99.6% (98.5 – 99.9)
PPV	84.5 (73.1 – 91.6)	93.5 (82.5 – 97.8)	92.3% (75.9 – 97.9)
NPV	98.9 (97.5 – 99.5)	100 (99.2 – 100)	99.6% (98.5 – 99.9)
OCC	97.3 (95.5 – 98.4)	99.4 (98.3 – 99.8)	99.2% (98.0-99.7)
Kappa	86.0 (77.4 – 94.6)	96.3 (87.7 – 100)	91.9% (83.3-100)

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GenoType® MTBDR*sl* Line Probe Assay shortens time to diagnosis of XDR-TB in a high-throughput diagnostic laboratory.

	Culture-based DST		Molecular based DST
Smear	1 day	Smear	1 day
Primary MGIT culture	12 days (range 6 to 47 days)	(Smear +) MTBDR*plus*	2 days (range 1 to 4 days)
2nd line culture	32 days (range 13 to 82 days)	(Smear +) MTBDR*sl*	1 day
Total	45 days (range 27 to 122 days)	(Smear +) Total	4 days (range 2 to 6 days)
		(Smear -) Total	15 days (range 8 to 52 days

(Mann-Whitney U two-tailed test, $p < 0.001$)

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“Diagnostic Delay Drivers”

104 specimen cultures were either contaminated or had lost viability

Culture-based DST

Guidelines: new specimen must be obtained

Molecular-based DST

102 (98%) gave a valid LPA result for OFX,
98 (94%) gave a valid LPA result for AMK.

Increase in the yield of DST results:
20.1% for OFX ($p < 0.001$)
19.3% for AMK ($p < 0.001$).

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Take Home Message

Rapid diagnosis of AMI and OFX resistance

Significantly reduced turn-around-time

Improved case detection

Pharmacogenetic information

Fits into the current diagnostic algorithm

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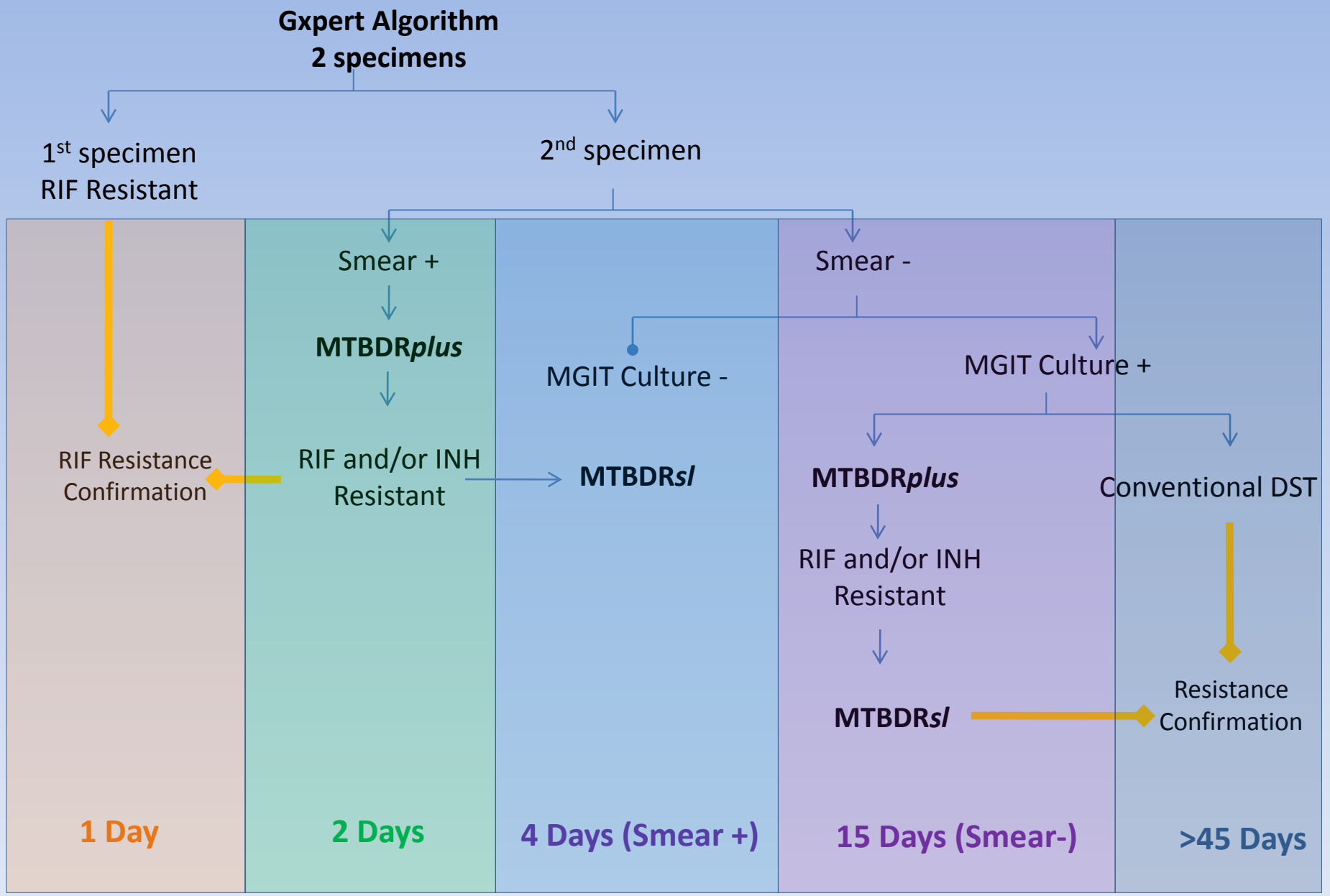
“Diagnostic Fit”



Thank You

Rob Warren,
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Lizma Streicher,
Marlein Bosman,
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Paul van Helden
Rick O'Brien