



Clinical performance of Xpert MTB/RIF Results from evaluation and demonstration studies

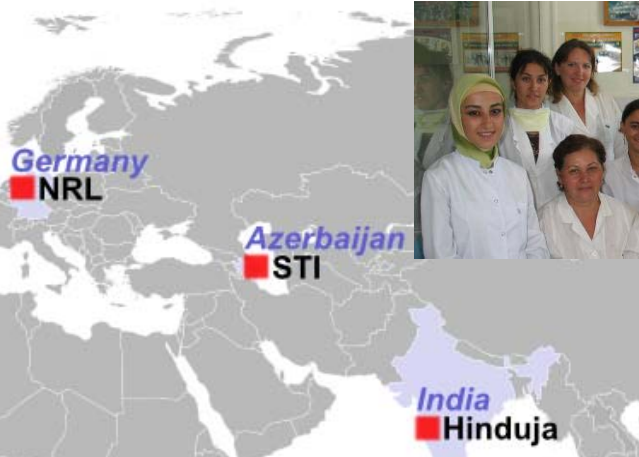
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Multi-center evaluation study

5 reference laboratories with high quality gold standard

Geographically diverse populations (HIV, TB & MDR TB prevalence)

	UPCH
HIV	2%
TB (C+)	61%
MDR TB	7%



	STI
HIV	5%
TB (C+)	42%
MDR TB	31%



Peru
UPCH



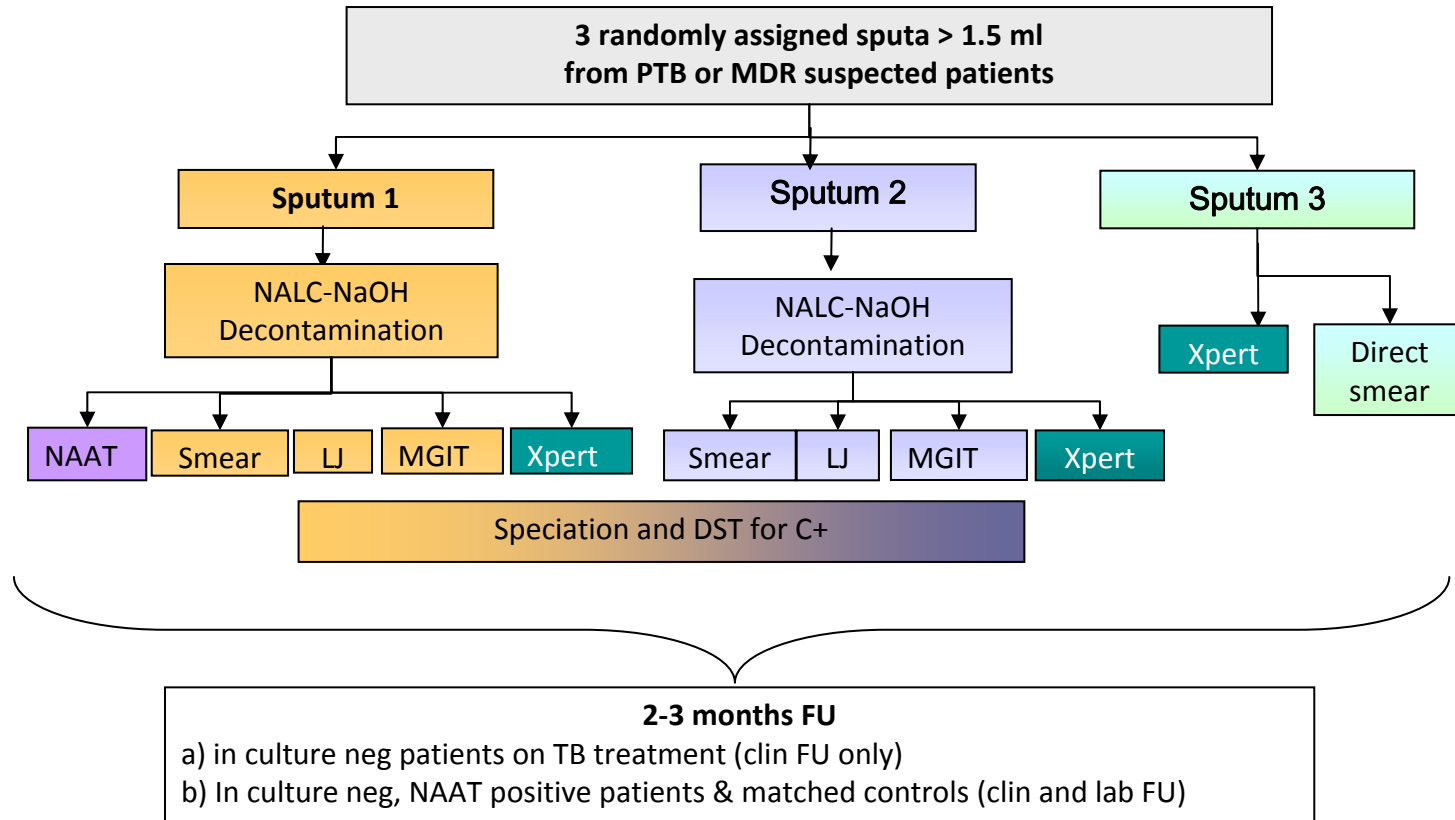
	Hinduja
HIV	5%
TB (C+)	60%
MDR TB	67%

	UCT	SAMRC
HIV	77%	72%
TB (C+)	39%	13%
MDR TB	10%	9%



Patient and specimen flow

- Enrolment of 1730 PTB or MDR suspected patients (4386 samples)



Overall performance: per patient analysis

	Sensitivity All C+	Sensitivity S+C+	Sensitivity S-C+	Specificity Non-TB
UPCH, Peru				
%	99.1	100.0	83.3	100.0
(Correct / total)	(209 / 211)	(199 / 199)	(10 / 12)	(102 / 102)
[95 CI]	[96.6 – 99.7]	[98.1 – 100.0]	[55.2 – 95.3]	[96.4 – 100.0]
Borstel & STI, Azerbaijan				
%	96.6	100.0	92.8	97.1
(Correct / total)	(144 / 149)	(80 / 80)	(64 / 69)	(68 / 70)
[CI]	[92.4 – 98.6]	[95.4 – 100.0]	[84.1 – 96.9]	[90.2 – 99.2]
UCT, South Africa				
%	95.9	99.0	90.4	98.4
(Correct / total)	(142 / 148)	(95 / 96)	(47 / 52)	(186 / 189)
[CI]	[91.4 – 98.1]	[94.3 – 99.8]	[79.4 – 95.8]	[95.4 – 99.5]
SAMRC, South Africa				
%	95.6	100.0	86.7	97.3
(Correct / total)	(43 / 45)	(30 / 30)	(13 / 15)	(213 / 219)
[CI]	[85.2 – 98.8]	[88.6 – 100.0]	[62.1 – 96.3]	[94.2 – 98.7]
Hinduja, India				
%	98.4	100.0	88.5	97.2
(Correct / total)	(185 / 188)	(162 / 162)	(23 / 26)	(35 / 36)
[CI]	[95.4 – 99.5]	[99.7 – 100.0]	[71.0 – 96.0]	[85.8 – 99.5]
Total (<i>Three</i> Xpert MTB/RIF)				
%	97.6	99.8	90.2	98.1
(Correct / total)	(723/741)	(566/567)	(157/174)	(604/616)
[CI]	96.2 – 98.5	99.0 – 100.0	84.9 – 93.8	96.6 – 98.9

Sensitivity & specificity of a single, direct Xpert; 1462 patients

Table 3: Sensitivity and specificity of a single, direct Xpert as compared to culture (2 solid and 2 liquid cultures).

Site	TP	FP	FN	TN	Sensitivity in C+ (95 CI)	Specificity in C- (95 CI)
Lima, Peru	201	0	8	101	96 (93-98)	100 (96-100)
Baku, Azerbaijan	123	1	24	68	84 (77-89)	99 (92-100)
Cape Town, SA	136	1	10	185	93 (88-96)	99 (97-100)
Durban, SA	36	3	7	215	84 (70-92)	99 (96-99)
Mumbai, India	179	35	8	35	96 (92-98)	100 (90-100)
Total	675	5	57	604	92 (90-94)	99 (98-100)

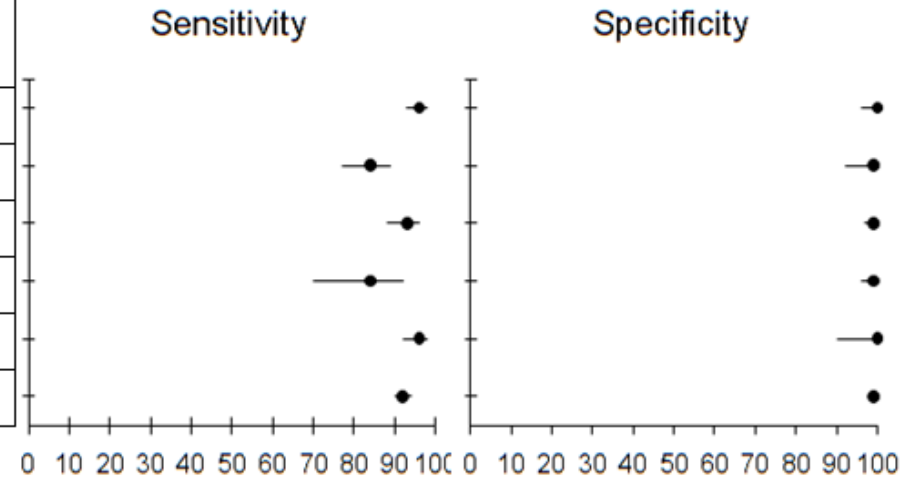


Table 6: Comparison of the overall sensitivity of a single LJ culture, a single MGIT culture and a single, direct Xpert using the results of 3 smears and 4 cultures per patient as a reference standard.

Patient group	Single LJ	Single MGIT	Single, direct Xpert
Smear-positive, Culture-positive	93.0% (1016/1092)	97.7% (1104/1130)	98.2% (551/561)
Smear-negative, Culture-positive	69.3% (205/296)	84.4% (276/327)	72.5% (124/171)
All Culture-positive	88.0% (1221/1388)	94.7% (1380/1457)	92.2% (675/732)

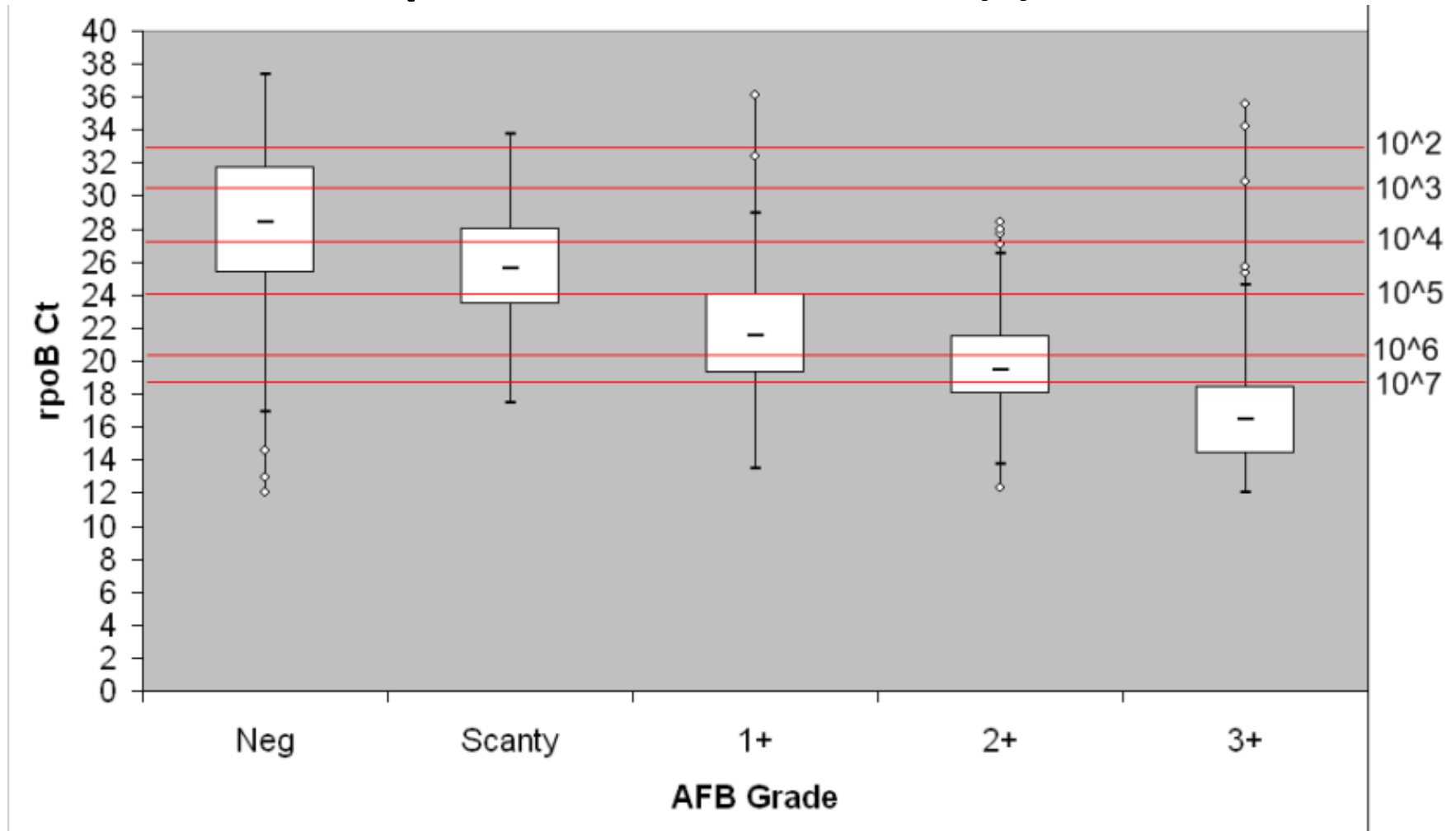
Rifampicin resistance detection

Table 7: Sensitivity and specificity of Xpert for the detection of rifampicin resistance as compared to phenotypic drug-susceptibility testing.*

Site	TP	FP	FN	TN	Sensitivity (95 CI)	Specificity (95 CI)
Lima, Peru	16	3	0	190	100	98
Baku, Azerbaijan	47	4	2	90	96	96
Cape Town, SA	15	0	1	126	94	100
Durban, SA	3	0	0	38	100	100
Mumbai, India	119	3	2	61	100	100
Total	200	10	5	505	98 (94-99)	98 (96-99)

1. Taking sequencing results for 15 discrepant cases into account, Xpert correctly detected rifampicin resistance in 209 of 211 patients (99.1% sensitivity) and in all 506 patients with rifampicin susceptibility (100% specificity).
2. 97.6% (200/205) of rifampicin resistant cases were confirmed to have multi-drug resistance.

Correlation of semiquantitative results of Xpert and smear (I)



Demonstration study sites

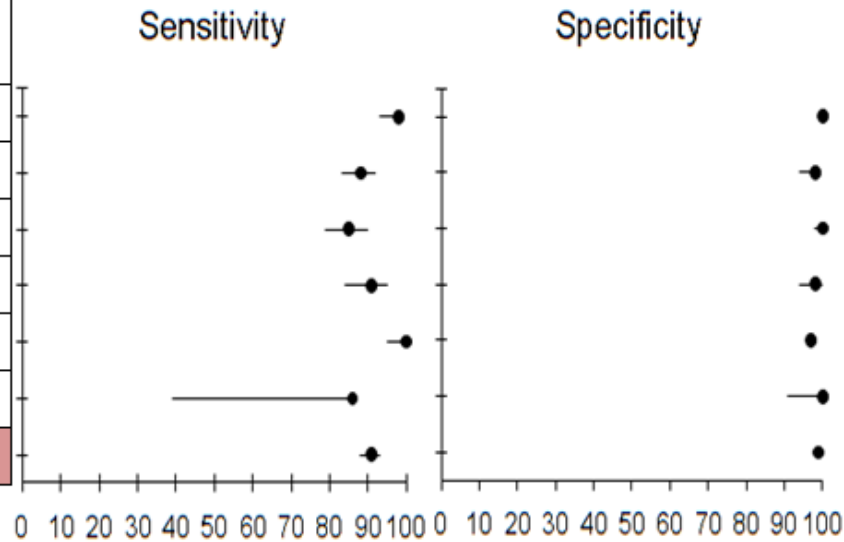
Table 9: Description of study sites, available infrastructure and laboratory capacity

Country / Site	Location	Level of the health system	Average # smears/day	Electricity	Biosafety cabinet	Infrastructure	Prior skills of Xpert operators	Operating temperature
Lima, Peru (supervised: by Instituto Nacional de Salud and Universidad Peruana Cayetano Heredia)								
HSJL	Urban	District Hospital (ZN, Ogawa)	25	Stable with occasional short interruptions	BSC 1	1 lab room, 1 storage room	ZN, Ogawa, No computer skills	Min: 17°C Max: 32°C, No AC
CSPL	Urban	Health Center (ZN)	15	Stable with occasional short interruptions	No	1 lab room	ZN, Basic computer skills	Min: 14°C Max: 31°C, No AC
HXV	Suburban	Health Center (ZN)	12	Stable with weekly short interruptions	No	1 lab room	ZN, Basic computer skills	Min: 19°C Max: 33°C, No AC
Vellore, India (supervised by Christian Medical College, Vellore)								
CHAD	Suburban	Sub-District TB Unit (ZN)	20	Stable with daily short interruptions	BSC 2	1.5 lab rooms	ZN, Basic computer skills	Min: 19°C Max: 42°C, intermittent AC
Baku, Azerbaijan								
STI	Urban	Prison Referral Center (ZN, LJ, MGIT)	60	Stable weekly short interruptions	BSC 1	4 lab rooms	ZN, No computer skills	Min: 12°C Max: 34°C Average: 21°C ; AC
Cape Town, South Africa (supervised by NHLS laboratory Groote Schuur and University of Cape Town)								
Paarl	Urban	Provincial Laboratory (FM)	300	Stable with occasional short interruptions	BSC 1	3 lab rooms	FM; basic LJ; Basic computer skills	Min: 16°C Max: 29°C, AC
MSF KH	Urban	Health Center (FM)	30	Stable with weekly short interruptions	BSC 1	2 lab rooms	FM, No computer skills	Min: 14°C Max: 28°C, AC
Kampala, Uganda (supervised by National Reference Laboratory and FIND Uganda)								
Mulago ER	Urban	Referral Hospital, Emergency unit (ZN)	30	Stable with weekly short interruptions	No	1 room	Basic ZN, Basic computer skills	Min: 19°C Max: 32°C, no AC
Manila, Philippines (supervised by Tropical Disease Foundation)								
LCP	Urban	Referral Hospital (ZN, Ogawa)	10	Stable	BSC 1	3 rooms	ZN, Ogawa, Intermediate computer skills	Min: 19°C Max: 25°C, AC

Sensitivity & specificity of a single, direct Xpert

Table 13: Sensitivity and specificity of a single, direct Xpert as compared to culture (1 to 4 cultures depending on the respective setting).

Site, Country	TP	FP	FN	TN	Sensitivity in C+ (95 CI)	Specificity in C- (95 CI)
Lima, Peru	123	1	3	557	98 (93-99)	100 (99-100)
Baku, Azerbaijan	158	3	21	134	88 (83-92)	98 (94-99)
Cape Town, SA	130	2	22	368	85 (79-90)	100 (98-100)
Kampala, Uganda	108	2	11	124	91 (84-95)	98 (94-100)
Vellore, India	73	18	0	620	100 (95-100)	97 (96-98)
Manila, Philippines	8	0	4	40	67 (39-86)	100 (91-100)
Total	600	26	61	1843	91 (88-93)	99 (98-99)



A single, direct Xpert (90.8%) identified more culture-positive patients than did a single LJ culture (89.8%).

Robustness

- No DNA contamination events
- No lot-to-lot variation
- Indeterminate rate (2.5%) lower than culture
- High operating temperature and short-term storage temperature had no effect on assay performance
- 2 days training adequate
- Requires stable power supply, annual calibration
- Simpler than microscopy: less workload dependent

Thank you