

Online data supplement: Test performance with the probable TB group excluded from the analysis, differences in test performance data and detailed cost effectiveness and sensitivity analyses methodologies and data

Do adjunct TB tests, when combined with Xpert MTB/RIF, improve accuracy and the cost of diagnosis in a resource-poor setting?

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Diagnostic accuracy tables

Table S1. The performance of different diagnostic tests (smear microscopy, Xpert MTB/RIF, CXR, TSPOT-TB, and QFT-GIT), alone or in combination with one another, for the detection of TB stratified by HIV status [individuals with ‘probable TB’ (i.e. no microbiological evidence for TB but placed on anti-TB treatment by the attending clinician) are omitted from performance calculations].

	Frontline performance in all TB suspects*					
	All patients n=480		HIV-uninfected n=286 [†]		HIV-infected n=130 [‡]	
	sens. [†]	spec. [§]	sens. [†]	spec. [§]	sens. [†]	spec. [§]
Xpert MTB/RIF	77.2% 115/149	95.5% (22/9/241)	81.0% 68/84	95.2% (140/147)	70.0% 35/50	95.0% (51/55)
Smear microscopy	68.5% 102/149	99.6% (240/241)	77.4% 65/84	100.0% (47/47)	52.0% 26/50	98.2% (54/55)
Smear microscopy combined with Xpert MTB/RIF (performed if smear-negative)	81.9% 122/149	94.6% (228/241)	85.7% 72/84	95.2% (140/147)	74.0% 37/50	90.9% (50/55)
CXR for active TB	100.0% 106/106	36.1% (52/144)	100.0% 59/59	40.5% (34/84)	100.0% 37/37	36.1% (13/61)
CXR followed by Xpert MTB/RIF if radiology is compatible with active TB	77.4% 82/106	97.2% 140/144	83.1% 49/59	96.4% (81/84)	64.9% 24/37	97.2% 35/36
Smear microscopy followed by CXR (performed if smear-negative), followed by Xpert MTB/RIF (performed if the radiograph is compatible with active TB)	83.0% 88/106	96.5% 138/143	89.8% 53/59	96.4% 80/83	67.6% 25/37	94.4% 34/36
TSPOT.TB	85.0% 91/107	44.7% (68/152)	85.9% 55/64	36.2% (34/94)	82.4% 28/34	65.7% (23/35)
QFT-GIT	84.9% 90/106	40.7% (70/172)	87.7% 57/65	36.6% (41/112)	80.6% 25/31	48.5% (16/33)
	PPV	NPV	PPV	NPV	PPV	NPV
Xpert MTB/RIF	90.6% 115/127	89.4% (228/225)	90.7% 68/75	92.3% (140/156)	89.7% 35/39	83.5% (51/66)
Smear microscopy	99.0% 102/103	83.6% 240/287	100.0% 65/65	88.6% 147/166	96.3% 26/27	69.2% (54/78)
Smear microscopy combined with Xpert MTB/RIF (performed if smear-negative)	90.4% 122/135	66.9% (228/341)	91.1% 72/79	92.1% 140/152	88.1% 37/42	79.4% (50/63)
CXR for active TB	53.5% 106/198	100.0% 52/52	54.1% 59/109	100.0% 34/34	61.7% 37/60	100.0% 13/13
CXR followed by Xpert MTB/RIF if radiology is compatible with active TB	95.3% 82/86	85.4% 140/164	94.2% 49/52	89.0% 81/91	96.0% 24/25	72.9% 35/48
Smear microscopy followed by CXR (performed if smear-negative), followed by Xpert MTB/RIF (performed if the radiograph is compatible with active TB)	94.6% 88/93	88.5% 138/156	94.6% 53/56	93.0% 80/86	92.6% 25/27	73.9% 34/46
TSPOT.TB	52.0% 91/175	81.0% 68/84	47.8% 55/155	79.1% 34/43	70.0% 28/40	79.3% 23/29
QFT-GIT	46.9% 90/192	81.4% 70/86	44.5% 57/128	83.7% 41/49	59.5% 25/42	72.7% 16/22

*Liquid culture positivity for *Mycobacterium tuberculosis* served as a reference standard

†54 Xpert MTB/RIF-negative individuals were of unknown HIV status (test refused or data missing)

‡ Test sensitivity was calculated by dividing the number of individuals positive for the adjunct test(s) by the number of culture-positive individuals who had received the same adjunct test(s) (i.e. only the non-TB group). Not all individuals received the same combination of tests.

§Test specificity was calculated by dividing the number of culture-negative individuals negative for the adjunct test(s) by the number of culture-negative individuals who had received the same adjunct test(s) but did not have treatment initiated based on clinical suspicion (i.e. only the non-TB group). Not all individuals received the same combination of tests.

Table S2. Performance of different diagnostic tests stratified by HIV status for the detection of TB in individuals negative for a single Xpert MTB/RIF test [individuals with ‘probable TB’ (i.e. no microbiological evidence for TB but placed on anti-TB treatment by the attending clinician) are omitted from performance calculations].

	Performance in Xpert MTB/RIF-negative individuals*					
	All patients n=350		HIV-uninfected n=209 [†]		HIV-infected n=91 [†]	
	sens. [‡]	spec. [§]	sens. [‡]	spec. [§]	sens. [‡]	spec. [§]
Smear microscopy	20.6% 7/34	99.6% 228/229	25.0% 4/16	100.0% 140/140	13.3% 2/15	98.0% 50/51
CXR for active TB	100.0% 24/24	36.7% 51/139	100.0% 10/10	41.3% 33/80	100.0% 13/13	37.1% 13/25
Smear microscopy combined with CXR (performed if smear-negative)	100.0% 24/24	36.7% 51/139	100.0% 10/10	41.3% 33/80	100.0% 13/13	37.1% 13/35
TSPOT.TB	74.1% 20/27	44.2% 65/147	73.3% 11/15	36.3% 33/91	77.8% 7/9	63.6% 21/33
QFT-GIT	80.0% 20/25	41.5% 68/164	84.6% 11/13	36.8% 39/106	77.8% 7/9	51.6% 16/31
	PPV	NPV	PPV	NPV	PPV	NPV
Smear microscopy	77.8% 7/9	66.9% 228/341	80.0% 4/5	68.6% 140/204	66.7% 2/3	56.8% 50/88
CXR for active TB	21.4% 24/112	100.0% 56/56	17.5% 10/57	100.0% 26/26	37.1% 13/35	100.0% 15/15
Smear microscopy combined with CXR (performed if smear-negative)	21.4% 24/112	100.0% 51/51	17.5% 10/57	100.0% 33/33	37.1% 13/35	100.0% 13/13
TSPOT.TB	19.6% 20/102	90.3% 65/72	15.9% 11/69	89.2% 33/37	36.8% 7/19	91.3% 21/23
QFT-GIT	17.2% 20/116	93.2% 68/73	14.1% 11/78	95.1% 39/41	31.8% 7/22	88.9% 16/18

*Liquid culture positivity for *Mycobacterium tuberculosis* served as a reference standard

[†]41 Xpert MTB/RIF-negative individuals were of unknown HIV status (test refused or data missing)

[‡] Test sensitivity was calculated by dividing the number of Xpert MTB/RIF-negative individuals positive for the adjunct test(s) by the number of Xpert MTB/RIF-negative, culture-positive individuals who had received the same adjunct test(s) (i.e. only the non-TB group). Not all individuals received the same combination of tests.

[§]Test specificity was calculated by dividing the number of Xpert MTB/RIF-negative, culture-negative individuals negative for the adjunct test(s) by the number of Xpert MTB/RIF-negative, culture-negative individuals who had received the same adjunct test(s) but did not have treatment initiated based on clinical suspicion (i.e. only the non-TB group). Not all individuals received the same combination of tests.

Table S3. Differences in overall performance between different diagnostic strategies

	Percentage change in performance between different diagnostic strategies*					
	All patients		HIV-uninfected		HIV-infected	
	sens. (95% CI)	spec. (95% CI)	sens. (95% CI)	spec. (95% CI)	sens. (95% CI)	spec. (95% CI)
Smear microscopy followed by Xpert MTB/RIF vs. smear microscopy alone	13.4 (3.7, 23.1) p<0.01	-4.2 (-6.8, -1.6)	8.3 (-3.3, 20.0)	-4.0 (-7.2, -0.7)	22.0 (3.6, 40.4) p<0.05	-5.0 (-10.8, 0.8)
Smear microscopy followed by Xpert MTB/RIF vs. Xpert MTB/RIF alone	4.7 (-4.4, 13.8)	-0.6 (-3.8, 2.7)	4.8 (-6.5, 16.0)	0.1 (-4.2, 4.2)	4.0 (-13.6, 21.6)	-1.3 (-8.4, 5.9)
CXR followed by Xpert MTB/RIF vs. Xpert MTB/RIF alone	0.2 (-10.2, 10.6)	1.3 (-1.9, 4.6)	2.1 (-10.6, 14.8)	1.1 (-3.4, 5.5)	-5.1 (-25.1, 14.8)	3.1 (-2.8, 9.1)
Smear microscopy followed by CXR followed by Xpert MTB/RIF vs. smear microscopy followed by Xpert MTB/RIF[†]	1.1 (-8.3, 10.1)	1.5 (-2.0, 4.5)	4.1 (-6.6, 14.9)	1.1 (-3.4, 5.6)	-6.4 (-25.8, 12.9)	2.6 (-4.6, 9.9)
Smear microscopy followed by CXR followed by Xpert MTB/RIF vs. CXR followed by Xpert MTB/RIF[†]	5.7 (-5.0, 16.4)	-0.4 (-3.9, 3.0)	6.8 (-5.5, 19.1)	0.0 (-4.7, 4.7)	2.7 (-18.8, 24.2)	-1.8 (-7.9, 4.3)
	PPV (95% CI)	NPV (95% CI)	PPV (95% CI)	NPV (95% CI)	PPV (95% CI)	NPV (95% CI)
Smear microscopy followed by Xpert MTB/RIF vs. smear microscopy alone	-9.4 (-15.7, -3.6)	4.6 (0.2, 9.0) p<0.05	-9.2 (-17.4, -10.4)	6.0 (-4.3, 16.3)	-8.2 (-20.3, 3.9)	8.5 (-2.5, 19.6)
Smear microscopy followed by Xpert MTB/RIF vs. Xpert MTB/RIF alone	-0.7 (-8.4, 7.0)	1.8 (-2.4, 6.0)	1.7 (-8.7, 12.1)	1.8 (-3.1, 6.6)	-1.6 (-15.3, 12.0)	1.7 (-8.9, 12.3)
CXR followed by Xpert MTB/RIF vs. Xpert MTB/RIF alone	3.7 (-4.1, 11.5)	-0.5 (-5.5, 4.4)	4.6 (-6.2, 15.5)	3.0 (-2.1, 8.1)	6.2 (-6.0, 18.4)	-2.9 (-15.1, 9.2)
Smear microscopy followed by CXR followed by Xpert MTB/RIF vs. smear microscopy followed by Xpert MTB/RIF[†]	3.9 (-3.8, 11.7)	0.0 (-4.5, 4.5)	3.6 (-6.5, 13.7)	1.3 (-3.6, 6.1)	4.5 (-9.4, 18.4)	-3.7 (-15.7, 8.3)
Smear microscopy followed by CXR followed by Xpert MTB/RIF vs. CXR followed by Xpert MTB/RIF[†]	-0.4 (-8.3, 7.4)	2.3 (-2.9, 7.5)	0.6 (-9.9, 11.2)	2.8 (-2.9, 8.6)	-3.4 (-15.9, 9.1)	0.9 (-12.4, 14.3)

*Performance data from Table 1 is used to calculate the percentage change in performance.

†The smear microscopy followed by CXR followed by Xpert MTB/RIF strategy and had the same diagnostic accuracy as the CXR followed by smear microscopy followed by Xpert MTB/RIF strategy.

Cost analysis methodology, figures and tables

The cost analysis was performed from a healthcare provider perspective to the diagnostic test costs and outcomes of Xpert MTB/RIF testing on its own or in combination with various pre-screening tests.

Model

A decision tree model was constructed to investigate six different diagnostic screening scenarios: (i) smear microscopy only; (ii) Xpert MTB/RIF only; (iii) smear microscopy followed by Xpert MTB/RIF (performed if smear-negative); (iv) CXR followed by Xpert MTB/RIF (performed if the chest radiograph was suggestive of TB); (v) a combination of smear microscopy, followed by CXR (performed if smear-negative) and Xpert MTB/RIF (performed if the chest radiograph was suggestive of TB); (vi) a combination of CXR, followed by smear microscopy (performed if CXR is suggestive of active TB) and Xpert MTB/RIF testing (performed if smear-negative) (Figure 1). The decision tree was constructed using TreeAge Pro 2011 (TreeAge Software Inc., Williamston, USA) and calculations were performed using Excel 2007 (Microsoft, USA). Tests results inputted into the model were normalised from our diagnostic accuracy data shown in Table 1.

Test Costs

Smear microscopy costs were obtained from the National Health Laboratory Service in South Africa and represent the actual costs incurred by the South African government. CXR costs specific for South Africa were taken from the literature (Vassal and Cobelens, StopTB presentation 2011, <http://www.stoptb.org/wg/gli/assets/documents/Mtg3pres/Day%201/session%203/Xpert%20MTB%20RIF%20%20scenarios%20for%20cost%20effectiveness%200A%20Vassall.pdf>). The cost of a single Xpert MTB/RIF test was calculated using WHO estimates (1) for equipment and consumables. These costs represent the compassionate pricing offered by Cepheid to low income countries. Other cost components such as

technician salary and other capital expenses were calculated using South Africa specific cost data. Capital costs were annualised at a discount rate of 3% and an assumed useful lifetime of 8 years for a Gene Xpert MTB/RIF IV machine. The cost per Xpert MTB/RIF test was calculated as the total annual cost of the machine plus the total cost of tests done in a year divided by the total number of valid tests run in a year. All prices are quoted in 2011 \$US dollars at an exchange rate of \$US 1 = ZAR 7.05. Test costs are shown in Table S1 and cost components of an Xpert MTB/RIF test are shown in Table S2.

Cost of diagnosis

In addition to the test costs, the number of TB cases detected by each strategy was also reported. The cost per TB case detected was calculated using the incremental cost of each strategy (compared to smear microscopy) divided by the number of TB cases correctly diagnosed by that strategy compared to smear microscopy.

Univariate and multivariate sensitivity analyses

A univariate sensitivity analysis was performed by varying test sensitivities and specificities by ~15-20%. Xpert MTB/RIF test costs were varied using private costs as the high estimate and 50% of the compassionate base case cost as the lower estimate. CXR costs were doubled for the high estimate and halved for the low estimate. Additionally, the cost of performing sequential smears was investigated. The incremental increase or decrease in sensitivity of serial smear examinations has been reported in another South African study (2). This data was used to calculate the sensitivity of either performing one smear (low estimate) or three smears (high estimate) in our cohort. We also incorporated the cost of the additional smear exams in our sensitivity analysis. A multivariate analysis was also performed using effectiveness inputs from a large multicentre study to determine the cost effectiveness of these strategies in a different setting (i.e. Xpert MTB/RIF sensitivity and specificity in smear-positive individuals of 92% and 99%, respectively and 77% and 99%, respectively in smear-

negative individuals). Overall costs, the number of TB cases detected and the cost per TB case detected by each strategy were assessed in the multivariate analysis.

Table S4. Costs and the relevant source(s) used for the cost analysis (US\$1=ZAR7.05)

Item	Cost (US\$)	Source
Smear microscopy	\$3.81	South African National Health Laboratory Service
Chest X-ray	\$18.12	StopTB, City of Cape Town
Xpert MTB/RIF (cost of a single test)	\$21.39	Calculated from WHO (1)

Table S5. Unit costs and relevant data for calculation of the per test price of a single Xpert MTB/RIF assay.

Item	Cost (US\$)	Source
GeneXpert IV machine and workstation	\$19,100	WHO (2)
Other capital and administrative costs	\$7,314.35	University of Cape Town (10% of total annual cost)
Maintenance (per year)	\$1800	WHO (2)
Cartridge and consumables	\$16.86	WHO (2)
Technician salary [based on hands-on time required to perform the assay (estimated at 2 hours/day)]	\$5,236.50	WHO (2), Provincial Government of Western Cape 2010 -2011 salary scales
Training	\$161.10	WHO (2), Cepheid
Input	Value	Source
Discount rate	3% per annum	Assumed
Life years of machine	8 years	Assumed
Number of tests per year (15 tests/day and 250 days per year)	3750	WHO (2)
Number of evaluable tests/year (assuming 5% of tests are lost due to damaged or incorrect usage)	3562	WHO (2)

Table S6. Costs and outcomes of different Xpert MTB/RIF strategies in HIV-uninfected patients

	Smear microscopy alone	Xpert MTB/RIF alone	Smear microscopy followed by Xpert MTB/RIF (performed if smear-negative)	Chest X-ray followed by Xpert MTB/RIF (performed if CXR suggestive of active TB)	Smear microscopy, followed by chest X-ray (performed if smear-negative), followed by Xpert MTB/RIF (performed if CXR suggestive of active TB)	CXR, followed by smear microscopy (performed if CXR suggestive of active TB), followed by Xpert MTB/RIF (performed if smear-negative)
Total test cost	\$7,420.00	\$21,389.75	\$23,798.87	\$35,300.07	\$30,751.83	\$38,357.38
Incremental cost vs. smear microscopy alone	-	\$13,969.75	\$16,378.87	\$27,880.07	\$23,331.83	\$30,937.38
Number of TB cases detected by each strategy	227.27	236.93	251.75	260.64	281.91	281.91
Additional number of TB cases detected vs. smear microscopy alone	-	9.66	24.48	33.37	54.64	54.64
Cost per TB case detected (compared to smear microscopy)	-	\$1,445.98 ^{#5}	\$669.19 ^{#3}	\$835.59 ^{#4}	\$426.99 ^{#1}	\$566.18 ^{#2}

[#]Superscripts ¹⁻⁵ indicate the cost- ranking of each strategy; ^{#1} indicates the most costly strategy while ^{#5} indicates the least costly strategy.

Table S7. Costs and outcomes of different Xpert MTB/RIF strategies in HIV-infected patients

	Smear microscopy alone	Xpert MTB/RIF alone	Smear microscopy followed by Xpert MTB/RIF (performed if smear-negative)	Chest X-ray followed by Xpert MTB/RIF (performed if CXR suggestive of active TB)	Smear microscopy, followed by chest X-ray (performed if smear-negative) , followed by Xpert MTB/RIF (performed if CXR suggestive of active TB)	CXR, followed by smear microscopy (performed if CXR suggestive of active TB), followed by Xpert MTB/RIF (performed if smear-negative)
Total test cost	\$7,420.00	\$21,389.75	\$24,367.26	\$36,022.29	\$34,072.89	\$39,119.93
Incremental cost vs. smear microscopy alone	-	\$13,969.75	\$16,947.26	\$28,602.29	\$26,652.89	\$31,699.93
Number of TB cases detected by each strategy	200.00	269.23	284.62	260.87	271.74	271.74
Additional number of TB cases detected vs. smear microscopy alone	-	69.23	84.62	60.87	59.24	59.24
Cost per TB case detected (compared to smear microscopy)	-	\$201.79 ^{#2}	\$200.29 ^{#1}	\$469.89 ^{#4}	\$449.92 ^{#3}	\$535.12 ^{#5}

[#]Superscripts ¹⁻⁵ indicate the cost- ranking of each strategy; ^{#1} indicates the most costly strategy while ^{#5} indicates the least costly strategy.

Table S8. Univariate sensitivity analysis. The cost per TB case detected compared to screening with smear microscopy alone was reported here.

Diagnostic accuracy variables used	Xpert MTB/RIF alone	Smear microscopy followed by Xpert MTB/RIF (performed if smear-negative)	Chest X-ray followed by Xpert MTB/RIF (performed if radiograph compatible with TB)	Smear microscopy, followed by chest X-ray (performed if smear-negative) , followed by Xpert MTB/RIF (performed if chest radiograph compatible with TB)	Chest X-ray, followed by smear microscopy (performed if chest radiograph compatible with TB) followed by Xpert MTB/RIF (performed if smear-negative)
Base case analysis*	\$515.81 ³	\$401.06 ¹	\$697.94 ⁵	\$423.85 ²	\$ 531.40 ⁴
Xpert MTB/RIF sensitivity					
90%	\$208.89 ¹	\$401.06 ²	\$697.94 ⁵	\$423.85 ³	\$ 531.40 ⁴
65%	-	\$401.06 ¹	\$697.94 ⁴	\$423.85 ²	\$ 531.40 ³
Xpert MTB/RIF specificity					
99%	\$515.81 ³	\$401.06 ¹	\$697.94 ⁵	\$423.85 ²	\$ 531.40 ⁴
80%	\$515.81 ³	\$401.06 ¹	\$697.94 ⁵	\$423.85 ²	\$ 531.40 ⁴
Xpert MTB/RIF sensitivity in smear negatives					
70%	\$515.81 ³	\$243.80 ¹	\$697.94 ⁵	\$423.85 ²	\$ 531.40 ⁴
30%	\$515.81 ²	\$568.88 ⁴	\$697.94 ⁵	\$423.85 ¹	\$ 531.40 ³
Xpert MTB/RIF specificity in smear negatives					
99%	\$515.81 ³	\$401.06 ¹	\$697.94 ⁵	\$423.85 ²	\$ 531.40 ⁴
80%	\$515.81 ³	\$401.06 ¹	\$697.94 ⁵	\$423.85 ²	\$ 531.40 ⁴
Xpert MTB/RIF sensitivity in CXR suspected of TB					
90%	\$515.81 ⁴	\$401.06 ²	\$345.68 ¹	\$423.85 ³	\$ 531.40 ⁵
65%	\$515.81 ³	\$401.06 ¹	\$183,557.27 ⁵	\$423.85 ²	\$ 531.40 ⁴
Xpert MTB/RIF specificity in CXR suspected of TB					
99%	\$515.81 ³	\$401.06 ¹	\$697.94 ⁵	\$423.85 ²	\$ 531.40 ⁴
80%	\$515.81 ³	\$401.06 ¹	\$697.94 ⁵	\$423.85 ²	\$ 531.40 ⁴
Xpert MTB/RIF sensitivity in smear negatives with a CXR suspected of TB					
60%	\$515.81 ³	\$401.06 ²	\$697.94 ⁵	\$327.95 ¹	\$ 531.40 ⁴
25%	\$515.81 ²	\$401.06 ¹	\$697.94 ⁵	\$583.94 ⁴	\$ 531.40 ³
Xpert MTB/RIF specificity in smear negatives with a CXR suspected of TB					
99%	\$515.81 ³	\$401.06 ¹	\$697.94 ⁵	\$423.85 ²	\$ 531.40 ⁴
80%	\$515.81 ³	\$401.06 ¹	\$697.94 ⁵	\$423.85 ²	\$ 531.40 ⁴

Xpert MTB/RIF sensitivity with a CXR suspected of TB in smear negatives						
60%	\$515.81 ⁴	\$401.06 ¹	\$697.94 ⁵	\$423.85 ³	\$406.33 ²	
25%	\$515.81 ³	\$401.06 ¹	\$697.94 ⁴	\$423.85 ²	\$740.19 ⁵	
Xpert MTB/RIF specificity with a CXR suspected of TB in smear negatives						
99%	\$515.81 ³	\$401.06 ¹	\$697.94 ⁵	\$423.85 ²	\$ 531.40 ⁴	
80%	\$515.81 ³	\$401.06 ¹	\$697.94 ⁵	\$423.85 ²	\$ 531.40 ⁴	
CXR sensitivity						
90%	\$515.81 ³	\$401.06 ¹	\$904.65 ⁵	\$423.88 ²	\$656.64 ⁴	
CXR specificity						
40%	\$515.81 ³	\$401.06 ¹	\$2,201.73 ⁵	\$424.18 ²	\$1,138.84 ⁴	
10%	\$515.81 ⁵	\$401.06 ²	\$414.46 ³	\$423.54 ⁴	\$319.67 ¹	
Smear specificity						
80%	\$515.81 ³	\$401.06 ²	\$697.94 ⁵	\$397.97 ¹	\$548.53 ⁴	
# of smears						
1 smear	\$256.77 ¹	\$401.06 ³	\$389.00 ²	\$527.28 ⁴	\$633.27 ⁵	
3 smears	\$2,798.11 ⁵	\$401.06 ¹	\$1,433.73 ⁴	\$459.13 ²	\$580.67 ³	
Xpert MTB/RIF cost						
\$142.52	\$4,988.31 ⁵	\$2,672.25 ³	\$3,157.39 ⁴	\$1,641.78 ¹	\$1,973.58 ²	
\$10.70	\$121.11 ¹	\$200.63 ²	\$480.89 ⁵	\$317.79 ³	\$404.13 ⁴	
CXR costs						
\$36.24	\$515.81 ²	\$401.06 ¹	\$1,144.39 ⁵	\$657.57 ³	\$837.98 ⁴	
\$9.06	\$515.81 ⁵	\$401.06 ³	\$474.71 ⁴	\$307.00 ¹	\$378.12 ²	
TB prevalence						
10%	\$1,601.15 ²	\$1,471.45 ¹	\$3,039.31 ⁵	\$2,153.10 ⁴	\$2,131.51 ³	
50%	\$320.23 ³	\$208.18 ¹	\$658.12 ⁵	\$309.76 ²	\$385.62 ⁴	

*See Table 1 for the performance data used in the base-case
Superscripts ¹⁻⁵ indicate the cost ranking of each strategy; ¹ indicates the strategy with the lowest cost per TB case detected while ⁵ indicates the strategy with the highest cost per TB case detected

Table S9. Multivariate sensitivity analysis. Using Xpert MTB/RIF performance data from Boehme *et al.* (2011) (sensitivity in smear-positive and smear-negatives of 90% and 77% respectively)

	Smear microscopy alone	Xpert MTB/RIF alone	Smear microscopy followed by Xpert MTB/RIF (performed if smear-negative)	Chest X-ray followed by Xpert MTB/RIF (performed if radiograph compatible with TB)	Smear microscopy, followed by chest X-ray (performed if smear-negative), followed by Xpert MTB/RIF (if radiograph compatible with TB)	Chest X-ray followed by Smear microscopy (if radiograph compatible with TB), followed by Xpert MTB/RIF (performed if smear-negative)
Total test cost	\$7,420.00	\$21,390.00	\$24,130.94	\$35,746.94	\$32,471.85	\$38,402.35
Incremental cost vs. smear microscopy alone	-	\$13,970.00	\$16,710.94	\$28,326.94	\$25,051.85	\$30,982.35
Number of correctly diagnosed non-TB cases	683.33	682.69	676.50	651.23	661.76	661.76
Number of correctly diagnosed TB cases	212.50	285.58	287.90	253.09	305.15	305.15
Additional number of TB cases correctly diagnosed vs. smear microscopy alone	-	73.08	75.40	40.59	92.65	92.65
Cost per TB case detected (compared to smear microscopy)	-	\$191.15 ^{#1}	\$221.64 ^{#2}	\$697.94 ^{#5}	\$270.38 ^{#3}	\$334.39 ^{#4}

[#]Superscripts ¹⁻⁵ indicate the cost- ranking of each strategy; ^{#1} indicates the most costly strategy while ^{#5} indicates the least costly strategy.

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