Comparing laboratory costs of smear/culture and Xpert® MTB/RIF-based tuberculosis diagnostic algorithms

Authors:

Pren Naidoo[1], Rory Dunbar[1], Elizabeth du Toit[1], Margaret van Niekerk[1], S. Bertel Squire[2], Nulda Beyers[1], Jason Madan[3]

Affiliations:

[1]Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Faculty of Medicine and Health Sciences, Stellenbosch University, South Africa

[2]Liverpool School of Tropical Medicine, Liverpool, United Kingdom

[3]Warwick Medical School, University of Warwick, United Kingdom

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ABSTRACT

Setting: Cape Town, South Africa, where Xpert® MTB/RIF was introduced as a screening test for all presumptive tuberculosis (TB) cases in primary health services.

Study Aim: To compare laboratory costs of smear/culture- and Xpert MTB/RIF-based TB diagnostic algorithms in routine operational conditions.

Methods: Economic costing was undertaken from a laboratory perspective. We used an ingredients-based costing approach with test costs based on the cost per unit and quantities utilised for buildings, equipment, consumables, staff and overheads. Cost allocation was based on reviews of standard operating procedures and laboratory records, observation and timing of test procedures, measurement of laboratory areas and manager interviews. We analysed electronic laboratory test data to compare overall costs and cost per pulmonary TB and MDR-TB case diagnosed. All costs were expressed as 2013 CPI-adjusted values.

Results: Total TB diagnostic costs increased by 43% from $440,967 in the smear-culture-based algorithm (April-June 2011) to $632,262 in the Xpert-based algorithm (April-June 2013). The cost per TB case diagnosed increased by 157% from $48.77 to $125.32 with 1601 and 1281 cases diagnosed respectively. The total cost per MDR-TB case diagnosed was similar at $190.14 and $183.86 in respective algorithms and the number of cases diagnosed increased by 13%, from 95 to 107.

Conclusion: The introduction of the Xpert-based algorithm resulted in substantial cost increases. This was not matched by the expected increase in TB diagnostic efficacy, calling into question the sustainability of this expensive new technology.

INTRODUCTION

New molecular diagnostic tests for tuberculosis (TB) such as GenoType® MTBDRplus line probe assay (Hain LifeScience GmbH, Nehren, Germany) (LPA) and Xpert® MTB/RIF (Cepheid, Sunnyvale, CA, USA) (Xpert) hold the promise of improving TB and multidrug-resistant (MDR)-TB diagnosis as both are sensitive and faster than culture and conventional drug susceptibility tests (DST). The accuracy of these tests is well established from laboratory and demonstration studies[1,2]. A meta-analysis of ten LPA studies showed high sensitivity (98.1% (95% CI 95.9 to 99.1)) and specificity (98.7% (95% CI 97.3 to 99.4)) for rifampicin resistance and lower, more variable sensitivity of 84.3% (95% CI 76.6 to 89.8) and specificity of 99.5% (95% CI 97.5 to 99.9) for isoniazid resistance[3]. A Cochrane Review of fifteen studies where Xpert was used as the initial test replacing smear microscopy, showed a pooled sensitivity of 88% (95%CrI 83% to 92%) and specificity of 98% (95% CrI 97% to 99%) for detecting *Mycobacterium tuberculosis* (MTB). In eleven of these studies, pooled sensitivity was 94% (95% CrI 87% to 97%) and specificity 98% (95% CrI 97% to 99%) for rifampicin resistance[4].

Policy recommendations[5,6] have been based mainly on accuracy data from laboratory and demonstration studies[7–9]. However demonstration studies tend not to reflect the realities of a test being used within an operational context[8,9]. There is a tendency to over-estimate effectiveness partly due to greater resource availability than would be found in routine settings[8]. Insufficient emphasis is placed on costs and an over-estimate of effectiveness may provide a more optimistic view of cost-effectiveness than would be found in routine settings.

Cost estimates are essential to making decisions on the most effective use of limited resources. One of the challenges to evaluating costs and cost-effectiveness is the lack of standard accepted evaluation methods[10,11]. Current guidelines are too broad and generalised and poor adherence to guidelines contributes to the failure to provide consistent and comparable cost data to policy makers[12]. For example, two studies in South Africa reported Xpert costs of $25.90 (in 2010 $US)[13] and $14.93 (in 2012 US$)[14] respectively. Differences in costs were partly attributable to the exclusion of cartridge shipping costs and specimen transport costs in the latter.

A guideline on laboratory costs[15] emphasises the importance of an ingredients-based approach to costing that includes all resource elements, including quality assurance and control. It emphasises the need to accurately allocate overhead costs and deal with capital assets in a way that takes “time preference” into account i.e. that $1 in 2 years is worth less than $1 today, reflecting a societal and individual preference to have money and resources today rather than in the future. Capital costs need to be discounted to reflect this preference[16].

Xpert is an expensive test and making the case for additional expenditure requires empirical data to supplement the estimates used in decision-making. Operational data can help improve the reliability of estimates used in cost and cost-effectiveness analyses and is particularly important in high-burden settings with resource constraints.

The aim of this study was to compare laboratory costs for the diagnosis of pulmonary TB and MDR-TB in a new Xpert-based algorithm to that in the previous smear/culture-based algorithm within a routine operational context. The study was part of a PROVE IT (Policy Relevant Outcomes from Validating Evidence on ImpacT) evaluation (http://www.treattb.org/) to assess the impact of new molecular diagnostic tests.

METHODS

Setting

The study was undertaken in Cape Town, South Africa, a city with a high TB and MDR-TB burden with 28,644 TB cases (752/100,000 population) and 1,020 MDR-TB cases notified in 2011. In comparison, 25,846 TB cases (663/100,000 population) and 1,134 MDR-TB cases were notified in 2013. Human immunodeficiency virus (HIV) co-infection rates amongst TB cases were 47% (97% tested) and 44% (98% tested) in respective years (Source: J. Caldwell, Routine TB Programme Data, Cape Town Health Directorate, April 2016).

Free TB diagnostic services were provided at 142 primary health care facilities in eight sub-districts. All sputum specimens collected at primary health care facilities were sent by courier to the National Health Laboratory Services (NHLS). Test results were entered into a networked, electronic laboratory database.

TB diagnostic algorithms

A smear/culture-based algorithm (Figure 1) was used in the “comparator” period (April to June 2011=T1). All presumptive TB cases were evaluated by smear microscopy from two spot sputum specimens, taken 1-hour apart. In high MDR-TB risk cases (>four weeks previous TB treatment, from congregate settings or with an MDR-TB contact), the second specimen underwent liquid culture (BACTEC™ MGIT™ 960) and drug susceptibility testing (DST) using the GenoType® MTBDRplus line probe assay (LPA) and second line testing as required. Smear-negative, HIV-infected, low MDR-TB risk cases were required to submit a third specimen for culture.

An Xpert-based algorithm was used in the “intervention” period (April to June 2013=T2) with Xpert replacing smear microscopy for all presumptive TB cases (Figure 1). Two sputum specimens were evaluated: the first was tested with Xpert; if MTB was detected the second underwent smear microscopy. In HIV-infected cases with negative Xpert tests, the second specimen underwent culture. Confirmatory LPA and second line DST were undertaken for cases with rifampicin resistance.

Costing methods

Economic costing was undertaken from a laboratory perspective for the high throughput central laboratory in Cape Town. Only costs related to the dedicated TB laboratory were assessed. Costs were calculated from the time the courier collected specimens from health facilities to the time results were returned. Costs were assessed only for pulmonary TB (PTB) tests for smear, culture, LPA and Xpert.

An excel-based costing tool was developed, based on that used in the Foundation for Innovation and Development (FIND) GenoType® MTBDRplus demonstration study. We used an ingredients-based costing

approach with test costs based on the cost per unit and quantities utilised for buildings, equipment, consumables, staff and overheads. Cost allocation was determined by reviews of standard operating procedures and laboratory records, direct observation and timing of the test procedures outlined in Figure 2, measurement of laboratory areas used for test processes and interviews with managers. Quality assurance samples were included in batch costs and outputs adjusted accordingly.

Building costs per square metre, including air-conditioning and consoles, were provided by the Council for Scientific and Industrial Research for a Level 2 laboratory for 2013. Equipment and consumables costs were sourced from laboratory financial records and quotes from suppliers for 2013. These costs were corrected by the consumer price index (CPI) to derive 2011 costs[17]. Staff and overheads costs were provided from laboratory financial records for both years. Overhead costs included costs for buildings, equipment, consumables and staff involved in specimen sorting and registration, results processing, procurement, stores, training, supervision and management. Specimen transport, electricity, water, sanitation, municipal and biohazardous waste disposal, cleaning and janitorial services, security services and telephone and internet costs were also included. Further information on costs is provided in online appendices 1, 2 and 3.

Building and equipment costs were spread over their expected lifespan and discounted to present values at a "risk-free" rate of 3%[11,18] with maintenance based on expenditure or estimated at 10% of annual costs. Laboratory utilisation was based on a 10-hour weekday for 21 days per month and a 4-hour Saturday shift. The cost of staff time was based on a 40-hour week for 46 weeks of the year with efficiency estimated at 80%.

All costs were calculated in local currency (ZAR). For comparative purposes, 2011 costs were expressed as 2013 CPI-adjusted values and converted to US$ based on average United Nations treasury operational rates in 2013 (ZAR9.75 = US$1.00)[19].

Study population and analysis

All sputum specimens processed in the laboratory in T1 (smear/culture-based algorithm) and T2 (Xpert-based algorithm) and resources related to the processing of these specimens were included in the assessment of laboratory and test costs. Overall laboratory costs were based on the cost per test and test volumes for microscopy (bleach-treated specimens), microscopy and culture, LPA and Xpert.

We used laboratory data for presumptive PTB cases from five of the eight sub-districts to estimate the cost per TB and MDR-TB case diagnosed. These sub-districts were included in a prior analysis of TB yield and their selection criteria have been described elsewhere[20]. The analysis required the full sequence of tests undertaken for presumptive TB cases. We therefore identified cases with specimens submitted in May 2011 and May 2013 and linked all diagnostic tests from the preceding and following months to identify the full sequence of tests undertaken for each case. Linkage was undertaken with MS-SQL using a combination of facility name, patient folder number, name, surname and age or birth-date.

We defined a *TB case* as an individual with one or more smears positive and / or culture positive for MTB and / or MTB detected on Xpert. An *MDR-TB case* was defined as an individual with rifampicin resistance on

LPA or Xpert. We compared the mean cost per patient diagnosed with TB and MDR-TB in each algorithm. MDR-TB costs were reported as additional to a TB diagnosis.

Ethics statement

The Health Research Ethics Committee at Stellenbosch University (IRB0005239) (N10/09/308) and Ethics Advisory Group at The International Union Against Tuberculosis and Lung Disease (59/10) approved the study. A waiver of informed consent was granted for use of routine data. The City of Cape Town Health Directorate, Western Cape Health Department and National Health Laboratory Service granted permission to use routine health data.

RESULTS

Comparison of total laboratory costs and activities

In T1, 79,544 specimens were tested at the central laboratory compared to 59,238 in T2. The majority (96% and 94% respectively) were for PTB tests.

Total laboratory costs for PTB tests increased from $440,967 in T1 to $632,262 in T2 (Table 1). Costs for bleach treated smears decreased by 49% from $128,916 to $65,799; smear and culture costs decreased by 35% from $247,771 to $161,707 and LPA by 50% from $64,279 to $32,339, all driven by decreased test volumes. The increase in total cost was attributable to Xpert test which accounted for 59% of total laboratory costs in the Xpert-based algorithm.

Annual overhead costs increased by 12% from $137,101 in T1 to $153,628 in T2. The largest contributors to the increase were specimen transport costs, utilities, biohazardous waste and janitorial services (Online Appendix 3). Overhead costs were allocated based on test volume as this was identified as the key driver for these costs. Overhead costs per test were increased by 47% from $1.80 in the smear/culture-based algorithm to $2.63 in the Xpert-based algorithm, due to both increases in overhead costs and reductions in test volumes.

Comparison of test costs (Table 1)

Smear microscopy costs (per bleach-treated specimen) increased from $2.85 in the smear/culture-based algorithm to $3.70 in the Xpert-based algorithm. Overhead costs were the main driver, accounting for 63% of costs in the smear/culture-based algorithm and 71% in the Xpert-based algorithm.

Microscopy and culture costs (per sodium hydroxide/sodium citrate-treated specimen) increased from $8.75 in the smear/culture-based algorithm to $9.62 per test in the Xpert-based algorithm. Consumables (44% and 40% in respective algorithms), staff costs (25% and 23% respectively) and overheads (21% and 27% respectively) were the key cost drivers. The highest cost component for consumables was for BACTEC MGIT tubes and supplement.

MTBDRPlus Line Probe Assay costs per test were similar at $16.12 in the smear/culture-based algorithm and $16.98 per test in the Xpert-based algorithm. Most tests were done on culture isolates and culture costs

have not been included in these totals. Consumables were the greatest cost-driver (79% and 75% in respective algorithms) due mostly to the cost of the GenoType® MTBDRplus kit.

Xpert MTB/RIF cost per test was $19.03. The largest cost driver was consumables (77%), due mostly to the cost of the XpertMTB/RIF cartridges.

Cost per TB case diagnosed

In May 2011 7,842 presumptive TB cases were tested through the smear/culture-based algorithm. The full sequence of tests for these individuals included 10,472 bleach-treated microscopy tests, 5,347 sodium hydroxide/sodium citrate-treated microscopy and culture tests and 980 tests for MTB culture confirmation at a total cost of $78,080. The mean cost per TB case diagnosed (n = 1601) was $48.77 (Table 2).

In May 2013 7,714 presumptive TB cases were tested through the Xpert-based algorithm. The full sequence of tests for these individuals included 2,711 bleach-treated microscopy tests, 3,689 sodium hydroxide/sodium citrate-treated microscopy and culture tests, 431 tests for MTB culture confirmation and 6,009 Xpert tests at a total cost of $160,536. The mean cost per TB case diagnosed (n = 1281) was $125.32.

The cost per TB case is influenced by the proportion of TB cases identified, which decreased in the Xpert-based algorithm (probably due to a decline in prevalence – see discussion for further details). We assessed a scenario where TB diagnostic yield in the Xpert-based algorithm was similar to that in the smear/culture-based algorithm which reduced the cost per TB case diagnosed to $101.94.

Cost per MDR-TB case diagnosed

There were 833 LPA tests done for TB cases in the smear/culture-based algorithm at a cost of $13,430 and mean additional cost per MDR-TB case (n = 95) of $141.37 (Table 2). In comparison 369 LPA tests were done amongst TB cases in the Xpert-based algorithm at a cost of $6,264 and mean additional cost per MDR-TB case (n=107) of $58.54. When these costs were added to the “base” cost of the TB diagnosis, the total cost per MDR-TB case diagnosed was $190.14 in the smear-culture-based algorithm compared to $183.86 in the Xpert-based algorithm.

As our prior analysis showed no difference in TB yield between the algorithms[20], we apportioned all additional costs to the additional MDR-TB cases diagnosed. This produced an incremental cost-effectiveness ratio (ICER) of $6,274 per additional MDR-TB case diagnosed.

DISCUSSION

The use of the more sensitive Xpert test[4,21,22] as a replacement for smear microscopy was expected to increase the number of TB cases diagnosed and simultaneous drug-susceptibility screening for all presumptive TB cases (not only those at high MDR-TB risk) expected to increase the number of MDR-TB cases diagnosed. A modelling study in South Africa, estimated that at full coverage Xpert would increase annual TB diagnostic costs by 53-57% to $48-70 million per year but that this would be partially off-set by a 30% to 37% increase in TB and 69 to 71% increase in MDR-TB cases diagnosed annually[23].

Our study found a 43% increase in PTB laboratory costs, from $440,967 in the smear-culture-based algorithm to $632,262 in the Xpert-based algorithm for 3-month periods. However, the increase in laboratory costs was not matched by an increase in TB diagnostic efficacy. Although the number of presumptive TB cases evaluated was similar in the smear/culture (n=7842) and Xpert-based algorithms (n=7714), the proportion of TB cases diagnosed (yield) decreased from 20.4% (n=1601) to 16.6% (n=1281). A prior stepped-wedge analysis undertaken as part of PROVE IT for 2010-2013 showed a temporal decline in TB diagnostic yield in both algorithms[20]. This may have been partly attributable to a declining TB prevalence, due perhaps to the rapid scale-up of anti-retroviral treatment in South Africa. When estimates were adjusted for the temporal trend, the study showed no significant difference in TB yield between the algorithms.

The increase in total costs and decrease in number of cases identified in the current study increased the cost per TB case diagnosed by 157% from $48.77 in the smear/culture-based algorithm to $125.32 in the Xpert-based algorithm. On the other hand, even a scenario with a similar proportion of TB cases identified in the Xpert-based algorithm to that in the smear/culture-based algorithm would increase the cost per TB case diagnosed by 109% (to $101.94).

The cost per MDR-TB case diagnosed was similar at $190.14 in the smear/culture based algorithm and $183.86 in the Xpert-based algorithm. In the smear and culture-based algorithm, drug susceptibility testing was only undertaken in high MDR-TB risk presumptive TB cases. One of the advantages of Xpert is that it provides simultaneous screening for TB and rifampicin resistance. The use of Xpert for all presumptive TB cases contributed to the 13% increase in the number of MDR-TB cases identified. Whilst these additional cases may have been diagnosed later in the smear/culture-based algorithm (i.e. after 1st line treatment failed), early diagnosis potentially reduces transmission, avoids the amplification of drug resistance and reduces patient morbidity and mortality. This modest benefit has to be weighed against the heavy overall expenditure, as shown by the MDR-TB ICER of $6,274. This figure needs to be viewed with some caution as possible changes in TB and thus MDR-TB prevalence has not been taken into consideration. Additional studies are required to assess whether Xpert or other drug susceptibility tests can be targeted more cost-effectively.

The cost-effectiveness of newly introduced laboratory tests is influenced by how services are re-organised and whether under-utilised assets can be redeployed. In the short-term it may be difficult to reduce costs until new systems and workloads are well established; however in the future efforts could be made to reduce overhead costs. Overhead costs per test could be reduced by increasing test volumes (through additional case-finding efforts for example). However, consumable costs were by far the greatest cost-drivers – accounting for 40% and 60% of total costs in respective algorithms. It remains to be seen whether global increases in test volumes or the availability of generic tests can reduce these costs substantially.

Strengths and limitations

The major strength of the analysis was that we collected detailed information to accurately estimate the cost per TB and MDR-TB case diagnosed. By including the full sequence of tests undertaken for individuals we

reflected the real-life variation found in diagnostic practices, including for example additional culture testing for smear and Xpert-negative cases in respective algorithms.

The extent to which our results can be generalised is limited by the setting as Cape Town has a relatively good laboratory and health infrastructure. Additional evidence is required from poorly-resourced settings including where culture is not available (as the benefit of Xpert may be greater in areas previously using only smear microscopy) and from rural settings (where specimen transport costs may be higher, economies of scale cannot be readily achieved and expertise may differ). The possible difference in TB prevalence between the two time-periods is a limitation, and has been taken into consideration in the analysis. The analysis was undertaken from a laboratory perspective only; the impact of new molecular diagnostic tests on patient costs is important and has been reported elsewhere[24].

Implications for policy and practice

The increase in total laboratory costs is in a similar range to that projected by two South African studies[13,23]. However we did not find the expected increases in TB-yield. Our findings are in keeping with a national study showing an 8% decrease in the number of laboratory confirmed PTB cases from 2011 to 2012, despite the introduction of Xpert[25]. Even when temporal trends of a possible declining prevalence were taken into account in our study, increased costs were not matched with increased TB diagnostic efficacy. It is difficult to justify the increased laboratory costs incurred through the introduction of Xpert and cost implications should not be underestimated. If the $160,411 spent on TB diagnosis in the Xpert-based algorithm was used for testing as per the smear/culture-based algorithm, the number of presumptive TB cases screened could have been increased by over 100% (from 7,714 to 16,158).

There is strong impetus to increase the use of Xpert. To mid-2014, 7.5 million Xpert cartridges were procured internationally with more than half being procured by South Africa[26]. However, the broader impact of Xpert remains questionable. Although studies have reported early TB[21,27,28] and MDR-TB[29,30] treatment initiation, Xpert had no impact on TB morbidity and mortality[27,31,32]. This together with the increased costs warrants a review of the role of Xpert in TB diagnosis.

Having invested heavily in this new technology, a reversion to a smear/culture-based algorithm is unlikely. Thus either technical adjustments need to be sought to improve Xpert sensitivity and / or the price of Xpert has to be substantially reduced to improve cost-effectiveness in our setting. Urgent efforts need to be made to optimise costs through improved efficiency of the Xpert-based algorithm, including exploring alternative options. Theron et al, for example, showed that pre-screening with smear reduced the cost of a TB diagnosis in their model by more than 20%[33]. A discrete event simulation model has been developed and validated as part of PROVE IT and will be used to evaluate more cost-effective diagnostic options.

This study highlights the need for thorough costing during early implementation to inform scale-up. As new diagnostic technologies become available, consideration should also be given to the wider costs of serial implementation of different technologies, overlapping of different technologies and redundancies that are created when existing technologies are also retained[9].

CONCLUSION

Economic costing is a key component in the decision to implement new TB diagnostic tests and careful consideration should be given to cost implications, particularly in resource-constrained, high-burden settings. The introduction of the Xpert-based algorithm has resulted in substantial increases in cost which are in line with modelling exercises undertaken in South Africa. However these were not matched by an increase in TB diagnostic efficacy; massive cost increases persist even when temporal trends of a possible declining TB prevalence were taken into consideration. One of the benefits of the Xpert-based algorithm was the modest increase in the number of MDR-TB cases diagnosed, which comes at high cost.

In view of the limited benefits, we have serious concerns about the sustainability of this expensive, new technology. More sensitive tests that are comparable to culture and that are substantially cheaper than Xpert (at current prices) are required, particularly if TB screening is to be substantially scaled up as suggested by the draft Global Plan to Stop TB 2016-2020[34].

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Author contributions:

All authors were involved in the study design. PN, RD and MVN collected the data. PN, RD and JM analysed the data. PN wrote the manuscript. All authors provided input to the manuscript and approved the final draft for submission.

Conflicts of interest:

The authors declare that they have no conflicts of interest.

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Table 1: Comparison of test costs in the smear/culture and Xpert-based algorithms

		Smear microscopy (Bleach treated)	**Smear microscopy & culture**	**Culture confirmation**	**MTBDRPlus Line Probe Assay**	**Xpert MTBRif**
Smear/culture-based algorithm (April – June 2011)(T1)	Building space	$0.02	$0.14	$0.05	$0.15	-
	Equipment	$0.11	$0.72	$0.02	$0.17	-
	Consumables	$0.36	$3.87	$0.84	$12.67	-
	Staff	$0.55	$2.21	$0.57	$1.34	-
	Overheads	$1.80	$1.80	$0.00	$1.80	-
	Cost per test	**$2.85**	**$8.75**	**$1.49**	**$16.12**	-
	Number of tests	45 252	27 508	4 747	3 987	-
	Total costs	**$128 916**	**$240 706**	**$7 065**	**$64 279**	-
Xpert-based algorithm (April – June 2013)(T2)	Building space	$0.02	$0.14	$0.05	$0.15	$0.06
	Equipment	$0.13	$0.74	$0.02	$0.18	$0.40
	Consumables	$0.36	$3.87	$0.84	$12.67	$14.62
	Staff	$0.55	$2.21	$0.57	$1.34	$1.32
	Overheads	$2.64	$2.64	$0.00	$2.64	$2.64
	Cost per test	**$3.70**	**$9.62**	**$1.49**	**$16.98**	**$19.03**
	Number of tests	17 770	16 503	2 020	1 905	19 565
	Total costs	**$65 799**	**$158 700**	**$3 007**	**$32 339**	**$372 418**

Test costs and volumes are for the central National Health Laboratory only. Total laboratory costs were $440,967 in the smear-culture-based algorithm compared to $632,262 in the Xpert-based algorithm for respective 3-month periods. All costs are expressed in 2013 CPI-adjusted values.

494 **Table 2: Costs per pulmonary TB and MDR-TB case diagnosed in the smear/culture and Xpert-based algorithms**

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	Costs in the smear/culture-based algorithm	Costs in the Xpert-based algorithm	Changes with the Xpert-based algorithm
Smear microscopy (Bleach treated)	$29 833.23 (n=10,472)	$10 038.29 (n=2,711)	-$19 794.94
Smear microscopy & culture (Sodium hydroxide/sodium citrate-treated)	$46 788.44 (n=5,347)	$35 475.12 (n=3,689)	-$11 313.32
Culture confirmation	$1 458.51 (n=980)	$641.53 (n=431)	-$816.98
Xpert MTB Rif	_	$114 380.73 (n=6,009)	$114 380.73
Total TB diagnostic costs	$78 080.18	$160 535.67	$82 455.50
Number of presumptive TB cases evaluated	7 842	7 714	-128
Number TB cases identified	1 601	1 281	-320
Mean cost per TB case identified	$48.77	$125.32	$76.55
Total costs for MTBDRPlus Line Probe Assay	$13 429.75 (n = 833)	$6 264.02 (n = 369)	-$7 165.73
Number of MDR-TB cases diagnosed	95	107	12
Mean additional cost per MDR-TB case diagnosed	$141.37	$58.54	-82.82
Mean total cost per MDR-TB case diagnosed	$190.14	$183.86	-$6.27

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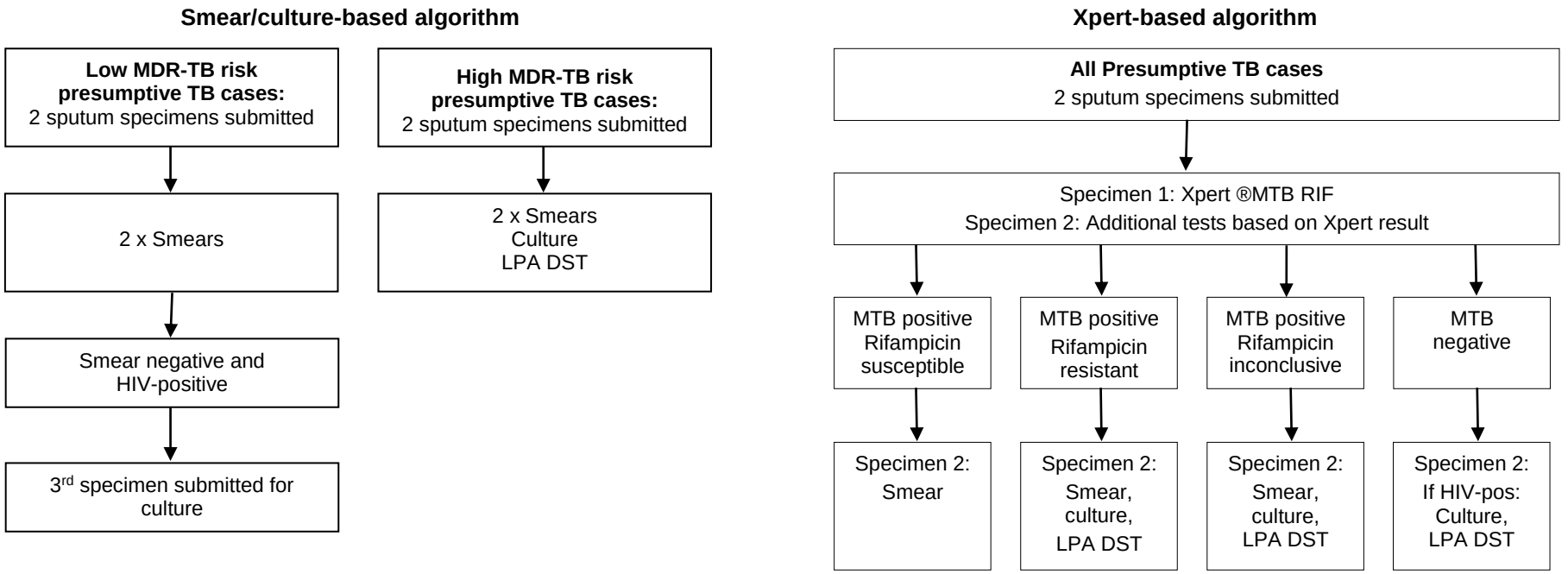
Figure 1: Testing protocols in TB diagnostic algorithms



The simplified sequence of diagnostic tests in each algorithm and the action taken based on test results is shown. Abbreviations: TB - tuberculosis; LPA – Genotype MTBDRPlus line probe assay; DST - drug susceptibility testing; HIV – human immunodeficiency virus; MTB – mycobacterium tuberculosis. Reprinted from: Naidoo P, Dunbar R, Lombard C, du Toit E Caldwell J et al. Comparing tuberculosis diagnostic yield in smear/culture and Xpert® MTB/RIF-based algorithms using a non-randomised stepped-wedge design. PLoS One. 2016;11(3):e0150487.

Figure 2: Laboratory workflow and test processes