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Market assessment of tuberculosis diagnostics in South Africa, 2012–2013

TB Diagnostics Market Analysis Consortium*

SUMMARY

OBJECTIVE: To assess the current served available market of tuberculosis (TB) diagnostics in South Africa in the public and private sectors.

DESIGN: Public and private sector test volumes and unit costs were collected for tuberculin skin tests, interferon-gamma release assays, smear microscopy, culture, speciation, Xpert® MTB/RIF, other nucleic acid amplification tests, drug susceptibility testing and adenosine deaminase tests.

RESULTS: In 2012, during Xpert scale-up, the public and private sectors performed a total of 9.2 million TB diagnostic tests, at an estimated total value of US$98 million. The public sector accounted for 93% of the overall test volume and value. There were no major differences in the types of tests performed in both sectors, with microscopy and culture accounting for the majority of tests performed (72%). In 2013, the public sector market value increased to US$101 million (a 10% increase over 2012): Xpert volumes increased by 166%, while total TB test volumes decreased by 12% compared to 2012.

CONCLUSION: South Africa has a substantial TB diagnostic market in terms of both volume and value. The roll-out of Xpert provides insights into how markets change in volume and value with the introduction of new tools.

KEY WORDS: tests; costs; volume; diagnosis

TUBERCULOSIS (TB) is a major public health problem worldwide, with 5.7 million new TB cases notified annually.[1] The total burden of TB is even higher, as an estimated 3 million new TB cases are not being diagnosed or notified to national TB programmes (NTPs).[1]

Although new TB diagnostics such as the Xpert® MTB/RIF assay (Cepheid Inc, Sunnyvale, CA, USA) are being scaled-up,[2] a great need remains for new TB diagnostic tests,[3] and in particular tests that can be used at various levels of the health care system to provide a rapid and actionable result for clinical management during the patient's first clinical encounter.[4]

While the technology pipeline has many new products, there is uncertainty on the current and potential market size for such technologies.[5,6] In 2006, the Foundation for Innovative New Diagnostics (FIND, Geneva, Switzerland) and The Special Programme for Research and Training in Tropical Diseases (TDR, World Health Organization [WHO], Geneva, Switzerland) estimated the global demand and market potential for TB diagnostics.[7] They showed that over US$1 billion was spent worldwide on TB diagnostics annually. However, much has changed in TB technology in the last decade;[8] updated analyses are thus underway.[9,10] Although regional and global market figures were reported, test manufacturers appreciate country-specific data, especially for the so-called BRICS countries (Brazil, Russia, India, China, South Africa), which are not only high TB burden countries, they are also growing economies that have the potential to invest in new technologies.[11] The national roll-out of Xpert in South Africa is a good example of this potential.

After India and China, South Africa has the third highest number of TB cases globally, with 349 582 notified TB cases in 2012 (5.7% of the global total).[1] South Africa's TB prevalence and incidence rates rank highest globally, and the country has the world's largest population of human immunodeficiency virus (HIV) infected individuals, and a large number of multidrug-resistant TB (MDR-TB) cases.[1]

*See Acknowledgements for Consortium members.

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In the present study, the current served available market (SAM) for TB diagnostics in South Africa was assessed for the 2012–2013 period. The volume and cost of the various tests in use for the diagnosis of latent tuberculous infection (LTBI) and active TB, drug susceptibility testing (DST) and treatment follow-up, and their market segmentation in the public and private sectors, are described.

METHODS

Setting

The public laboratory network in South Africa is operated by the National Health Laboratory Service (NHLS, Johannesburg, South Africa), which serves 80% of the country's population (www.nhls.ac.za). In 2012, this centralised laboratory network consisted of 240 microscopy centres; 18 regional laboratories with culture, DST and line-probe assay (LPA) capabilities; and a central reference laboratory. A small number of private laboratory networks offered TB diagnostic services through a mechanism of private payments and medical aid reimbursement. It is estimated that only 16% of South Africans have access to private medical insurance, while 84% are dependent on public sector health care.[12]

In 2011, following WHO recommendations,[13] South Africa's Minister of Health, Dr Aaron Motsoaledi, announced that the Xpert assay would be implemented across the country.[14] Consequently the NHLS and the National Department of Health (NDOH) developed a phased national implementation plan for its rollout.[15] The clinical testing algorithm was revised (Appendix Figures A.1A and A.1B),* replacing smear microscopy by Xpert for initial diagnosis. Complete coverage with Xpert was achieved in September 2013.

Tests included

The volume of tests performed in the public and private sectors was collected for tests used for the diagnosis of LTBI, active TB, DST and treatment follow-up. These included the tuberculin skin test (TST), interferon-gamma release assays (IGRAs), sputum smear microscopy (SSM), culture, nucleic acid amplification tests (NAATs) such as the Xpert and line-probe assays (LPAs), commercial *Mycobacterium tuberculosis* speciation tests, first- and second-line phenotypic DST and adenosine deaminase (ADA) for extra-pulmonary (mostly pleural) TB.

Calculation of test volumes

A bottom-up approach was used to collect test volumes. For the public sector, volumes for all tests except TST were retrieved from the NHLS database. TST volumes were estimated via a top-down approach using the number of purified protein derivative vials sold by the single distributor in South Africa. An average of 10 tests per 1.5 ml vial was used to estimate the number of TSTs performed. IGRA testing was not routinely offered in the public sector, but was available in private laboratories.

For culture-based DST, records of the numbers of first- and second-line drugs tested were used and divided by the average number of drugs tested as panels (two drugs for first-line and three for second-line panels). The number of pyrazinamide tests was calculated separately, as these were performed individually. Test volume data for the public sector were collected for 2012 as well as 2013.

Data on test volumes performed in private sector laboratories and prices charged per test were collected for 2012, but not for 2013, using surveys that were sent to the three main private laboratory networks and another independent laboratory, all known to perform TB diagnostic testing. All private laboratories provided data for their entire networks.

As data collection was based on aggregated routine programme data not identifiable to individual persons, no ethical approval was sought.

Unit costs

Unit costs were collected in South African Rand (ZAR) for 2012 and then converted to 2012 USD using the average exchange rate of R8.12 = US$1.[16] The same costs were assumed for 2013. Costs for SSM, culture, LPA and DST performed in the public sector were estimated by the NHLS using the WHO STOP TB Planning and Budgeting Tool data.[17] Unit costs per test (Appendix Table A.1) included the cost for reagents and consumables, labour, instrument amortisation or leasing agreement, repeat testing for errors and invalid results, sample transport, laboratory operating expenses and organisational overheads (electricity, water, central management, etc.)

Costs for speciation tests and ADA were based on 2012 NHLS public sector charges.[18] Xpert costs were based on NHLS charges and adjusted to include equipment costs. Costs for TST were estimated by the project team and included labour, reagents and consumables.

The two main private laboratories provided the prices charged to the patient and these were used to calculate the average price per test. These prices were used as a proxy for the cost of testing for private laboratories.

Calculation of the served available market by public vs. private segmentation

Three different market values were calculated. First, the value of the public sector market was calculated for 2012 and 2013 by multiplying the volume of each

* The appendix is available in the online version of this article, at http://www.ingentaconnect.com/content/iuatld/ijtld/2015/00000019/00000002/art00017

Table 1 Unit costs per diagnostic test for the public sector, prices charged by the private sector per test and costs cited in the literature (USD)

Diagnostic test	Public sector Costs/test	Private sector Prices charged/test	Overall market Cost/test*	Sensitivity analysis Range in cost per test
TST	10.06	18.29	10.06	No other sources known
IGRA	—	77.76	39.53	No other sources known
Sputum smear microscopy	5.94	11.41	5.94	1.68[20]–5.94[†]
Culture (liquid)	14.89	57.02	14.89	7.54[‡]–16.99[20]
Speciation test	11.27	—[§]	11.27	No other sources known
Xpert	21.94	105.09	21.94	13.36[19]–21.94[†]
LPA	30.25	113.22	30.25	20.56[‡]–35.12[†]
PCR	—	49.74	15.35	No other sources known
First-line DST (SIRE, average 2 drugs per test)	36.93	97.44	36.93	16.72[‡]–43.68[20¶]
PZA susceptibility test	27.25	—	27.25	No other sources known
Second-line DST (average 3 drugs per test)	48.12	175.10	48.12	25.08[‡]–48.12[†]
ADA	4.82	7.69	4.82	No other sources known

* Public sector test costs except for IGRA and PCR. IGRA costs were provided by the Clinical Lab Services, University of the Witwatersrand, Johannesburg, who had experience with conducting this assay for clinical trial purposes. PCR test costs were estimated by dividing the price charged by private laboratories for this test by the average private price-to-public test cost ratio.
† Cost values based on our study, as these were higher than that of other published micro-costing studies.
‡ NHLS state price.
§ There were no separate prices for speciation tests as these tests were performed in conjunction with culture and were included in the price of culture.
¶ Cost for first-line DST were based on all four SIRE drugs
USD = United States dollar; TST = tuberculin skin test; IGRA = interferon gamma release assay; LPA = line-probe assay; PCR = polymerase chain reaction; DST = drug susceptibility testing; SIRE = streptomycin, isoniazid, rifampicin, ethambutol; PZA = pyrazinamide; ADA = adenosine deaminase test; NHLS = National Health Laboratory Service.

test in the public sector by the unit costs of the public sector. Second, the value of the private sector market for 2012 was calculated by multiplying private sector test volumes by the average private sector price charged. Finally, the value of the overall TB diagnostic market for 2012 was calculated by multiplying the total number of each test performed in both sectors by the public sector cost. The public sector test cost was used for the overall market value, as these costs were thought to best reflect the cost of performing the test.

For IGRAs and polymerase chain reaction (PCR) tests, it was necessary to estimate the costs, as these tests were not performed routinely in the public sector. IGRA costs were estimated by the Clinical Lab Services (CLS), University of the Witwatersrand, Johannesburg, South Africa, which has experience in conducting this assay for clinical trial purposes. PCR costs were estimated by dividing the price charged by private laboratories for this test by the average private price-to-public test cost ratio. All unit costs are shown in Table 1.

Sensitivity analysis

Sensitivity analyses of the overall market value were undertaken for the plausible range in unit cost of SSM, culture, DST, LPA and Xpert. Lower and upper limits were derived from recent publications for South Africa,[19,20] usually based on primary data collection, or from the NHLS charges.

RESULTS

According to the quarterly reports of the NDOH, a total of 2.12 million people with presumptive TB were tested in the public sector and a total of 296 996 new TB cases were diagnosed in South Africa in 2012,[1] representing a 7:1 suspect to case ratio.

2012 TB diagnostic test volumes

The total volume of TB diagnostic tests conducted in the public sector amounted to 8.5 million individual tests (Figure 1A). A further 0.6 million TB tests were performed in the private laboratory networks (Figure 1B), for a total of 9.2 million tests (Figure 1C). The public sector accounted for 93% of the total TB test volumes.

Testing practices in the public and private sectors were similar. In both sectors, SSM (diagnostic and treatment monitoring) accounted for about half of the test volumes (n = 4.9 million, 54%), followed by liquid culture (n = 1.6 million tests, 18%). The use of Xpert and LPA was more predominant in the public sector. The public sector alone performed 749 288 Xpert tests in 2012 (8.8% of test total test volume in the public sector), while private laboratories used other commercial molecular tests (PCR, n =15 530) in addition to Xpert (n = 34 979, 5.5% of the total test volume in the private sector) and LPAs (n = 8091). Tests for LTBI accounted for 12% of the test volume in the public sector (TST only) and 20% of the test volume in the private sector in 2012 (TST and IGRA).

Served available market in 2012, segmented by health sector

Prices charged by private laboratories were on average three times higher than the estimated cost for the same test in the public sector. For 2012, the public sector TB diagnostic market value was estimated at 91 million USD, representing 19% of

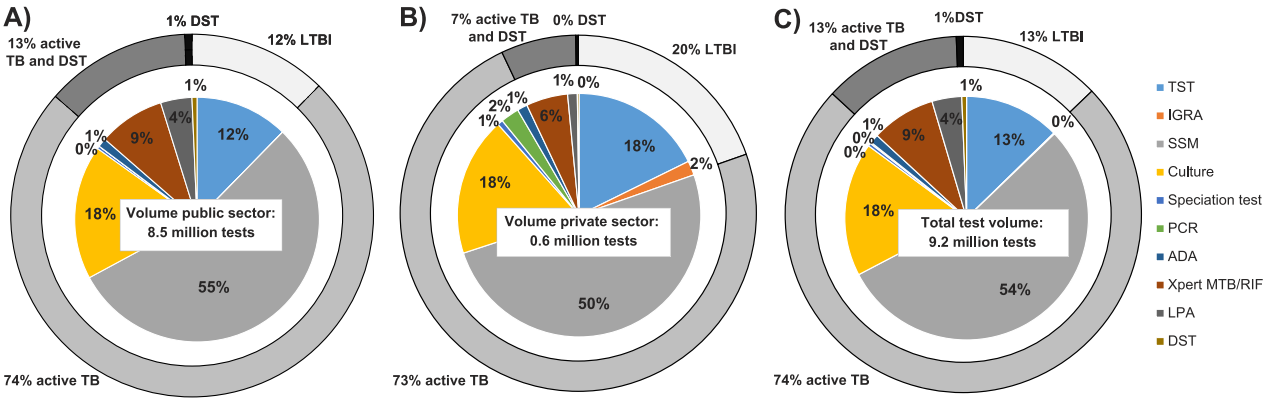

Figure 1 Volumes of TB diagnostic tests performed in the public and private sectors and both sectors combined, South Africa, 2012, by test and diagnostic purpose. Percentages were rounded to the nearest integer. Inner circles show the proportion of each TB diagnostic of the total test volumes in **A)** the public sector, **B)** the private sector or **C)** both sectors. Outer circles show the TB diagnostic test volumes by diagnostic purpose. Tests for the diagnosis of LTBI included TST and IGRA. Tests for active TB included SSM, culture, speciation tests, PCR and ADA. Tests for active TB and DST referred to tests that can detect both *M. tuberculosis* as well as resistance to one or more first-line drugs, including Xpert and LPA. DST included both first- and second-line phenotypic DST tests. DST = drug susceptibility test; LTBI = latent tuberculous infection; TB = tuberculosis; TST = tuberculin skin test; IGRA = interferon gamma release assay; SSM = sputum smear microscopy; PCR = polymerase chain reaction; ADA = adenosine deaminase test; LPA = line-probe assay. This figure can be viewed in color in the online version of this article at http://www.ingentaconnect.com/content/iuatld/ijtld/2015/00000019/00000002/art00017

the NTP budget in South Africa for the 2012–2013 financial year.[1] SSM (US$27.8 million) accounted for 30% of the value, and slightly less was spent on culture (US$22.5 million, Figure 2A). Molecular diagnostics, including Xpert and LPAs, contributed 30%.

In the private sector, the TB diagnostic market value was estimated at almost US$19 million (Figure 2B). The highest expenditure was on culture (US$6.6 million, 35%), followed by Xpert (US$3.7 million, 20%) and SSM (US$3.6 million, 19%), while tests to diagnose LTBI accounted for 16% of the total value. The overall TB diagnostic market value, including both sectors, was estimated at US$98 million in South Africa in 2012 (Figure 2C). As in the case of the volumes of tests, the private sector accounted for 7% of the overall expenditure on TB diagnostics.

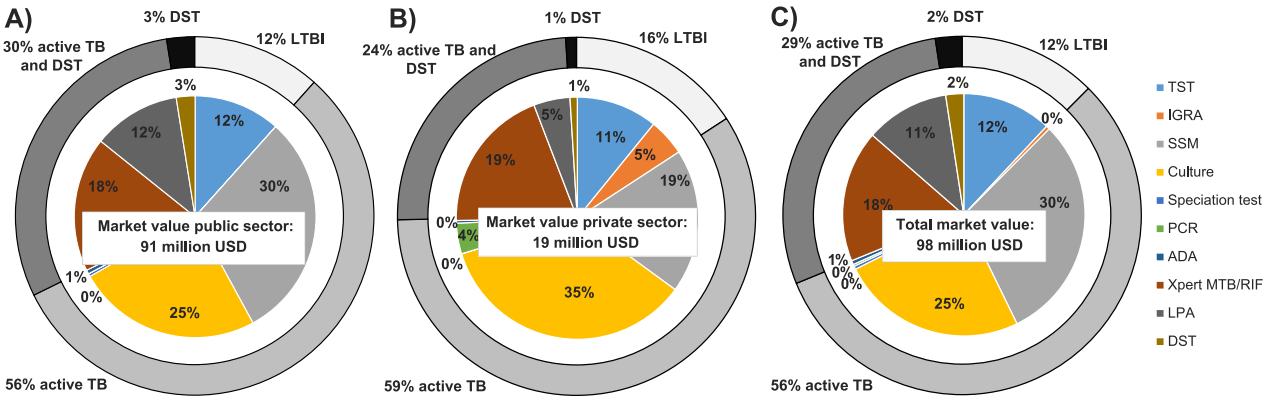

Figure 2 Market value of TB diagnostics in the public sector, the private sector and both sectors, South Africa, 2012 by test and diagnostic purpose. Percentages were rounded to the nearest integer. Inner circles show the proportion of the market value by different tests performed in **A)** the public sector, **B)** the private sector or **C)** both sectors. Market value costs per test in the public sector were based on costing data from the NHLS, while those for the private sector were based on the prices charged to patients for each test. Costs for the overall market value (both sectors combined) were mainly based on public sector costs. See Table 1 for further details. Outer circles show the TB diagnostic test volumes by diagnostic purpose. Tests for the diagnosis of LTBI included TST and IGRA. Tests for active TB included SSM, culture, speciation tests, PCR and ADA. Tests for active TB and DST referred to tests that can detect both *M. tuberculosis* as well as resistance to one or more first-line drugs, including Xpert and LPA. DST included both first- and second-line phenotypic DST tests. DST = drug susceptibility test; LTBI = latent tuberculous infection; TB = tuberculosis; TST = tuberculin skin test; IGRA = interferon gamma release assay; SSM = sputum smear microscopy; PCR = polymerase chain reaction; ADA = adenosine deaminase test; LPA = line-probe assay. This figure can be viewed in color in the online version of this article at http://www.ingentaconnect.com/content/iuatld/ijtld/2015/00000019/00000002/art00017

Table 2 Total overall tuberculosis diagnostic market value for the public and private sectors combined using public sector test costs, South Africa, 2012, USD

Diagnostic test	Public sector *n*	Private sector *n*	Tests performed *n*	Public sector %	Private sector %	Costs/test USD	Overall market value USD	% of total value	Sensitivity analysis: lower-upper range*
TST	1 051 700	111 979	1 163 679	90.4	9.6	10.06	11 710 623	12.0	11 710 623
IGRA	—	12 009	12 009	—	100	39.53	474 699	0.5	474 699
Sputum smear microscopy	4 676 768	318 018	4 994 786	93.6	6.4	5.94	29 646 275	30.3	8 372 370–26 669 029
Culture (liquid)	1 514 133	116 563	1 630 696	92.9	7.1	14.89	24 279 693	24,8	12 295 448–27 705 525
Speciation test	31 654	4 645	36 299	87.2	12.8	11.27	408 972	0.4	408 972
Xpert	749 288	34 979	784 267	95.5	4.5	21.94	17 209 598	17.6	10 477 807–17 209 598
LPA	353 547	8 091	361 638	97.8	2.2	30.25	10 941 201	11.2	7 435 277–12 700 727
PCR	—	15 530	15 530	—	100	15.35	257 812	0.3	257 812
First-line DST (SIRE, average 2 drugs per test)	34 609	892	35 501	97.6	2.4	36.93	1 372 561	1.4	593 577–1 550 586
PZA susceptibility test	2 256		2 256			27.25			61 476
Second-line DST (average 3 drugs per test)	19 740	549	20 289	97.3	2.7	48.12	976 368	1.0	508 848–976 368
ADA	99 705	8 548	108 253	92.1	7.9	4.82	522 146	0.5	522 146
Total	8 533 400	631 803	9 165 203	93.1	6.9		97 799 949	100	53 119 055–103 247 560

* For the lower and upper range for sensitivity, the cost values as listed in Table 1 were applied.
USD = United States dollar; TST = tuberculin skin test; IGRA = interferon gamma release assay; LPA = line-probe assay; PCR = polymerase chain reaction; DST = drug susceptibility testing; SIRE = streptomycin, isoniazid, rifampicin, ethambutol; PZA = pyrazinamide; ADA = adenosine deaminase test.

Results of the sensitivity analysis are shown in Table 2. On changing the unit costs for SSM, culture, DST, Xpert and LPAs, which accounted for 86% of the total test volumes, the overall market value ranged between US$53.1 and US$103 million.

2013 public sector test volumes and market value

Nationwide scale-up of Xpert and use of a new testing algorithm resulted in a 166% increase in Xpert tests in 2013 compared to 2012 (Figure 3), corresponding to 2.0 million Xpert tests and a market value of US$43.7 million for Xpert alone in 2013 (Appendix Table A.2). In contrast, test volumes for SSM, culture and LPA fell by respectively 46%, 19% and 32% in 2013, while TST volumes increased by 27%. Altogether, these changes led to a decrease of 12% in total test volumes, while the market value increased to US$101 million in 2013 (10% higher than in 2012) in the public sector.

DISCUSSION

This study reveals that in 2012 the TB diagnostic landscape in South Africa included a wide range of diagnostics that encompassed a total volume of 9.2 million individual tests, at an estimated cost of US$98 million. In 2013, the market value for the public sector increased by 10% due to the scale-up of Xpert as a replacement test for SSM for initial TB diagnosis. In comparison with the market analysis conducted by FIND and others in 2003–2004, TB test volumes in South Africa had increased considerably.[7] A total of 1.5 million smears and 0.77 million cultures were previously estimated for the entire country, of which respectively 11% and 8% were performed in the private sector (M Perkins, FIND, personal communication). Our results suggest that smear and culture volumes had each increased by more than 200% in 2012, suggesting investments by the NTP and NHLS to expand coverage of diagnostic testing. Nevertheless, 38% of estimated prevalent TB cases in South Africa are currently not notified.[1]

In recent years, the South African NTP has undergone revitalisation, with strong emphasis on improving access to diagnosis and active case finding, treatment and care, as well as the integration of TB and HIV services. The national plan for Xpert rollout was developed based on cost modelling, which provided detailed budget estimates and laboratory-specific indications for the number and size of Xpert instruments required.[15] This market analysis demonstrates that the new algorithm that recommends Xpert as the test for initial diagnosis resulted in a shift in the type of tests performed and a slight increase in spending on TB diagnostics by the public sector.

The successful implementation of Xpert in South Africa has shown that there is a market for new TB

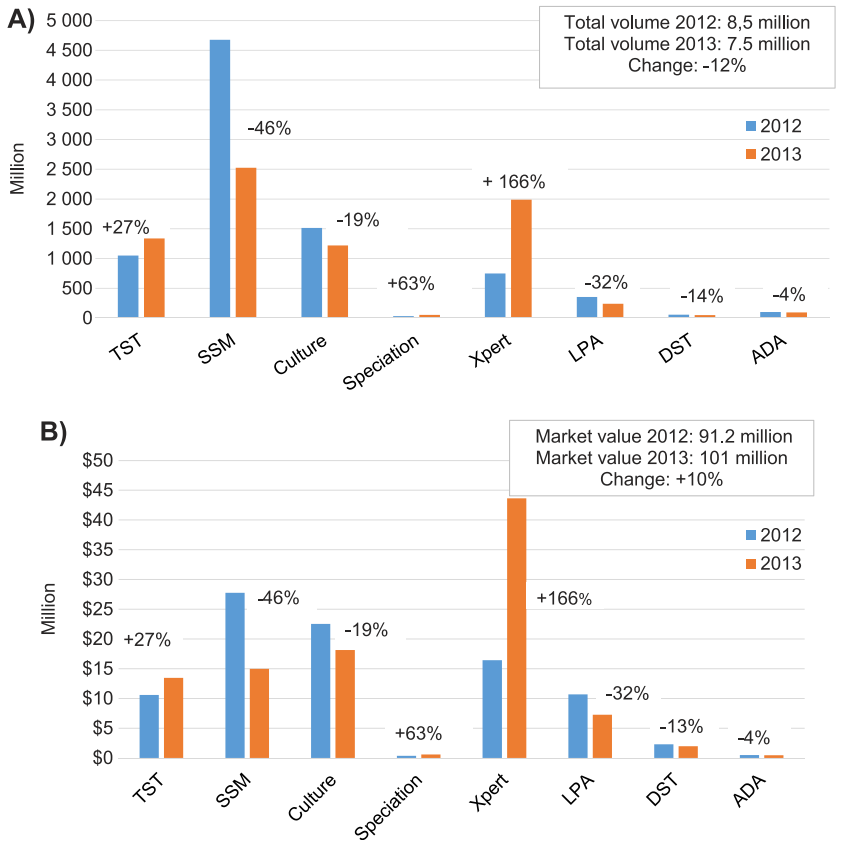

Figure 3 Changes in **A)** TB diagnostic testing volumes and **B)** market value (in USD) in the public sector, South Africa, 2012 and 2013. TST = tuberculin skin test; SSM = sputum smear microscopy; LPA = line-probe assay; DST = drug susceptibility testing; ADA = adenosine deaminase test. This figure can be viewed in color in the online version of this article at http://www.ingentaconnect.com/content/iuatld/ijtld/2015/00000019/00000002/art00017

diagnostic tools with increased sensitivity and faster turnaround times. In addition to new point-of-care diagnostics for the detection of pulmonary TB, there is a need for alternative test target product profiles (TPP), including a rapid biomarker-based test that detects extra-pulmonary TB and pulmonary TB in both adults and children, a triage test that can be used at lower levels of care to identify individuals who need confirmatory testing, and a rapid DST employed at the level of microscopy centres.[3] Consensus on the key characteristics of TPPs for TB diagnostics was recently reached at a meeting convened by the WHO/Global Laboratory Initiative and New Diagnostics Working Group. Beyond estimating the current SAM at individual country levels,[10] efforts are ongoing to project the potential market for future diagnostics on a country or even larger scale.[9] These efforts aim to encourage the growing interest of test developers and donors in TB diagnostics.

This study has some limitations. First, information on some types of tests (e.g., chest radiography, blood culture and histopathology) was not collected and will therefore have led to an underestimation of the total TB diagnostic market. Second, first- and second-line DST volumes in the public sector may be over- or under-estimated, as the number of drugs tested in each panel varied according to clinical request. Third, unit costs used in this study came from different sources and did not include the same components. However, we conducted a sensitivity analysis around unit costs to address this issue. Finally, private sector test volumes for 2013 were not collected. Furthermore, the exact indication for some of the tests used in the private sector was not ascertained (e.g., whether IGRAs were used for LTBI or active TB).

In conclusion, this market analysis of TB diagnostics demonstrated that South Africa has a substantial TB diagnostics market in terms of both volume and value that includes a broad range of tests. As the analysis covered the period of Xpert roll-out, it provides insights into how markets change in volume and value with the introduction of new tools.

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Conflicts of interest: C C Boehme and M D Perkins are employed by FIND, a non-profit organization that collaborates with industry partners, including Cepheid and Hain Diagnostics, for the development, evaluation and demonstration of new diagnostic tests for poverty-related diseases.

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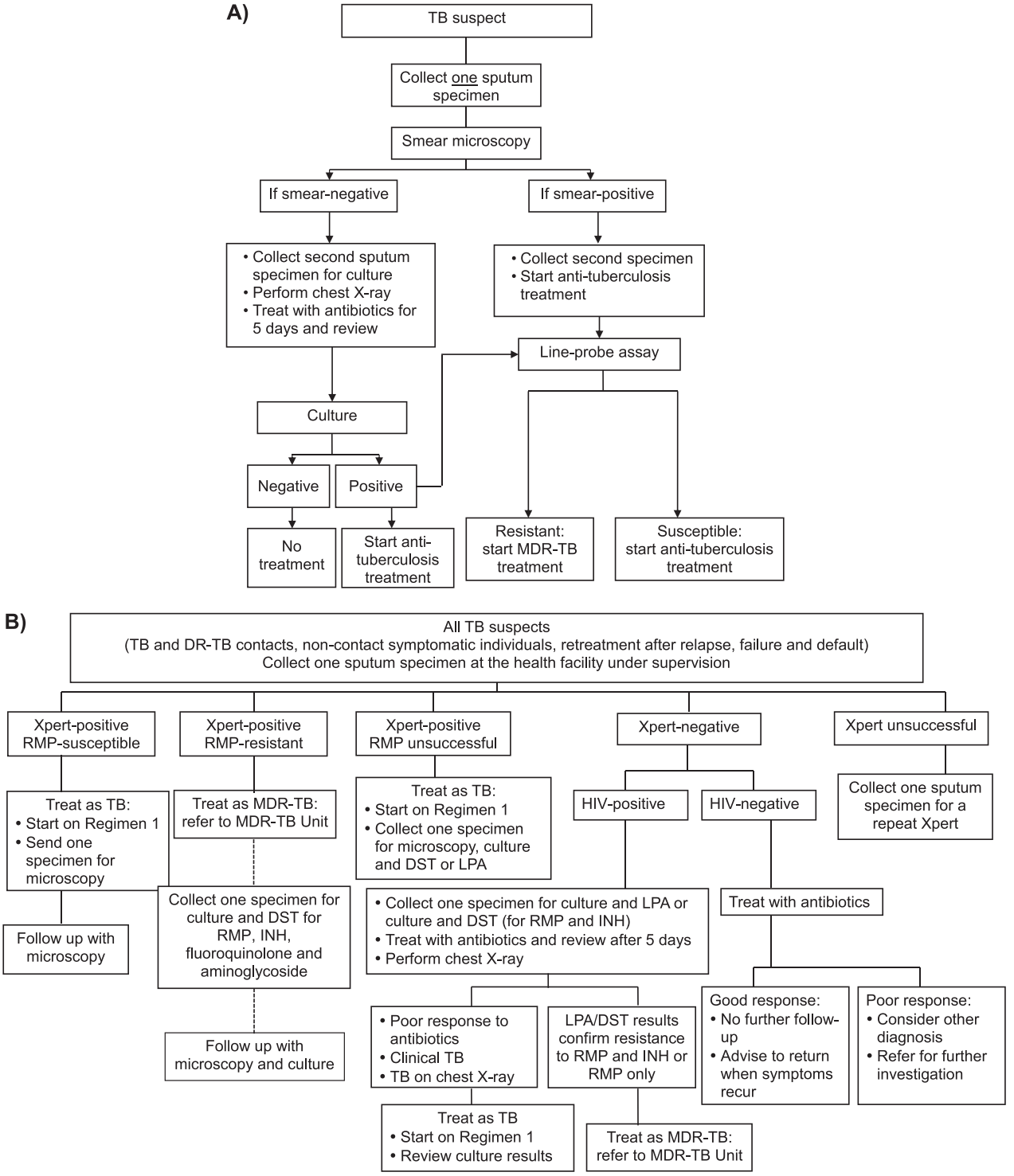
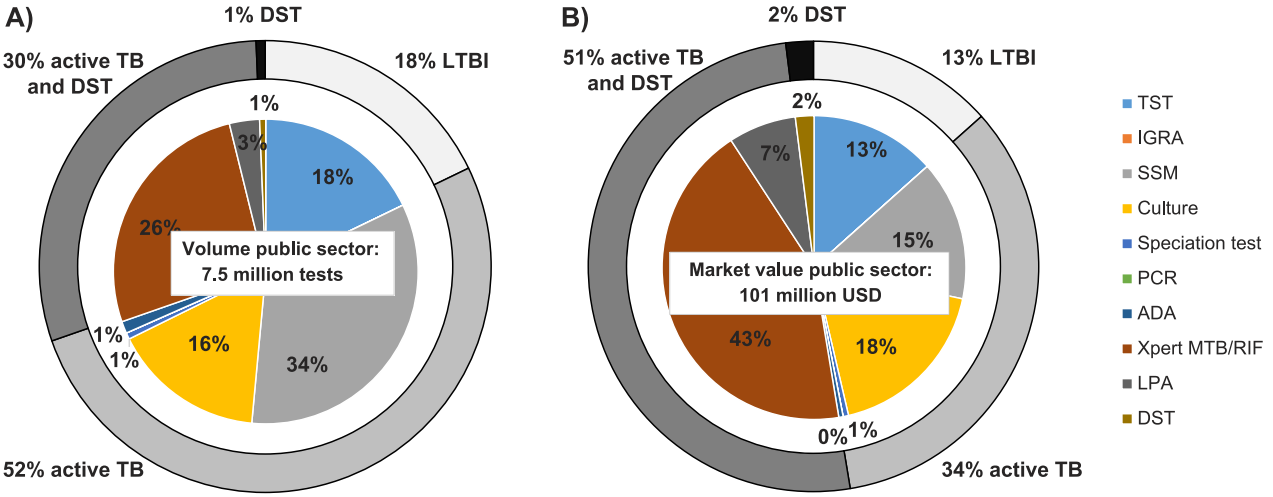
References

1 World Health Organization. Global tuberculosis report, 2013: WHO/HTM/TB/2013.11. Geneva, Switzerland: WHO, 2013.
2 World Health Organization. WHO monitoring of Xpert MTB/RIF roll-out 2013. Geneva, Switzerland: WHO, 2013.
3 Kik S V, Denkinger C M, Casenghi M, Vadnais C, Pai M. Tuberculosis diagnostics: which target product profiles should be prioritised? Eur Respir J 2014; 44: 537–540.
4 Pai N P, Vadnais C, Denkinger C, Engel N, Pai M. Point-of-care testing for infectious diseases: diversity, complexity, and barriers in low- and middle-income countries. PLOS Med 2012; 9: e1001306.
5 Pai M. Tuberculosis diagnostics: test developers' FAQs. Int J Tuberc Lung Dis 2013; 17: 570–571.
6 UNITAID. Tuberculosis: diagnostics technology and market landscape. 2nd ed. Geneva, Switzerland: UNITAID, 2013.
7 World Health Organization/Special Programme for Research and Training in Tropical Diseases/Foundation for Innovative New Diagnostics. Diagnostics for tuberculosis: global demand and market potential. Geneva, Switzerland: WHO, 2006.
8 Cobelens F, van den Hof S, Pai M, Squire S B, Ramsay A, Kimerling M E. Which new diagnostics for tuberculosis, and when? J Infect Dis 2012; 205 (Suppl 2): S191–S198.
9 Kik S V, Denkinger C M, Chedore P, Pai M. Replacing smear microscopy for the diagnosis of tuberculosis: what is the market potential? Eur Respir J 2014; 43: 1793–1796.
10 TB Diagnostics Market Analysis Consortium. Market assessment of tuberculosis diagnostics in Brazil in 2012. PLOS ONE 2014 [In press].
11 Pai M. Diagnostics for tuberculosis: what test developers want to know. Expert Rev Mol Diagn 2013; 13: 311–314.
12 McIntyre D. What healthcare financing changes are needed to reach universal coverage in South Africa? S Afr Med J 2012; 102: 489–490.
13 World Health Organization. Fact sheet. Expanding and accelerating access to diagnostics for patients at risk of multidrug-resistant tuberculosis. Geneva, Switzerland: WHO, 2010: pp 1–2.
14 Motsoaledi A. Health budget vote policy speech presented at the National Assembly by the Minister of Health. Johannesburg, South Africa: Government of South Africa, 2011.
15 Meyer-Rath G, Schnippel K, Long L, et al. The impact and cost of scaling up GeneXpert MTB/RIF in South Africa. PLOS ONE 2012; 7: e36966.
16 World Bank. World Bank data official exchange rate. Washington DC, USA: World Bank, 2012.
17 World Health Organization. Planning and budgeting for TB control activities. Geneva, Switzerland: WHO, 2010.
18 National Health Laboratory Service. State pricing catalogue 2011–2012. Pretoria, South Africa: Department of Health, 2011.
19 Shah M, Chihota V, Coetzee G, Churchyard G, Dorman S E. Comparison of laboratory costs of rapid molecular tests and conventional diagnostics for detection of tuberculosis and drug-resistant tuberculosis in South Africa. BMC Infect Dis 2013; 13: 352.
20 Vassall A, van Kampen S, Sohn H, et al. Rapid diagnosis of tuberculosis with the Xpert MTB/RIF assay in high burden countries: a cost-effectiveness analysis. PLOS MED 2011; 8: e1001120.

APPENDIX



Appendix Figure A.1 **A)** Smear (old) testing algorithm in place in the public sector, South Africa, 2012. **B)** Xpert (new) testing algorithm in place in the public sector, South Africa, 2012. TB = tuberculosis; MDR-TB = multidrug-resistant TB. DR-TB = drug-resistant TB; RMP = rifampicin; DST = drug susceptibility testing; LPA = line-probe assay; HIV = human immunodeficiency virus; INH = isoniazid.



Appendix Figure A.2 Volume of TB diagnostic tests performed and their market value in the public sector, South Africa, 2013, by different tests and their diagnostic purpose. Inner circles show the proportion of **A)** the total test volume or **B)** the market value, by different tests performed in the public sector, South Africa, 2013. 2012 Public sector costs were used to calculate the market value. Outer circles show **A)** the proportion of test volumes or **B)** the market value, by tests according to their detection purpose. Tests for LTBI diagnosis included TST and IGRA. Tests for active TB included SSM, culture, speciation tests, PCR and ADA. Tests for active TB and DST referred to tests that can both detect *M. tuberculosis* as well as resistance to one or more first-line drugs, including Xpert and LPA. DST included first- and second-line phenotypic DST tests.TST = tuberculin skin test; IGRA = interferon gamma release assay; SSM = sputum smear microscopy; PCR = polymerase chain reaction; ADA = adenosine deaminase test; LPA = line-probe assay; DST = drug susceptibility testing; LTBI = latent tuberculous infection.

Appendix Table A.1 Unit costs for tuberculosis diagnostic tests from the public sector perspective; breakdown by components, South Africa, 2012, in USD

	TST USD	Sputum smear USD	IGRA USD	Culture* USD	Speciation tests USD§	Xpert USD	LPA USD	First-line DST† USD	PZA testing USD	Second-line DST‡ USD	ADA USD§
Consumables	2.77	1.43	Based on costing	5.60	Based on NHLS	14.18¶	16.56	22.98	14.31	32.27	Based on NHLS
Instrument utility	NA	0.12	estimation by CLS	1.16	state price	2.33	0.65	2.87	1.44	4.31	state price
Labor	6.64	3.38		4.77		2.27	6.17	5.35	5.35	5.35	
Overhead costs (non-reportable results, repeats, sample transport and laboratory operating expenses)	0.66	1.00		3.36		3.17	6.87	5.73	6.15	6.19	
Total	10.06	5.94	39.53	14.89	11.27	21.94	30.25	36.93	27.25	48.12	4.82

* Average of the cost of a liquid culture with growth and that of a liquid culture with no growth.
† Based on an average of 2 drugs tested per run.
‡ Based on an average of 3 drugs tested per run.
§ Based on the most recent NHLS State charges and cannot therefore be broken down by cost item.
¶ Consumables including Xpert cartridge at $US9.98.
USD = United States dollar; TST = tuberculin skin test; IGRA = interferon gamma release assay; LPA = line-probe assay; DST = drug susceptibility testing; PZA = pyrazinamide; ADA = adenosine deaminase test; NA =not applicable; CLS = Clinical Lab Services, University of the Witwatersrand, Johannesburg; NHLS = National Health Laboratory Service.

Appendix Table A.2 Test volumes and market value of tuberculosis diagnostics tests in the public sector in 2012 and 2013, South Africa, USD

Diagnostic test	Tests performed in 2012 *n*	Tests performed in 2013 *n*	Change in test volume %	Costs per test USD	Market value 2012 USD	Market value 2013 USD	Change in market value %
TST	1 051 700	1 338 850	+27	10.66	10 583 728	13 473 447	27
IGRA	—	—		—	—		
Sputum smear microscopy	4 676 768	2 525 507	−46	5.94	27 758 697	14 990 007	−46
Culture (liquid)	1 514 133	1 218 888	−19	14.89	22 544 168	18 148 218	−19
Speciation test	31 654	5 588	+63	11.27	356 638	581 229	+63
Xpert	749 288	1 989 460	+166	21.94	16 442 035	43 655 804	+166
LPA	353 547	240 172	−32	30.25	10 696 412	7 266 300	−32
PCR	—	—		—	—	—	
First-line DST (SIRE, average 2 drugs per test)	34 609	26 611	−21	36.93	1 278 151	982 757	−21
PZA susceptibility test	2 256	2 464		27.25	61 467	67 134	
Second-line DST (average 3 drugs per test)	19 740	19 408	−2	48.12	949 948	933 972	−2
ADA	99 705	95 281	−4	4.82	480 916	459 577	−4
Total	8 533 400	7 221 079	−12		91 152 159	100 558 445	+10

USD = United States dollar; TST = tuberculin skin test; IGRA = interferon gamma release assay; LPA = line-probe assay; PCR = polymerase chain reaction; DST = drug susceptibility testing; SIRE = streptomycin, isoniazid, rifampicin, ethambutol; PZA = pyrazinamide; ADA = adenosine deaminase test.

RESUME

OBJECTIF : Evaluer le marché actuel des diagnostics de tuberculose (TB) disponibles en Afrique du Sud dans le secteur public et privé.

SCHÉMA : Les volumes de tests et le coût unitaire du secteur public et privé ont été recueillis pour les tests cutanés à la tuberculine, les tests de libération de l'interféron-gamma, la microscopie de frottis, les cultures, la spéciation, le test Xpert® MTB/RIF, d'autres tests d'amplification des acides nucléiques, les tests de pharmaco sensibilité et les tests d'adénosine désaminase.

RÉSULTATS : En 2012, lors de l'expansion du Xpert, les secteurs public et privé ont effectué un total de 9,2 million de tests diagnostiques de la TB pour une valeur estimée totale de US$98 millions. Le secteur public était à l'origine de 93% du volume et de la valeur de l'ensemble des tests. Il n'y a pas eu de différences majeures dans les types de tests réalisés dans les deux secteurs, la microscopie et la culture représentant la majorité des tests effectués (72%). En 2013, la valeur marchande au niveau du secteur public a atteint US$101 millions (10% d'augmentation par rapport à 2012), tandis que les volumes du Xpert augmentaient de 166% et que le total du volume des tests TB diminuait de 12% par rapport à 2012.

CONCLUSION : L'Afrique du Sud a un marché substantiel en termes de diagnostic de la TB autant en volume qu'en valeur. Le déploiement du Xpert montre comment les marchés se modifient en volume et en valeur avec l'introduction de nouveaux outils.

RESUMEN

OBJETIVO: Evaluar el mercado vigente para los métodos diagnósticos de la tuberculosis (TB) en Suráfrica en el sector público y el sector privado.

MÉTODO: En los sectores público y privado se recogió información sobre los volúmenes de pruebas utilizadas y los costos unitarios de la prueba cutánea de la tuberculina, la prueba de liberación de interferón γ, el examen microscópico de extendidos, los cultivos, la determinación de la especie, la prueba Xpert® MTB/RIF, otras pruebas de amplificación de ácidos nucleicos, la prueba de sensibilidad a los medicamentos y la determinación de la adenosina desaminasa.

RESULTADOS: En el 2012, durante la ampliación de escala de la aplicación de la prueba Xpert, se practicaron 9,2 millones de pruebas diagnósticas en el sector público y el sector privado, con un valor total estimado en US$98 millones. Al sector público correspondió el 93% global del volumen de pruebas y del costo. No se observaron diferencias considerables en los tipos de pruebas realizadas en ambos sectores; la mayoría de las pruebas practicadas correspondió al examen microscópico y el cultivo (72%). En el 2013, el valor del mercado del sector público aumentó a US$101 millones (un aumento de 10% con respecto al 2012). Los volúmenes de la prueba Xpert aumentaron un 166% y los volúmenes totales de pruebas de diagnóstico de la TB disminuyeron un 12%, en comparación con el 2012.

CONCLUSIÓN: En Suráfrica existe un mercado considerable para las pruebas diagnósticas de la TB, desde el punto de vista del volumen y del valor. El despliegue de la prueba Xpert ofrece información sobre las modificaciones del volumen y el valor del mercado que ocurren con la introducción de nuevas herramientas diagnósticas.