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Market assessment of tuberculosis diagnostics in India in 2013

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SUMMARY

BACKGROUND: India represents a significant potential market for new tests. We assessed India's market for tuberculosis (TB) diagnostics in 2013.

METHODS: Test volumes and unit costs were assessed for tuberculin tests, interferon-gamma release assays, sputum smear microscopy, serology, culture, speciation testing, nucleic-acid amplification tests (i.e., in-house polymerase chain reaction, Xpert® MTB/RIF, line-probe assays) and drug susceptibility testing. Data from the public sector were collected from the Revised National TB Control Programme reports. Private sector data were collected through a survey of private laboratories and practitioners. Data were also collected from manufacturers.

RESULTS: In 2013, India's public sector performed 19.2 million tests, with a market value of US$22.9 million. The private sector performed 13.6 million tests, with a market value of US$60.4 million when prices charged to the patient were applied. The overall market was US$70.8 million when unit costs from the ingredient approach were used for the 32.8 million TB tests performed in the entire country. Smear microscopy was the most common test performed, accounting for 25% of the overall market value.

CONCLUSION: India's estimated market value for TB diagnostics in 2013 was US$70.8 million. These data should be of relevance to test developers, donors and implementers.

KEY WORDS: tests; costs; volumes; diagnosis

TUBERCULOSIS (TB) affected an estimated 9 million people in 2013, and caused 1.5 million deaths.[1] About 3 million TB patients globally were not diagnosed or notified to any of the national TB programmes in 2013, with India accounting for 1 million missed patients.[1] There has been a concurrent rise in the prevalence of multidrug-resistant TB (MDR-TB), with many of these cases being undetected and therefore unreported.[2]

India has both a high TB and a high MDR-TB burden, and accounts for 24% of the world's incident TB cases.[1] India's TB landscape is different from other BRICS countries (Brazil, Russia, India, China and South Africa), such as China, Brazil and South Africa, due to the major role played by the private sector in TB diagnosis and treatment. It is estimated that nearly 50% of India's TB patients are managed in the private sector, and diagnostic delays are common.[3,4]

There is a great need for new TB diagnostic tools.[5] Recently introduced diagnostics, such as Xpert® MTB/RIF (Cepheid Inc, Sunnyvale, CA, USA), are essential in the fight against TB, and are helping countries move towards the goal of universal drug susceptibility testing (DST).[6] Without state-of-the-art diagnostics combined with other novel interventions, it will be difficult to reduce TB incidence.[7]

Point-of-care (POC) diagnostics, allowing for the specific and sensitive diagnosis of TB at first contact with the patient, will be crucial for reducing diagnostic delays and reducing transmission.[8] Most of the high TB burden countries have significant rural populations, as seen in India, where 69% of the population is rural,[9] further emphasising the need for POC diagnostics that can be deployed for use at lower levels of the health care system.

While the TB diagnostics pipeline in 2015 looks promising,[10] product developers and donors will benefit from detailed analyses of the diagnostics market and dynamics.[11] The size of the global market and the market potential were first assessed in 2006 by 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).[12] The report found the overall expenditure on TB diagnostics to be over US$1 billion. However, much has changed in the last decade,[13] which is why updated market analyses have been performed.[14–16] According to recent market assessments by our

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Consortium in Brazil,[14] China[15] and South Africa,[16] the annual national (in 2012/2013) TB diagnostic market was worth US$17 million in Brazil, US$294 million in China and US$98 million in South Africa. In this study, the served available market (SAM) was estimated for TB diagnostics in India for 2013.

METHODS

Details of our methods for the estimation of SAM are similar to the methods used by FIND and TDR in their 2006 analysis of the TB diagnostics market,[12] and are described in detail in our previous market assessment publications.[14–16]

Setting and testing infrastructure

India's Revised National TB Control Programme (RNTCP), its public TB programme, offers free TB diagnosis and treatment across the entire country. The RNTCP has over 13 000 designated microscopy centres (DMCs), each serving a population of 50 000 to 100 000 people. India also has a national network of public TB laboratories (Appendix Figure A.1).[17**] There are six national reference laboratories (NRLs) that perform tests and which are also responsible for the supervision of 30 intermediate reference laboratories (IRLs), with periodic training of the IRL staff in culture, DST and external quality assessment (EQA). There is one IRL per state that monitors and supervises EQA activities and performs culture and DST. Overall, there are 62 culture and DST laboratories under the RNTCP. The RNTCP also partners with the Microbiology Departments of medical colleges to provide MDR-TB services. These medical colleges report all sputum smear microscopy (SSM) results to the RNTCP; however, no comparable reporting process for the diagnosis of MDR-TB exists.

According to key stakeholders, India's private sector accounts for 60% of all TB diagnostic services. There are no precise data on the number and type of laboratories in the private sector. There are five large, private network laboratories that use a hub-and-spoke model of collection and franchise centres feeding into centralised laboratories. Similar but smaller networks exist at the regional (state) level. In addition, there are laboratories within private hospitals and private medical colleges. Finally, there are a large number of small, individual, independently managed laboratories that are usually owned by a single person.

The private sector in India probably consists of over 40 000 poorly regulated independent laboratories and more than 60 000 collection centres (for network laboratories) as of 2011.[18] The National Accreditation Board for Testing and Calibration Laboratories (NABL) is an autonomous body under the Department of Science and Technology, tasked with the objective of providing third-party assessments for India's laboratories. Although some laboratories have been accredited, there is variation even in the meaning of accreditation: according to the NABL, 533 Indian laboratories currently have accreditation, which means that these laboratories may have been accredited for as few as one and up to all medical tests, and accreditation may not necessarily apply to TB tests.[19]

Testing algorithms

The RNTCP uses WHO-endorsed TB tests, including smear microscopy (Ziehl-Neelsen [ZN] staining and light-emitting diode [LED] fluorescence microscopy), Xpert, line-probe assay (LPA), solid and liquid culture and DST. Using the RNTCP's algorithm (Appendix Figure A.2), pulmonary TB is diagnosed when one of two sputum samples is smear-positive or when chest X-ray (CXR) is indicative of pulmonary TB.[20]

All persons presumed to have TB found to be smear-negative and with CXR results suggestive of TB, as well as those who are smear-negative but are classified by physicians as highly clinically suspicious or do not have reliable CXR results, are tested with Xpert, also known as the cartridge-based nucleic-acid amplification test (CBNAAT) under the Indian programme. Xpert test results are confirmed by LPA or culture. All people living with the human immunodeficiency virus and the acquired immunedeficiency syndrome, as well as those who are at risk of MDR-TB, are immediately tested using CBNAAT. This newer algorithm is shown in Appendix Figure A.3. It is noteworthy that the RNTCP algorithms do not include tests such as serology, interferon-gamma release assays (IGRAs) and in-house polymerase chain reaction (PCR).

The Indian private sector, which may be a contributor to the high number of undiagnosed and misdiagnosed patients, does not necessarily follow the RNTCP algorithm or protocols. Until 2012, serological, antibody-based rapid tests and enzyme-linked immunosorbent assays (ELISAs) were the most popular TB tests in the private sector in India.[21] After the negative WHO policy recommendation in 2011,[22] the Indian government banned commercial serological tests for TB in 2012.[23]

In 2013, the Clinton Health Access Initiative (CHAI) and partners launched the Initiative for Promoting Affordable and Quality TB Tests (IPAQT)[24] to replace suboptimal tests by WHO-endorsed TB tests in the private market and to reduce the price of tests such as Xpert and LPA by 30–50%. IPAQT now has 105 private laboratories, including

** The appendix is available in the online version of this article, at http://www.ingentaconnect.com/content/iuatld/ijtld/2016/00000020/00000003/art00007

four large network laboratories, engaged in the consortium. All these laboratories have to agree to a ceiling price and to notify confirmed cases to the RNTCP.

Tests included in the market analysis

Data on the volume of tests performed and unit test costs in both the private and public sectors were collected for diagnostics used for the detection of active TB, latent tuberculous infection (LTBI), and for follow-up testing: SSM, culture, speciation testing, nucleic acid amplification tests (NAATs)— which include LPAs (both first- and second-line), Xpert and in-house PCR— tuberculin skin tests (TSTs), IGRAs, and first- and second-line culture DST. Complete data on tests such as CXR for TB screening, adenosine deaminase test for pleural TB and blood culture for TB were not available for India in 2013, and were therefore excluded from the analysis. As the RNTCP does not currently report volumes of second-line culture DST, these tests were also excluded from this analysis.

Calculation of test volumes

Public sector

Data for India's public sector were estimated using RNTCP data and reports[17] and sales data from test manufacturers. A bottom-up approach (i.e., actual number of tests performed) was used for public sector volumes of solid and liquid culture, LPA and first-line DST. The 2014 RNTCP annual report provided test volume data for 9 months of 2013, and these values were extrapolated to account for the whole of 2013.

For liquid culture, sales volumes were provided by product manufacturers (i.e., top-down approach). As the RNTCP reported on the total number of cultures regardless of technique, the number of solid cultures could be estimated by subtracting the estimated number of liquid cultures from the total number of cultures.[17] Speciation tests are performed on all culture-positive samples by the RNTCP. To calculate the volume of speciation tests, the proportion of smear-positive samples reported as culture-positive was applied to the total volume of cultures performed. Volumes of Xpert and LPA used by the RNTCP in 2013 were provided by the manufacturers.

Sales data from the largest Indian purified protein derivative (PPD) manufacturer was used to estimate TST volumes stratified by public and private sectors. An average number of 10 tests per 1.5 ml vial or 35 tests per 5 ml vial of PPD, respectively, was used to determine the number of TSTs performed in each sector.

The total number of public sector smears was estimated based on data from the RNTCP on the total number of individuals with presumptive TB seen at their centres and the number of successfully treated cases in 2013.[17] Individuals with presumptive TB are supposed to have two sputum smears examined. However, because some individuals do not submit a second sputum sample we used an estimated 1.9 smears per initial presumed TB case. Follow-up smears include three samples taken over the course of 6 months according to RNTCP guidelines. To estimate the volume of follow-up smears, the RNTCP's treatment success rate of 85% was used,[17] multiplied by the number of TB patients.

Private sector

Private sector data were collected using a survey and from manufacturer data. A middle-out approach (i.e., some primary data collection) was used to estimate test volumes for SSM and serology in the private sector, through the analysis of survey data collected through an Indian Market Research Bureau (IMRB) survey study performed in collaboration with CHAI, India.[25] This study of private sector providers in India was conducted in January–March 2013. It included 307 private laboratories and 768 TB treating physicians, including qualified and unqualified doctors. Data collection was performed in 15 major Indian states.

Volumes of Xpert, LPA (both first- and second-line), liquid culture and TST test in the private sector were estimated using a top-down approach and based on the 2013 manufacturers' sales data. IGRA volumes were obtained through annual importation data from the Indian government. Locally produced IGRA was not included in our estimates due to its small market share in 2013.

The volume of testing with in-house PCR in the private sector was calculated using a middle-out approach, with test volumes from major Indian laboratory chains for IGRA and in-house PCR. Based on the similar costs and penetration of in-house PCR and IGRA, these laboratories' share of the IGRA market was assumed to be similar to their share of the in-house PCR market. The total in-house PCR volume could then be estimated based on these assumptions.

Unit costs

Unit costs were estimated in Indian rupees (INR), and were then converted to 2013 USD using the average exchange rate (58.60 INR = US$1) for 2013 (Table 1).[26] For the public sector, costs for SSM, liquid and solid culture, LPA, Xpert, first-line liquid DST and speciation were based on a recent study undertaken by FIND,[27] that reported unit costs per test to the health service provider using an ingredient approach. The ingredient approach is a bottom-up approach, which only factors-in resources directly observed by researchers. Each observation had a different number of specimens being tested. This study focused on five DMCs and two IRLs. The DMCs were used for costing SSM and Xpert, while the IRLs were used to

Table 1 Unit cost (in USD) per diagnostic test for the public sector and prices charged by the private sector

Diagnostic test	Public sector costs/test USD	Price charged in the private sector USD	Cost/test used to calculate overall market value USD*	Sensitivity analysis (range in cost/test)
TST	1.12	3.46	1.12	0.99–1.25
IGRA	—	42.74	42.74	37.59–47.85
Smear (ZN+fluorescence microscopy)	0.84†	1.71	0.84	0.6–1.1
Culture (liquid)	11.07	17.10	11.07	9.01–13.12
Culture (solid)	9.83	—	9.83	2.29–17.83
Speciation test	3.95	—	3.95	3.74–4.16
Xpert	12.29	29.07	12.29	11.61–12.89
LPA (first-line)	18.18	27.36	18.18	17.09–19.27
LPA (second-line)	18.18‡	27.36	18.18	17.09–19.27
PCR	—	32.43	32.43	28.59–36.39
Solid DST (first-line)	29.88	—	29.88	26.34–33.42
Serology	—	10.26	10.26	9.03–11.49

* Public sector test costs were used to calculate the overall market value, except for those tests that were not offered in the public sector and for which we did not have alternative cost estimates. Test costs estimated by FIND included SSM, solid and liquid culture, speciation, Xpert, first-line LPA and solid DST. We used our own similar cost estimate for TST. Tests not offered in the public sectors included IGRA, serology and PCR, for which private sector prices were used.
† The cost of smears is the average cost of ZN and fluorescence microscopy smears combined.
‡ Assumed cost of second-line LPA was equivalent to first-line LPA.
USD = United States dollar; TST = tuberculin skin test; IGRA = interferon-gamma release assay; ZN = Ziehl-Neelsen; LPA = line-probe assay; PCR = polymerase chain reaction; DST = drug susceptibility testing; FIND = Foundation for Innovative New Diagnostics; SSM = sputum smear microscopy.

estimate costs of solid culture, liquid culture, DST, LPA and the *Mycobacterium tuberculosis* rapid speciation test. All cost values include the costs for reagents and consumables, labour, instrument amortisation, laboratory operating expenses, and organisational overheads (electricity, water, central management, etc.). In the current study, the average test costs used were based on all observations in all laboratories combined.

We used a similar approach to estimate the cost of TSTs. Costs of a vial of PPD, as well as the syringe and gloves, were determined and added to costs of labour from the FIND study plus overheads, which was assumed to be 20%.

For the private sector, actual costs of tests were unknown; instead, the prices charged to patients by private laboratories had been collected by CHAI through an anonymous survey of 307 laboratories and 768 health care providers across 15 Indian states. The average price per test for each type of test was used when estimating the private sector market.

Calculation of the 2013 served available market by public vs. private segmentation

Similar to our previous analyses for Brazil,[14] China[15] and South Africa,[16] three different market values were calculated. First, the value of the public sector market was calculated by multiplying the unit costs with the volumes of each of the TB tests in the public sector. The value of the private sector market was then calculated by multiplying test volumes by the average prices charged by providers. Finally, the value of the overall TB diagnostic market was calculated by multiplying the total numbers of each test, the sum of both private and public sector volumes, by the public sector unit costs where public sector costs were available. Private sector prices for the tests were used for those tests that did not have public sector costs (IGRA, in-house PCR and serology).

Sensitivity analyses

Sensitivity analyses of the overall market value were undertaken for the plausible range in unit costs of SSM, culture, DST, LPA and Xpert. Lower and upper limits were derived from the costing study performed by FIND. Excluding culture, due to its large range, a mean percentage difference between the lower and upper cost limit of each test was derived (± 12%).This mean percentage difference was used to calculate the lower and upper limits for those tests that did not have data available for the sensitivity analysis, which included TST, IGRA, PCR and serology.

RESULTS

Public sector

Unit costs per test that were used to calculate the public sector, private sector and overall market value are shown in Table 1. In 2013, the total volume of all TB tests performed in the public sector amounted to 19.2 million (Figure 1A and Table 2). Specifically, a total of 17.1 million SSM tests were performed. Ninety-five percent of all smears were examined using traditional ZN staining techniques, while the remaining 5% were performed using LED microscopy.

For culture, 62% of the total volume of 240 446 were performed using solid media and the remaining 38% using liquid media. Speciation test volumes were 33.1% of the total culture volume, a value of 79 588 (0.4% of public sector tests). The volume of TST was estimated at 1.5 million (8.0% of public sector tests). The volume of Xpert tests was 167 410 (0.9% of public sector test volume), while the volume of first-

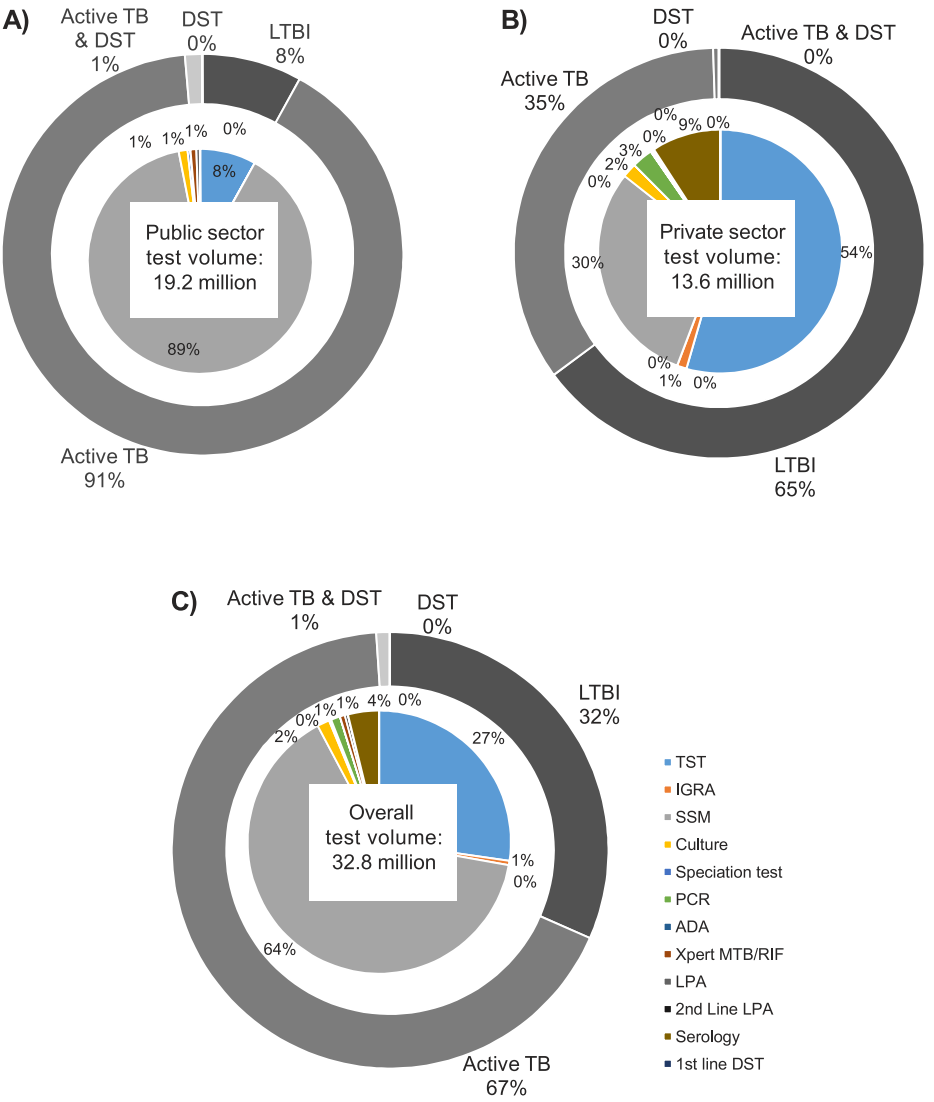

Figure 1 Volumes of TB diagnostic tests performed in the public and private sectors and combined, by test and diagnostic purpose, India, 2013. Percentages rounded to the nearest integer. Inner circles show the proportion of each TB diagnostic of the total test volumes in **A)** the public sector, **B)** the private sector or **C)** both sectors. Outer circles show the TB diagnostic test volumes by diagnostic purpose. Tests for the diagnosis of LTBI include TST, IGRA and serology. Tests for active TB include SSM, culture, speciation tests and PCR. Tests for active TB and DST refer to tests that can detect both *M. tuberculosis* as well as resistance to one or more first-line drugs, including Xpert and LPA. DST includes first-line DST on solid culture. TB = tuberculosis; DST = drug susceptibility testing; LTBI = latent tuberculous infection; USD = United States dollar; TST = tuberculin skin test; IGRA = interferon-gamma release assay; SSM = sputum smear microscopy; PCR = polymerase chain reaction; ADA = adenosine deaminase; LPA = line-probe assay. This image can be viewed online in colour at http://www.ingentaconnect.com/content/iuatld/ijtld/2016/00000020/00000003/art00007

line LPA was 96 483 (0.5% of public sector volume). First-line DST was estimated at 7734 (0.04% of public sector volume).

The total volume of 19.2 million tests resulted in a market value of US$22.9 million. This value represents 19% of the 2013–2014 RNTCP budget of US$121.1 million.[17] SSM volumes represented 88.9% of all tests in the public sector, and 62.4% of market value for this sector, making it the largest contributor in terms of both size and value (Figure 2A and Appendix Table A.1). Solid and liquid culture together accounted for 1.2% of the market test volumes and 10.9% of the public sector market value. Molecular tests (Xpert and LPA) accounted for 17.1% of the total public sector market value.

Private sector

In 2013, the private sector was estimated to have performed a total of 13.6 million TB tests (Figure 1B and Appendix Table A.2). A total of 7.4 million TSTs

Table 2 Total overall TB diagnostic market value (in USD) in India's public and private sectors, using unit costs for 2013

Diagnostic test	Volume in public sector	Volume in private sector	Total volume of tests performed	Proportion performed in public sector* %	Proportion performed in private sector* %	Unit cost USD	Overall market value million USD	Proportion of total value	Range of market value, based on sensitivity analysis million USD†
TST	1 543 927	7 398 090	8 942 017	17.3	82.7	1.12	10.0	14.1	8.9–11.2
IGRA	—	170 520	170 520	—	100	42.74	7.3	10.3	6.4–8.2
Smear (ZN+fluorescence microscopy)	17 072 298	4 061 214	21 133 512	80.8	19.2	0.84	17.8	25.1	12.7–23.2
Culture (liquid, does not include DST)	92 413	261 624	354 037	26.1	73.9	11.07	3.9	5.5	3.2–4.6
Culture (solid)	148 033	—	148 033	100	—	9.83	1.5	2.1	0.3–2.6
Speciation	79 588	—	79 588	100	—	3.95	0.3	0.4	0.3–0.3
Xpert	167 410	26 620	194 030	86.3	13.7	12.29	2.4	3.4	2.3–2.5
LPA (first-line)	96 483	32 064	128 547	75.1	24.9	18.18	2.3	3.3	2.2–2.5
LPA (second-line)	—	5 000	5 000	—	100	18.18	0.1	0.1	0.1–0.1
PCR	—	378 933	378 933	—	100	32.40	12.3	17.3	10.8–13.8
Solid first-line DST	7 734	—	7 734	100	—	29.88	0.2	0.3	0.2–0.3
Serology	—	1 244 476	1 244 476	—	100	10.26	12.8	18.0	11.2–14.3
Total	19 207 885	13 578 541	32 786 427	58.6	41.4	—	70.8	100	58.5–83.6

* Proportion of total test volumes.
† The sensitivity analysis was performed based on the range in costs listed in Table 1.
TB = tuberculosis; USD = United States dollar; TST = tuberculin skin test; IGRA = interferon-gamma release assay; ZN = Ziehl-Neelsen; DST = drug susceptibility testing; LPA = line-probe assay; PCR = polymerase chain reaction.

(54.5% of the total private sector volume) and 4.1 million SSM tests (29.9% of private sector volume) were performed. There were 261 624 liquid cultures (1.9% of private sector volume), 32 064 LPA tests (0.2% of private volume), 5000 second-line LPAs (0.03% of private volume) and 26 620 Xpert tests (0.2% of private volume). An estimated 378 933 in-house PCR tests were performed (2.8% of private volume). The volume of IGRAs conducted in 2013 was 170 520 (1.3% of private volume). Commercial serological tests were estimated to have a volume of 1.2 million (9.2% of private sector volume). Serology volumes in the private sector were estimated by taking half of the annual estimated value based on the assumption that the laboratories had stopped offering the test at the end of 2013 or the beginning of 2014. Although DST was performed by specific private laboratories, accurate data for private sector DST volumes were not available.

Using the price charged to the patient for performing individual tests, the overall private market value amounted to US$60.4 million; however, this figure includes laboratory profit margins. If the public sector costs were used for applicable tests (TST, SSM, liquid culture, Xpert and first- and second-line LPA), the private market value is estimated at US$47.9 million. Prices charged by laboratories in the private sector were consistently higher than the cost of the same test in the public sector. Prices charged for SSM, solid and liquid culture and LPA were all 45–55% higher when compared to test costs in the public sector. The price of Xpert was 135% higher than its estimated cost in the public sector.

Of the total private sector market value, estimated at US$60.4 million, the TST market was valued at US$15.3 million (25.4% the private sector market value, Figure 2B and Appendix Table A.2). SSM accounted for US$6.9 million (11.5% of private sector market value). In-house PCRs had an estimated value of US$12.3 million (20.3% of private sector market value). Serological tests accounted for US$12.8 million (21.1% of private sector market value). Liquid culture was estimated to have a market value of US$4.0 million (6.7% of private sector market value). IGRAs represented 1.2% of the total tests, but due to the high price per test (US$42.75), the market was estimated at US$7.3 million (12.1% of private sector market value).

Overall market and market segmentation

An estimated 32.8 million TB tests were performed in India in the public and private sectors combined (Figure 1C). To estimate the overall market value, the unit cost per test estimated for the public sector was applied to all test volume data. This generated an overall market value of US$70.8 million (Figure 2C).

With both sectors combined, the most common test in 2013 was SSM, with 21.1 million tests performed,

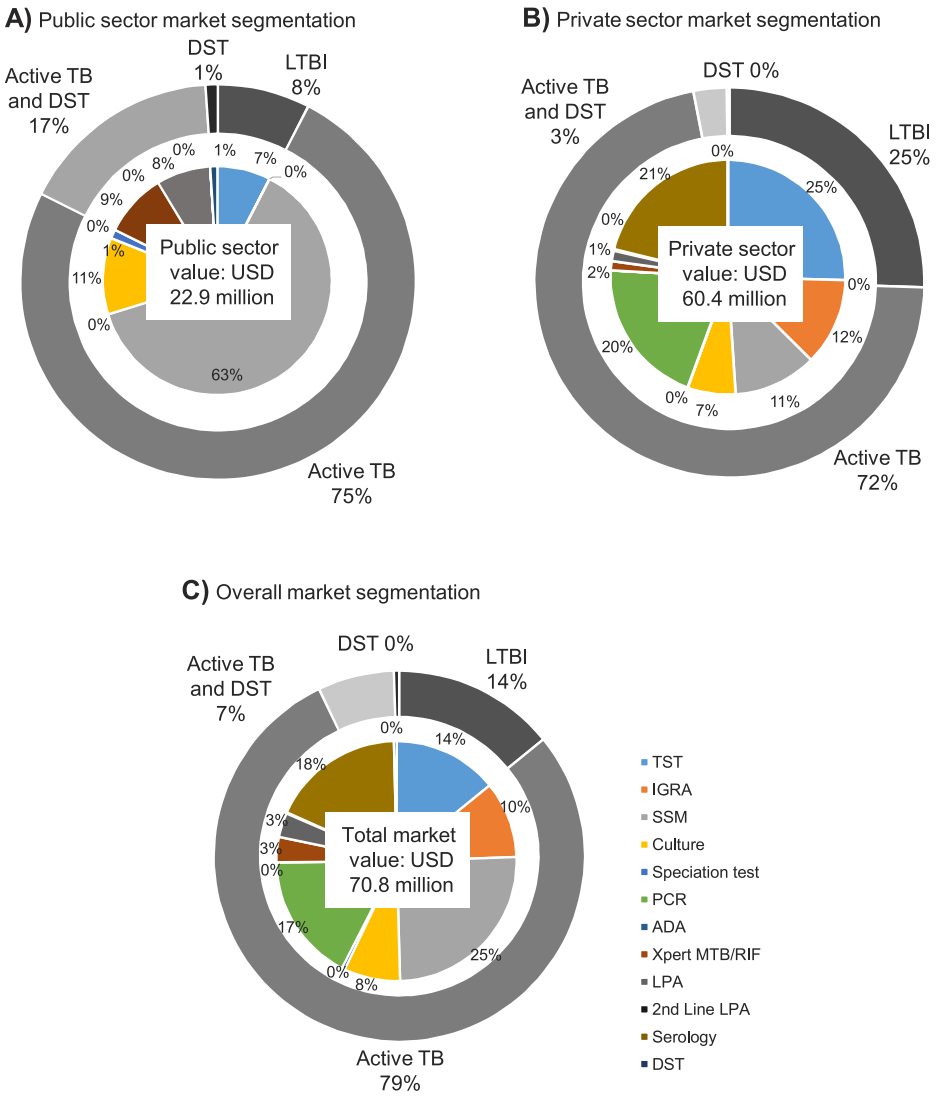

Figure 2 Market value of TB diagnostics in the public sector, the private sector and both sectors, by test and diagnostic purpose, India, 2013. Percentages rounded to the nearest integer. Inner circles show the proportion of the market value by different tests performed in **A)** the public sector, **B)** the private sector or **C)** both sectors. Market value costs per test in the public sector are based on costing data from the study performed by FIND, except for TST (which was performed exclusively for this study), while those for the private sector are based on the prices charged to patients for each test. Costs for the overall market value (both sectors combined) are 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 include TST, IGRA and serology. Tests for active TB include SSM, culture, speciation tests and PCR. Tests for active TB and DST refer to tests that can detect both *M. tuberculosis* as well as resistance to one or more first-line drugs, including Xpert and LPA. TB = tuberculosis; DST = drug susceptibility testing; LTBI = latent tuberculous infection; USD = United States dollar; TST = tuberculin skin test; IGRA = interferon-gamma release assay; SSM = sputum smear microscopy; PCR = polymerase chain reaction; ADA = adenosine deaminase; LPA = line-probe assay; FIND = Foundation for Innovative New Diagnostics. This image can be viewed online in colour at http://www.ingentaconnect.com/content/iuatld/ijtld/2016/00000020/00000003/art00007

representing a 64.5% share of nationwide tests. Using the public sector costs, the market value of SSM was US$17.8 million (25.1% of overall market value). In-house PCRs had a large share of the market value, with costs of US$12.3 million (17.3% of overall market value), which can be attributed to the high cost value of this test. In-house PCR volumes (n = 378 933) represented only 1.2% of the total test volume. Total culture volumes, including solid and liquid culture, were estimated at 502 070, representing 1.5% of total test volumes. The market value for culture-based testing in India was calculated to be US$5.4 million (7.6% of overall market value). TSTs represented 27.1% of nationwide tests, with an

overall value of US$10.0 million (14.1% of overall market value) when using the reduced public sector costs. Serological tests made up 3.8% of the total test volume, and due to the relatively high cost of this test (US$10.26), these tests were valued at US$12.7 million (18.0% of overall market value).

Tests conducted with the purpose of diagnosing active TB as well as for treatment monitoring (SSM, culture, speciation, PCR, serology) accounted for 68% of overall test volumes and 79% of the overall market value in 2013 (Figures 1C and 2C). Tests in which the detection of active TB and DST were combined in one (Xpert, first- and second-line LPA) represented 1% of overall test volumes and 7% of overall market value in 2013. Finally, LTBI tests (TST and IGRA) accounted for 31% of the overall test volumes and 14% of the overall market value.

Sensitivity analysis

The results of the sensitivity analysis are shown in Table 2. Market value was calculated using upper and lower limits of unit costs found in Table 1. The overall market value ranged between US$58.6 million and US$83.6 million.

DISCUSSION

An overall market value of US$70.8 million was calculated for the 32.8 million TB tests performed in India's public and private sectors. A previous analysis by some members of our group had estimated India's TB diagnostic market to be higher,[28] but were not able to precisely quantify test volumes in the private sector. The 2013 analysis was based on data provided by the RNTCP and communications with stakeholders in manufacturing and distribution of tests, as well as with private laboratory chains. The strength of our current 2013 study lies in the survey that was used as a basis for determining most of the private sector test volumes. Another big difference between the two analyses is that serological TB tests were widely used in 2011, while their use had greatly decreased by 2013 due to the 2012 ban by the government.

In the 2011 market analysis, serological tests made up a large proportion of the private testing market, estimated to be as high as 5.5 million tests in that year.[28] The Indian government banned these tests in January 2012; however, the ban did not have an immediate effect: serological tests were still manufactured and/or used in India in 2013, as confirmed through the survey conducted among private practitioners for this study. Fortunately, however, there has since been a clear decline in the number of serological tests being performed as well as a substantial reduction in serological tests being produced in India. This was verified through interviews with manufacturers, distributors and private laboratories.

India has a unique health care system, where private sector diagnosis of TB is very common. This differentiates India from many other high-burden countries, where the public sector is mostly responsible for TB care. For example, we observed that in South Africa and Brazil respectively 93% of 9.2 million tests and 91% of 2.4 million tests of the country's total TB diagnostic tests were performed in the public sector.[14,15] It is this private vs. public division that complicates the diagnostic landcape in India. Studies have found that private physicians and laboratories overuse CXR, underuse SSM, overprescribe TB drugs and prescribe irrational drug regimens.[21,29] The Indian private market purchases of first-line TB drugs were sufficient to treat 117% of India's incident cases in 2008.[30]

It is worth mentioning that India's ban on TB serology paved the way for an innovative effort to replace suboptimal TB tests in the private market with WHO-endorsed TB tests. The IPAQT initiative is attempting to increase the speed at which this transition is taking place.[24] The IPAQT business model is based on a shift from a high-margin, low-volume (premium) model to lower-margin, high-volume (mass market) pricing of WHO-endorsed tests such as Xpert, LPA and liquid culture. IPAQT member laboratories obtain test reagents and instruments at the same price as the public sector. In return, the private laboratories have agreed to not exceed negotiated, transparently advertised ceiling prices to patients. They have also agreed to notify all TB cases to the government, participate in EQA and avoid offering serological TB tests.

Because of this initiative, the cost of Xpert, LPA and liquid culture was reduced to approximately 30–50% less than private market prices before IPAQT was launched, and the prices are comparable to the banned TB ELISAs. Since its launch in April 2013, the IPAQT initiative has already achieved a pan-India presence, with over 105 laboratories providing these tests at affordable prices. Over 170 000 WHO-endorsed TB tests have been performed by IPAQT member laboratories.

The use of IGRAs in India's private sector has become a concern, as it seems to have increased in recent years. Indian physicians very rarely treat LTBI, and there is concern that IGRAs in India are primarily being used to diagnose active TB disease in the private sector.[31,32] This is speculated to be a consequence of the serology ban, and the preference for blood-based tests by private laboratories and doctors. Our results suggest that IGRAs account for about 12% of the private sector market value. The costs and consequences of this have been addressed in a recent modelling study.[33]

Our analysis has many limitations. First, all data from the private sector are imprecise estimates. As there is no comprehensive, organised data collection from the private sector, and as privately managed

patients are not routinely notified to the RNTCP, it is possible that we underestimated testing volumes. For example, India has a large number of private medical colleges and corporate hospitals, and their TB testing volumes are largely unknown. Second, data on DST are most likely underestimated. First-line DST volumes seem unusually low for India's high population and estimated MDR-TB burden. This is partly due to the lack of data on second-line culture DST values beyond the use of second-line LPAs in the public sector. DST also appears to be rare in the private sector, which was confirmed through the private sector survey, as most of the laboratories are unable to perform these tests. Although we are aware that some private laboratories offer liquid culture as well as second-line LPA, our data on these volumes may be an underestimate. Sales data from liquid culture manufacturers on first-line DST culture reagents led to an estimated volume of 7734 tests. The RNTCP states that 181 021 DST tests were performed in 2013; however, it does not specify how many of these were culture DST, Xpert and LPA.[17] This compromised an accurate estimation of culture-based first-line DST. The other limitation is the lack of data on CXR in both public and private sectors. All of these suggest that our overall TB market value may be underestimated.

Despite these limitations, our study provides the first estimate of the TB diagnostics market in India and suggests that the overall market for TB diagnostics in 2013 was US$70.8 million for over 32.7 million performed tests. Using the total market value and total patients notified in 2013 (1.4 million), the cost per patient notified was estimated to be US$51.

Given India's ambitious goal of universal access, ongoing plans to make universal DST available by 2019 and initiatives such as IPAQT, the TB diagnostics market is growing. Initial test numbers for 2014 show higher volumes of WHO/RNTCP-endorsed tests. In 2014, the combined volume for Xpert and LPA in the private sector was 118 900 tests as compared to 63 684 tests conducted in 2013. Volumes for Xpert grew by 175% in the private sector, likely driven by IPAQT. In 2014, 255 408 persons with presumed MDR-TB underwent DST in the public sector. This is approximately 40% more than the number of persons with presumed drug-resistant TB tested in 2013. About 108 609 first-line LPA tests were conducted in 2014 as compared to 96 483 tests in 2013. Given these trends, we intend to update our analysis in future.

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Conflicts of interest: The Clinton Health Access Initiative (CHAI), New Delhi, India, serves as the Secretariat of the Initiative for Promoting Affordable, Quality TB Tests (IPAQT) in India. C Denkinger, C Boehme, N Raizada and M D Perkins are employed by the Foundation for Innovative New Diagnostics (FIND, Geneva, Switzerland), a non-profit organisation that collaborates with industry partners, including Cepheid (Sunnyvale, CA, USA), Becton Dickinson (Sparks, MD, USA) and Hain LifeScience (Nehren, Germany), for the development and evaluation of new diagnostics for poverty-related diseases. MP serves as a consultant to the Bill & Melinda Gates Foundation, and on the Governing Council of IPAQT. He also serves on the Scientific Advisory Committee of FIND. He has no industry relations or conflicts.

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APPENDIX

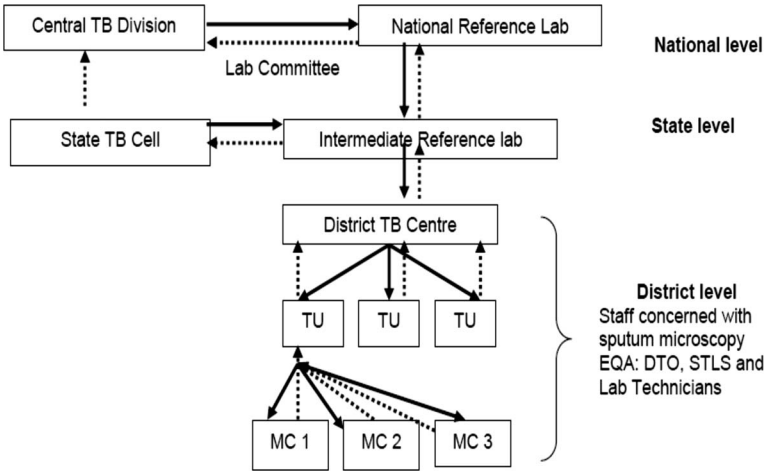

Figure A.1 Public sector laboratory network in India. (Source: Central TB Division, Ministry of Health and Family Welfare, Government of India). TB = tuberculosis; Lab = laboratory; TU = treatment unit; MC = microscopy centre; EQA = external quality assurance; DTO = District TB Officer; STLS = State TB Laboratory Supervisor.

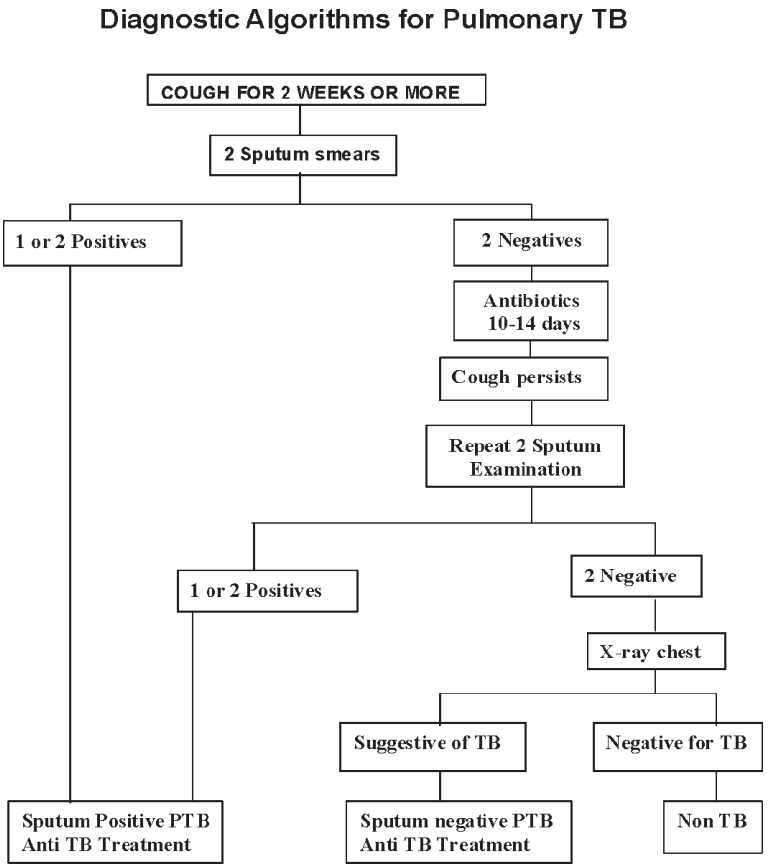

Figure A.2 Recommended diagnostic algorithm for sputum smear microscopy and chest X-ray for individuals with symptoms suggestive of PTB in India. (Source: Central TB Division, Ministry of Health and Family Welfare, Government of India). TB = tuberculosis; PTB = pulmonary TB.

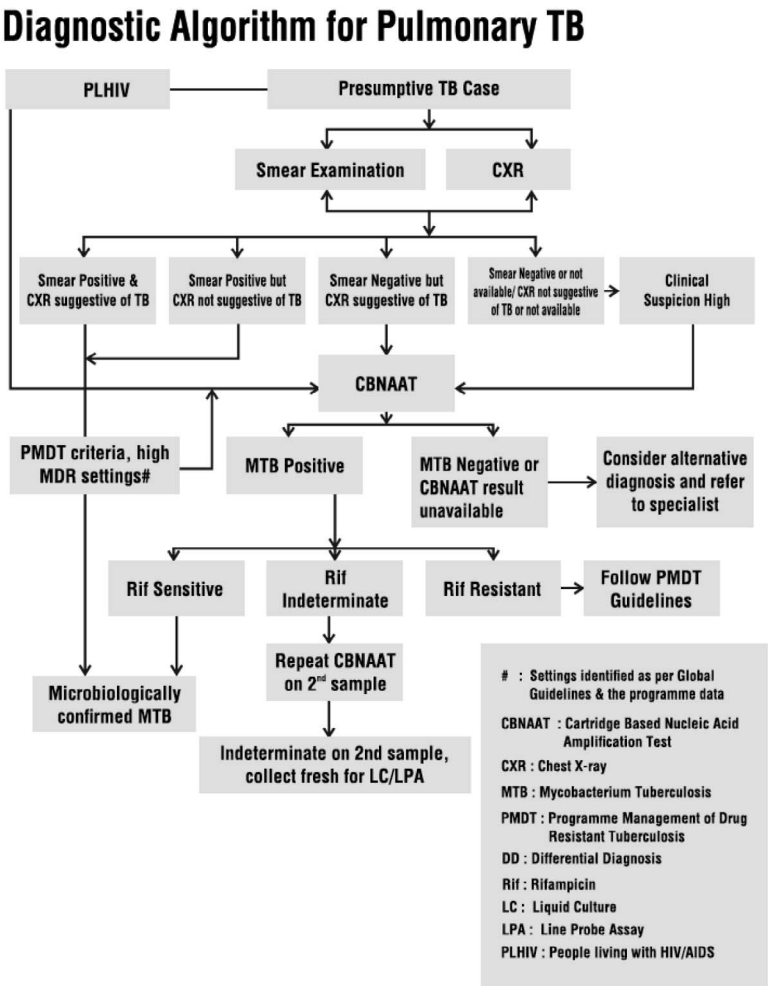

Figure A.3 Revised diagnostic algorithm for diagnosis of TB including DST, liquid culture testing and CBNAAT. (Source: Central TB Division, Ministry of Health and Family Welfare, Government of India). TB = tuberculosis; PLHIV = people living with human immunodeficiency virus/acquired immune-deficiency syndrome; CXR = chest X-ray; CBNAAT = cartridge based nucleic acid amplification test; PMDT = programmatic management of drug-resistant TB; MDR = multidrug-resistant; MTB = *Mycobacterium tuberculosis*; Rif = rifampicin; LC = liquid culture; LPA = line-probe assay.

Table A.1 Test volumes and market value of diagnostic tests for tuberculosis in the public sector, India, 2013.

Diagnostic test	Volume in public sector	Proportion of tests performed in public sector %	Unit cost USD	Market value of public sector million USD	Proportion of public sector value %
TST	1 543 927	8.0	1.12	1.7	7.4
IGRA	—	—	42.74	—	—
Smear (ZN+fluorescence microscopy)	17 072 298	88.9	0.84	14.3	62.4
Culture (liquid)	92 413	0.5	11.07	1.0	4.4
Culture (solid)	148 033	0.8	9.83	1.5	6.6
Speciation	79 588	0.4	3.95	0.3	1.3
Xpert	167 410	0.9	12.29	2.1	9.2
LPA (first-line)	96 483	0.5	18.18	1.8	7.9
LPA (second-line)	—	—	18.18	—	—
PCR	—	—	32.43	—	—
Solid first-line DST	7 734	0.04	29.88	0.2	0.9
Serology	—	—	10.26	—	—
Total	19 207 885	100	—	22.9	100%

USD = United States dollar; TST = tuberculin skin test; IGRA = interferon-gamma release assay; ZN = Ziehl-Neelsen; LPA = line-probe assay; PCR = polymerase chain reaction; DST = drug susceptibility testing.

Table A.2 Test volumes and market value of diagnostic tests for tuberculosis in the private sector, India, 2013

Diagnostic test	Volume in private sector	Proportion of tests performed in private sector %	Unit cost USD	Market value of private sector million USD	Proportion of private sector value %
TST	7 398 090	54.4	2.07	15.3	25.4
IGRA	170 520	1.3	42.74	7.3	12.1
Smear (ZN+fluorescence microscopy)	4 061 214	29.9	1.71	6.9	11.5
Culture (liquid)	261 624	1.9	15.35	4.0	6.7
Culture (solid)	—	—	11.07	—	—
Speciation	—	—	3.95	—	—
Xpert	26 620	0.2	29.07	0.8	1.3
LPA (first-line)	32 064	0.2	27.36	0.9	1.5
LPA (second-line)	5 000	0.03	27.36	0.1	0.2
PCR	378 933	2.8	32.43	12.3	20.3
Solid first-line DST	—	—	—	—	—
Serology	1 244 476	9.2	10.26	12.8	21.1
Total	13 578 541	100	—	60.4	100

USD = United States dollar; TST = tuberculin skin test; IGRA = interferon-gamma release assay; ZN = Ziehl-Neelsen; LPA = line-probe assay; PCR = polymerase chain reaction; DST = drug susceptibility testing.

RESUME

OBJECTIF : L'Inde représente un marché potentiel significatif pour les nouveaux tests. Nous avons évalué le marché indien des diagnostics de la tuberculose (TB) en 2013.

MÉTHODE : Les volumes de tests et leur coût unitaire ont été évalués pour le test cutané à la tuberculine, le test de libération de l'interféron gamma, la microscopie de frottis, la sérologie, les cultures, les tests de spéciation, les tests d'amplification de l'acide nucléique (la réaction polymérase en chaîne, le Xpert® MTB/RIF, tests de sondes en ligne) et les tests de pharmacosensibilité. Les données ont été obtenues à partir des rapports du Programme national révisé de lutte contre la TB. Les données du secteur privé ont été recueillies grâce à une enquête auprès des laboratoires et des praticiens privés ainsi qu'auprès des fabricants.

RÉSULTATS : En 2013, le secteur public d'Inde a réalisé 19,2 millions de tests pour un prix d'ensemble de US$22,9 millions. Le secteur privé en a réalisé 13,6 millions pour une valeur de US$60,4 millions lorsque les patients payaient les tests. La valeur totale du marché a été de US$70,8 millions en utilisant les coûts unitaires selon l'approche des matières actives pour les 32,8 millions de tests TB réalisés dans le pays tout entier. La microscopie de frottis a été le test le plus fréquemment réalisé, représentant 25% de la valeur totale du marché.

CONCLUSION : La valeur du marché estimé pour les diagnostics de TB en Inde a été en 2013 de US$70,8 millions. Ces données devraient s'avérer pertinentes pour les personnes qui élaborent les tests, les donateurs et ceux qui les mettent en oeuvre.

RESUMEN

MARCO DE REFERENCIA: La India representa un importante mercado potencial para las nuevas pruebas diagnósticas. Se analizó el mercado de la India para las pruebas de diagnóstico de la tuberculosis (TB) en el 2013.

MÉTODOS: Se evaluaron los volúmenes y los costos unitarios de la prueba cutánea de la tuberculina, las pruebas de liberación de interferón gama, la baciloscopia del esputo, las pruebas serológicas, los cultivos, las pruebas de identificación de especie, las pruebas de amplificación de ácidos nucleicos (es decir, una prueba interna de reacción en cadena de la polimerasa, la prueba Xpert® MTB/RIF y las pruebas con sondas en línea) y las pruebas fenotípicas de sensibilidad a los medicamentos. Los datos del sector público se obtuvieron a partir de los informes del Programa Nacional Revisado contra la Tuberculosis. Los datos del sector privado provinieron de una encuesta administrada a los laboratorios y los médicos privados. Se obtuvieron además datos de los fabricantes.

RESULTADOS: En el 2013 se realizaron 19,2 millones de pruebas en el sector público en la India, con un valor comercial de US$22,9 millones. En el sector privado se llevaron a cabo 13,6 millones de pruebas con un valor de US$60,4 millones, cuando se aplicaron los precios cobrados al paciente. Los 32,8 millones de pruebas de diagnóstico de la TB realizadas en todo el país representaron un mercado total de US$70,8 millones, al calcular los costos unitarios según el método de los ingredientes. La baciloscopia fue la prueba practicada con mayor frecuencia y correspondió al 25% del mercado total.

CONCLUSIÓN: Se estimó que el valor comercial del mercado de las pruebas diagnósticas de la tuberculosis en la India en el 2013 fue de US$70,8 millones. Estos datos son de interés para quienes se encargan del desarrollo de las pruebas, los donantes y las instancias que las ponen en práctica.