Xpert negative means no TB: A mixed-methods study into early implementation of Xpert in Puducherry, India

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Abstract

Introduction: Xpert MTB/RIF was implemented in 2016 as the initial diagnostic test for extrapulmonary, pediatric, and human immunodeficiency virus-associated tuberculosis (TB) and as an add-on test for sputum microscopy-negative patients under Revised National TB Control Programme, Puducherry, India. We intended to study the change in TB case notification rates (CNRs) after 2015 and explore the enablers and barriers for implementation of Xpert. Materials and Methods: Sequential mixed-methods study, quantitative phase followed by a descriptive qualitative phase (key informant interviews with healthcare providers in the program). Results: The TB (all forms) CNR increased in 2016 followed by a drop to 2015 levels in 2017. There was a reduction in patients notified as sputum-negative pulmonary TB and pediatric TB during 2016–2017. Healthcare providers used a negative Xpert result in ruling out TB among patients who would previously get diagnosed clinically. Perceived benefits of Xpert were efficiency, rapid results, and detecting resistance. Barriers included poor awareness among medical colleges and the private sector, difficulty in motivating sputum microscopy-negative patients for Xpert, and incompletely filled referral forms. Conclusion: Xpert-negative results should be interpreted cautiously after clinical assessment. Identified barriers should be addressed to ensure that all eligible undergo testing.

Keywords: Cartridge-based nucleic acid amplification test, India, initial diagnostic tool for TB, operational research, Structured Operational Research and Training Initiative

Introduction

Globally, there were an estimated 10.4 million new patients with tuberculosis (TB) in 2016 and 600,000 new patients with multidrug/rifampicin-resistant TB (MDR/RR-TB). Among the estimated patients with TB, 1 million (10%) were children and 1.2 million (11%) had human immunodeficiency virus (HIV)-associated TB. Extrapulmonary TB (EPTB) comprised 15% of the 6.6 million notified patients with TB.[¹]

India has the highest number of patients with TB and MDR/RR-TB. There were an estimated 2.8 million patients with TB (around half a million people died due to TB) with an estimated annual incidence of 211 per 100,000 population.[¹] Of the annually notified 1.4 million patients with TB from the public sector in 2016–2017, 5%–6% were children, 3% had HIV-associated TB, and 17%–18% had EPTB.[²,³]

Compared with microscopy, cartridge-based nucleic acid amplification test (CBNAAT), also widely known as Xpert MTB/RIF assay® (Cepheid, Sunnyvale, CA, USA), is an accurate diagnostic test for TB and also offers better sensitivity.
One qualitative study conducted on the implementation of Xpert among a pediatric population in four cities of India has elaborated challenges in implementation through interviews with treating physicians.\[^{13}\]

In 2016, India recommended the use of Xpert as the initial diagnostic test for HIV-associated TB, EPTB, and pediatric TB. The program also recommended Xpert as an add-on test for sputum microscopy–negative patients if chest radiography was suggestive of TB (we will henceforth use “targeted group for Xpert” to denote this group of patients).\[^{13}\] There is a need to assess implementation, including the changes in case notification rates (CNRs). We have limited information on enablers and barriers in introducing Xpert among this targeted group under programmatic setting. Understanding this requires a mixed-methods study design combining quantitative data collection with qualitative systematic enquiry. This is important as India moves toward the use of Xpert as the initial diagnostic test for TB among all clinically, geographically, and socioeconomically vulnerable populations.\[^{14}\]

This study was conducted in Puducherry, India, to assess the trends in CNRs of TB (all forms), sputum-negative pulmonary TB, pediatric TB, HIV-associated TB, EPTB, and MDR-TB before (2010–2015) and during (2016–2017) the implementation of Xpert. We also explored the enablers and barriers in using Xpert among the targeted groups from the providers’ perspective.

**Materials and Methods**

**Study design**

This was a sequential mixed-methods study where the quantitative phase (involving aggregate secondary data from the TB program) was followed by a descriptive qualitative phase.\[^{15}\]

**Study setting**

**General setting**

The study was conducted in the Union Territory of Puducherry (population ~1.4 million). It consists of four geographically separated districts: Puducherry, Yanam, Karaikal, and Mahe. Two districts are situated on the eastern coast and two on the western coast of the Indian peninsula.

The Revised National TB Control Programme (RNTCP) was first implemented in 2002. The district TB center in Puducherry district is the nodal administrative unit of RNTCP for all four districts. The Union Territory of Puducherry has seven subdistrict administrative units [tuberculosis units (TU) – four in Puducherry and one each in Yanam, Karaikal, and Mahe] and 27 designated microscopy centers (DMCs). Among the 27 DMCs, 9 are located in medical colleges, 4 in district-level hospitals, and 14 in primary- or secondary-level health centers.

**Specific setting**

Xpert machine was introduced for the targeted group in February 2016 at the Intermediate Reference Laboratory (IRL) in Puducherry district. The IRL is situated in the government hospital for chest diseases. The same facility has also been providing liquid culture for all forms of TB and line probe assay (LPA) for testing of MDR-TB (among patients with presumptive MDR-TB) since 2012, the details of which have been discussed elsewhere.\[^{15}\]

Samples from the targeted group for Xpert are received from DMCs in medical colleges or district-level hospitals. Facilities for sample collection for pediatric (induced sputum or gastric lavage) or extrapulmonary samples are available either at the medical colleges or at the government hospital for chest diseases. Samples of patients with presumptive TB among people living with human immunodeficiency virus (PLHIV) are referred from the antiretroviral therapy center which is located at the Indira Gandhi Medical College and Research Institute (a medical college under the Government of Puducherry). Samples of smear-negative and chest radiograph–positive patients are also mostly sent from DMCs in district-level facilities or medical colleges. Patients are referred here for chest radiography from the primary/secondary health centers.

After making an entry in the laboratory register of the DMC, samples are transported to the IRL by a nongovernmental organization or by a private medical college staff (distance range 0–25 km) or patient’s attendants (often a relative). Patients may also be asked by the DMCs and private sector to go to the IRL and provide the sample. Samples of patients from Karaikal, Mahe, and Yanam districts are referred to the nearby district hospitals with facility for Xpert. Since 2017, the new laboratory registers have been introduced at DMCs and give the option to enter the following details: sputum or nonsputum sample, HIV status, previous TB treatment history, whether patient belongs to a vulnerable population, and whether they were referred for Xpert/LPA, if applicable.\[^{15}\]

**Study population**

For the quantitative phase, the study population included all patients with TB notified (drug-susceptible and MDR/RR-TB) from the Union Territory of Puducherry between 1st January 2010 and 31st December 2017. For the qualitative phase, healthcare
providers involved in detection, testing, and management of presumptive TB among the targeted groups for Xpert in a program setting in Puducherry district (during March 2018 to April 2018) were purposively selected on the basis of their role in the program implementation.\[16\]

**Data variables, sources of data, and data collection**

**Quantitative phase**

Year-wise aggregate data that were collected from the program records included the following: number of notified TB (all forms, sputum-negative pulmonary TB, HIV-associated TB, pediatric TB, EPTB) and MDR/RR-TB, and population of Union Territory of Puducherry.

**Qualitative phase**

A total of 10 key informant interviews with medical officers (n = 5), microbiologists (n = 3), and laboratory technicians (n = 2) were conducted. Interviews ranged from 10 to 45 min. One participant was female, and the rest were males. Sample size was decided based on the saturation of information.

Five interviews were conducted each by AN (a male medical doctor (M.B.B.S., M.D) and KS (a female medical doctor (M.B.B.S., M.D). Both are trained in qualitative research and fluent in the local language (Tamil). Neither of them were from the program, but both worked as teaching faculty in a private medical college in the Puducherry district. The interviews were done on a date, time, and place convenient to the participants after informing them of the purpose of the study and establishing a rapport. All the interviews were audio-recorded. An interview guide with probing questions was used. During all the interviews, the participant, AN, and KS were present, where one investigator acted as an interviewer and the other as note-taker. At the end of the interview, debriefing was done between the investigators to ensure participant validation.\[16\]

**Data analysis and statistics**

**Quantitative phase**

The annual CNRs per 100,000 population segregated for all forms of TB, sputum-negative pulmonary TB, pediatric TB, HIV-associated TB, EPTB, and MDR/RR-TB from 2010 to 2017 were summarized using a line diagram.

**Qualitative phase**

Audio-recordings were transcribed and translated from Tamil into English by AN within 3 days of conducting the interviews. Manual coding and descriptive content analysis was done by two trained researchers (AN and EV), and categories and themes were developed. To strengthen interpretive credibility and to reduce subjective bias, categories and themes were reviewed by HDS and the disagreements were resolved through discussion.\[17-19\]

**Results**

**Quantitative phase**

The annual trend of TB CNR, all forms and among subcategories, is depicted in Figure 1. The TB (all forms) CNR reduced from 118 to 97 per 100,000 population between 2010 and 2017. There was an increase between 2015 and 2016 (from 97 to 106) followed by a decrease between 2016 and 2017 (from 106 to 97). The trend line of EPTB CNR during 2015–2017 was in the same direction as the TB (all forms) CNR. This was accompanied by a reduction in sputum-negative pulmonary (from 9 per 100,000 population to 6 per 100,000 population) and pediatric TB CNR (from 4 per 100,000 population to 2 per 100,000 population) during 2015–2017. The EPTB CNR was more or less constant over the study period.

**Qualitative phase**

Healthcare providers’ perceptions of the implementation of Xpert are presented below, under three major themes: perceptions of the trend in TB notification after implementation of Xpert among the targeted groups and the benefits and challenges of implementing Xpert.
I. Perceptions of trends in TB notifications
The quantitative results [Figure 1] were shared with healthcare providers during interviews, who were surprised to learn that the total case notification had decreased in 2017, especially for sputum-negative pulmonary TB and pediatric TB.

Many believed that this may be due to the fact that if a patient was diagnosed clinically as pulmonary TB before Xpert was implemented, further culture could take a minimum of 3 weeks. They described how previously many of these patients were empirically started on TB treatment without confirmation through culture. The same was the case for pediatric TB where most of the diagnosis was clinical before implementation of Xpert. Some doctors, such as the one cited below, thought that Xpert was the ‘gold standard’ test for all forms of TB and were not aware that the results may vary in extrapulmonary cases or if there were poor quality samples: “but if the CBNAAT is negative, they [doctors] won’t start the treatment thinking that it is the gold standard.”

Another reason for poor notification suggested by several interviewees, including the key informant cited below, was that many healthcare providers were not aware that Xpert was available.

Referral is not there. Some departments know and utilise it properly, but the rest of the medical colleges. We have not received samples from the rest of the medical colleges. The [lack of referral from the] private sector is one more reason. So far we have only received five or six samples. Their support is very … we can say almost nil. (Key informant, IRL)

A medical officer at a medical college believed that the decrease in notifications could be due to a decrease in the incidence of TB itself: “I feel like the existence is low. I feel paediatric TB is coming down in the community.”

II. Benefits of Xpert
Key informants discussed several benefits of Xpert, including efficiency, detecting resistance, and ease of use. The benefit of being able to detect rifampicin resistance was also noted.

Efficiency
Interviewees described how the implementation of Xpert enabled them to receive results more quickly, which in turn decreased the amount of time it took to initiate patients on treatment:

In CBNAAT, you can get the results same day itself, that is the main advantage. Second thing is identifying TB in pauci bacillary group, like in paediatric group, we may not have enough sputum. Even with minimal secretions we can process for CBNAAT. (Medical officer)

The healthcare providers appreciated same-day diagnosis as it was beneficial for the patient and believed it had wider community benefits in preventing the spread of TB.

Reporting was done quickly and communicated through email. Most key informants said that they receive the report in an average of 3 days:

If I am seeing a patient today it means he can give the sample tomorrow morning. The processing speed depends on the sample load in the IRL. Usually they load on the sample day itself. If not they will load it the next day. Then they have to write a report and give it to them which they do it on the next day. So usually it takes three days from the time of seeing the patient to arrival of report. Even though the result is available within two hours, because of these transport issues, like the patient has to go there and then with the result they have to come back here, which takes three days. (Medical officer)

However, as this microbiologist describes, the improved turnaround time also created increased demand, which in turn created delays in processing:

Initially many clinicians were not aware about the turnaround time. Once they came to know the turnaround time is just one and half hours, they started sending samples and created problems [delays in result]. Then we spoke with the administration, and we provided one person dedicated for this transportation.

Ease of use
Many key informants believed Xpert was beneficial, simple to operate, and ‘easy to handle’:

CBNAAT is a very simple machine to handle. You just have to add a solution and load the cartridge. This can be done easily in any setup. If you have a small room like this with a light and a fan you can operate a CBNAAT machine. (Medical officer)

A laboratory technician suggested that ‘experts’ were not needed to use the machine as long as technicians were given the appropriate training:

This [Xpert] is just a machine. If you load in a cartridge it will show the result. [A] simple training is enough; senior experts are not needed for this test.

III. Perceived challenges with implementing Xpert
The main reported challenges related to sample collection and transport, problems at the level of the IRL, and lack of knowledge about Xpert from healthcare providers.

Challenges related to sample collection and transport
Healthcare providers found it difficult to motivate sputum microscopy–negative patients to give sputum for Xpert testing. It was also difficult to collect and send two samples from people who had already traveled long distances to reach the medical college and district-level facility for chest radiography. These patients had to return with two specimens for CBNAAT testing. One suggestion was that it would be better to have a satellite collection center to help the patients and to reduce loss to follow-up.

First day they say they are not getting sputum. We ask them to come the next day. But due to distance they may
not come. They may feel that a tablet has been given, so why do we have to go once again? Moreover they don't understand the importance of this testing. We will miss the patient. (Laboratory technician)

It will be better if they could give their sputum in their nearest PHC from there shifting of the samples possible. We are transporting from here to the IRL every day. But on the patient point of view if they could be able to give the sample in the nearby PHC it would be better. (Laboratory technician)

Challenges at the level of IRL

According to the healthcare providers working in the IRL, Xpert testing request forms were not filled in completely or accurately, which made them difficult to return to the patients and referring doctors: “another challenge is filling the forms. Rarely doctors fill and submit the complete form.”

In addition, key informants reported that they received inadequate or poor quality samples and samples sent in nonsterile containers. Key informants working in laboratories, such as microbiologist, also reported an overload of work and samples and an overload in the processing of extrapulmonary samples:

Yes, we run three cycles right now [during duty hours]. We start the fourth circle before we close [the lab] and on the next morning we read the result. This is how we manage the case load.

Healthcare provider–related challenges

Some departments in medical colleges were not fully aware about Xpert and only a few medical colleges sent samples to the IRL. A poor response from private healthcare providers was reported, despite Xpert testing being free:

Partnerships are still lacking in the private sector. They are still sending samples to some other private labs. The only thing is they have to fill the form and they don't like it [because] it needs more details. They need to find much time to fill all those details. That is the only issue with private doctors or private nursing homes. Otherwise they are in a good position to send samples to our centre. It is absolutely free of cost. It is good for the patient also. They will get good results. [We] still need to sensitise them because many of them may not aware about this CBNAAT. (Medical officer)

Others mentioned that the number of requests for Xpert as an add-on test for sputum-negative presumptive TB was low despite many high-load settings having a large load of presumptive pulmonary TB. In some centers, doctors were available only in the morning hours and patients with presumptive pulmonary TB were followed up on alternate day, resulting in a delay in diagnosis or loss to follow-up of patients.

Discussion

This is an important mixed-methods study from a programmatic setting in India, where a qualitative systematic enquiry was done to explore the implementation of Xpert as an initial diagnostic test for extrapulmonary, pediatric, and HIV-associated TB and as an add-on test for sputum microscopy-negative patients. Key benefits and challenges in implementing Xpert were identified.

This study had some limitations. First, we could not perform a trend analysis which included an assessment of notifications post Xpert implementation against the projected trends. We did not have adequate numbers of annual notifications for MDR/RR-TB, pediatric TB, and HIV-associated TB. In addition, we only had two postimplementation years to assess the change in trend. Second, we did not include private practitioners in the study to further explore the reasons for limited referral from private sector. Third, we included key informants from Puducherry district and did not include those from Mahé, Yanam, and Karaikal districts. This was due to logistical reasons as these districts were geographically far away from each other. However, this appears to be a minor limitation as Puducherry district contributed to 80% population of Union Territory of Puducherry.

Limitations notwithstanding, the study had some key findings. First, the healthcare providers used Xpert in ruling out TB among patients who would previously get diagnosed clinically. This resulted in a relative reduction in the number of patients being notified as sputum-negative pulmonary TB and pediatric TB after 2016. Similar findings were reported in project settings in four major cities of India where Xpert was used for diagnosis in presumptive TB among children. However, when it comes to interpreting the negative Xpert results, providers should be cautious in their approach because of potential false-negative results. Although the specificity of the Xpert is consistently high, the sensitivity varies with the type of sample: add-on test following a negative sputum microscopy (68%), initial diagnosis among PLHIV (79%), and initial diagnosis of EPTB (lymph node tissue and aspirate – 85%, cerebrospinal fluid – 80%, gastric lavage – 84%, pleural fluid – 44%).

Second, globally noticed perceived benefits including efficiency, rapid results, and detecting resistance were also observed in our study. In addition, we explored the implementation of Xpert from the point of view of the laboratory technician at the Xpert facility (IRL). They found the machine easy to handle with minimal training. The Xpert machine was being utilized optimally. No logistic issues related to the Xpert machine in IRL were identified, unlike similar studies from Mongolia and Nigeria where training-related issues, frequent breakdown, and lack of cartridges were observed.

Third, a key concern of the healthcare providers was the difficulty in motivating the sputum microscopy-negative patients to return to the medical college or district-level health facility with two samples for Xpert testing, especially those who came from distant places. It is to be noted that initially these patients were referred to the nearest medical college or district-level health facilities for chest radiography. This was also corroborated by the fact that the providers perceived that the number of
Xpert requests for this indication (as an add-on test for sputum microscopy–negative chest radiograph positive) at the IRL was less than expected. It was suggested to have a “satellite collection center” (on a daily basis) so that patients could provide samples to the nearest centers instead of repeatedly visiting the medical college or district-level health facilities. Similar findings were seen in Bhopal, India (2017), where there were challenges faced in ensuring patients (diagnosed patients with TB who were eligible for drug susceptibility testing) return to the DMC with two samples. \[19\]

Fourth, another issue of concern was incompletely filled referral forms. Referral forms help in the documentation of important information about the patients as well as in the follow-up of patient and treating doctor, and help in fast dissemination of the result. This was also reported previously from Puducherry. \[19\] This problem needs to be addressed through proper sensitization and training among the healthcare providers. Unlike other studies where the reporting of the results from a central laboratory was identified as a problem, in our study reporting was done through email in addition to hard copies of documents, which was welcomed by the healthcare providers.

Finally, the lack of awareness about Xpert facility in medical colleges and poor response from private providers were identified as barriers. These need to be addressed by creating awareness and knowledge about the Xpert among the physicians in the medical colleges and private sectors.

**Conclusion**

In Puducherry, India, Xpert was implemented as the initial diagnostic test among a subgroup of patients with presumptive TB. Providers should be cautious in ruling out TB immediately after a negative result if Xpert is used for extrapulmonary and pediatric TB and as an add-on test after negative smear microscopy. This decision should be made after making a thorough clinical assessment. Barriers such as the lack of awareness regarding Xpert in the private sector and medical colleges need to be addressed. There is scope to improve the use of Xpert as an add-on test among sputum microscopy–negative and chest radiograph–positive patients.

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**Author’s contribution**

Conceived and designed the study: NA, HDS, EV, DK, KS; data collection: NA, KS, AJP; data analysis: NA, HDS, EV, MM; prepared first draft: NA, HDS, EV; reviewed and approved the final draft: all authors.

**Ethics approval and consent to participate**

Ethics approval was obtained from the Institutional Ethics Committee of the Pondicherry Institute of Medical Sciences, Puducherry (RC-17/98), India, and the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease (The Union), Paris, France (No. 94/17). Administrative approval was also obtained from the state tuberculosis officer (PSHM/RNTCP/acc/S2/2017-18/239). Written informed consent was obtained from all key informants before conducting the interviews and this process was approved by the ethics committees.

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**Conflicts of interest**

There are no conflicts of interest.

**References**

1. World Health Organization (WHO). Global Tuberculosis Report 2017 [Internet]. Geneva, Switzerland: 2017. Available from: http://apps.who.int/iris/bitstream/handle/10665/259366/9789241565516-eng.pdf;jsessionid=60411D83FABAC0A7F80DE05D6228EBB?sequence=1. [Last cited on 2018 Jan 24].

2. Revised national tuberculosis control programme (RNTCP); Central TB division; Ministry of Health and Family Welfare; Government of India. India TB Report 2018 [Internet]. New Delhi: 2018. Available from: https://tbcindia.gov.in/
showfile.php?lid=3314. [Last cited on 2018 Jan 24].

3. Revised national tuberculosis control programme (RNTCP); Central TB division; Ministry of Health and Family Welfare; Government of India. TB India 2017 [Internet]. New Delhi: 2017. Available from: http://www.tbcindia.nic.in/index1.php?lang=1&level=1&sublinkid=4738&lid=3275. [Last cited on 2018 Jan 24].

4. Kaur R, Kachroo K, Sharma JK, Vatturi SM, Dang A. Diagnostic Accuracy of Xpert Test in Tuberculosis Detection: A Systematic Review and Meta-analysis. Journal of global infectious diseases [Internet] 8:32-40. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27013842. [Last cited on 2018 Jan 24].

5. Detjen AK, DiNardo AR, Leyden J, Steingart KR, Menzies D, Schiller I, et al. Xpert MTB/RIF assay for the diagnosis of pulmonary tuberculosis in children: a systematic review and meta-analysis. The Lancet Respiratory medicine [Internet] 2015;3:451-61. Available from: http://linkinghub.elsevier.com/retrieve/pii/S2213260015000958. [Last cited on 2017 Sep 06].

6. Denkinger CM, Schumacher SG, Boehme CC, Dendukuri N, Pai M, Steingart KR. Xpert MTB/RIF assay for the diagnosis of extrapulmonary tuberculosis: A systematic review and meta-analysis. The European respiratory journal [Internet] 2014;44:435–46. Available from: http://erj.ersjournals.com/cgi/doi/10.1183/09031936.0007814. [Last cited on 2017 Sep 06].

7. Raizada N, Sachdeva KS, Swaminathan S, Kulsange S, Khaparde SD, Nair SA, et al. Piloting Upfront Xpert MTB/RIF Testing on Various Specimens under Programmatic Conditions for Diagnosis of TB & DR-TB in Paediatric Population. PloS one [Internet] 2015;10:e0140375. Available from: http://dx.plos.org/10.1371/journal.pone.0140375. [Last cited on 2017 Sep 06].

8. McDowell A, Raizada N, Khaparde SD, Rao R, Sarin S, Kalra A, et al. "Before Xpert I only had my expertise": A qualitative study on the utilization and effects of Xpert technology among pediatricians in 4 Indian cities. PloS one [Internet] 2018;13:e0193656. Available from: http://dx.plos.org/10.1371/journal.pone.0193656. [Last cited on 2018 Jun 11].

9. World Health Organization (WHO). Global Tuberculosis Report 2016 [Internet]. Geneva, Switzerland: 2016. Available from: http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:No+title#0. [Last cited on 2018 Jan 24].

10. Boehme CC, Nabeta P, Hillemann D, Nicol MP, Shenai S, Krapp F, et al. Rapid molecular detection of tuberculosis and rifampin resistance. The New England journal of medicine [Internet] 2010;363:1005-15. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20825313. [Last cited on 2018 Jan 24].

11. World Health Organization (WHO). Automated Real-Time Nucleic Acid Amplification Technology for Rapid and Simultaneous Detection of Tuberculosis and Rifampicin Resistance: Xpert MTB/RIF Assay for the Diagnosis of Pulmonary and Extrapulmonary TB in Adults and Children: Policy update [Internet]. Geneva, Switzerland: 2013. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25473701. [Last cited on 2018 Jan 24].

12. Rendell NI, Bekhbat S, Ganbaatar G, Dorjjavdan M, Pai M, Dobler CC. Implementation of the Xpert MTB/RIF assay for tuberculosis in Mongolia: A qualitative exploration of barriers and enablers. PeerJ [Internet] 2017;5:e3567. Available from: https://peerj.com/articles/3567. [Last cited on 2018 Jun 11].

13. Revised national tuberculosis control programme (RNTCP); Central TB division; Ministry of Health and Family Welfare; Government of India. Technical and operational guidelines for tuberculosis control in India. New Delhi: 2016.

14. Revised national tuberculosis control programme (RNTCP); Central TB division; Ministry of Health and Family Welfare; Government of India. Guidelines on Programmatic Management of Drug-Resistance Tuberculosis in India 2017. New Delhi: 2017.

15. Shewade HD, Govindarajan S, Sharath BN, Tripathy JP, Chinnakali P, Kumar AM V, et al. MDR-TB screening in a setting with molecular diagnostic techniques: Who got tested, who didn't and why? Public health action [Internet] 2015;5:132–9. Available from: http://openurl.ingenta.com/content/xref?genre=article&issn=2220-8372&volume=5&isue=s+&page=132. [Last cited on 2017 Sep 06].

16. Mack N, Woodsong C, McQueen KM, Guest G, Namey E. Qualitative Research Methods: A data collector’s field guide [Internet]. 2011. Available from: https://www.fhi360.org/sites/default/files/media/documents/Qualitative Research Methods - A Data Collector’s Field Guide.pdf [Last cited on 2018 Jan 24].

17. Creswell J, Plano Clark V. Designing and Conducting Mixed Methods Research. London (United Kingdom): Sage Publications Ltd; 2007.

18. Kvale S. Doing interviews. London (United Kingdom): SAGE Publications; 2007.

19. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): A 32-item checklist for interviews and focus groups. International journal for quality in health care: Journal of the International Society for Quality in Health Care / ISQua 2007;19:349-57.

20. Gidado M, Nwokoye N, Nwadike P, Ajiboye P, Eneogu R, Useni S, et al. Unsuccessful Xpert* MTB/RIF results: The Nigerian experience. Public health action [Internet] 2018;8:2-6. Available from: http://www.ingentaconnect.com/content/10.5588/pha.17.0080. [Last cited on 2018 Jun 11].

21. Monedero-Recuero I. Xpert implementation in challenging scenarios: A brand-new car running on the same bumpy old roads. Public health action [Internet] 2018;8:1. Available from: http://www.ingentaconnect.com/content/10.5588/pha.18.0012. [Last cited on 2018 Jun 11].

22. Shewade HD, Kokane AM, Singh AR, Parmar M, Verma M, Desikan P, et al. Provider reported barriers and solutions to improve testing among tuberculosis patients ‘eligible for drug susceptibility test’: A qualitative study from programmatic setting in India. PLOS ONE [Internet] 2018;13:e0196162. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29677210. [Last cited on 2018 Jun 13].