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# Combination of Xpert MTB/RIF and MTBDR*plus* for Diagnosing Tuberculosis in a Chinese District

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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**Background:** The incidence of tuberculosis (TB) remains high in many countries, including some middle- and high-income countries without financial constraints for diagnosis and treatment. The implementation of an improved algorithm for diagnosis using 2 rapid molecular tests should help reduce the TB burden.

**Material/Methods:** Between April 2018 and March 2019, sputum samples from 711 patients suspected of TB in Nanshan, Shenzhen, China, were included in this prospective study. All sputum samples were examined by smear microscopy, Mycobacterium Growth Indicator Tube (MGIT) 960 culture, and Xpert MTB/RIF. The sputum remnants of Xpert MTB/RIF were used for MTBDR*plus* to confirm the Xpert results both for the presence of TB bacilli and for resistance to rifampicin (RIF), and also to diagnose multidrug-resistant tuberculosis (MDR-TB).

**Results:** In total, 200 (28.1%) of the 711 sputa were positive for TB by Xpert MTB/RIF, and the sputum remnants were used for MTBDR*plus*. The simultaneous use of Xpert MTB/RIF and MTBDR*plus* directly on sputum samples permitted accurate bacteriologic confirmation of TB in 64% (119/187) of cases and detection of 70% (7/10) of strains that were MDR.

**Conclusions:** The implementation of 2 rapid nucleic acid-based tests on sputum samples could facilitate the prompt and appropriate treatment of most TB cases.

**MeSH Keywords:** **Molecular Diagnostic Techniques** • ***Mycobacterium tuberculosis*** • **Tuberculosis, Multidrug-Resistant**

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## Background

Tuberculosis (TB) is still the leading cause of death due to an infectious disease worldwide [1]. Of the estimated 10 million new global cases of TB in 2018, about half a million cases were multidrug-resistant (MDR-TB) (WHO 2019 Global TB report), but less than 40% of these were detected and less than a one-third started on appropriate treatment. The incidence of new MDR-TB cases has not declined despite efforts to implement rapid diagnosis and drug susceptibility testing (DST). MDR-TB is resistance to at least rifampicin (RIF) and Isoniazid (INH), while XDR-TB is defined as MDR plus additional resistance to any injectable agent and also any fluoroquinolone. Because antibiotic-resistant mutations generally affect essential enzymes in the major metabolic pathways, it was initially thought that drug-resistant strains would be less infectious and transmissible than drug-sensitive TB, but several studies have shown MDR-TB to be highly transmissible [2,3].

TB is endemic in many countries, including middle- and high-income countries such as China and India. Transmission of MDR-TB is a serious problem in the rapidly developing city of Shenzhen in Southern China [4]. Prompt identification of MDR-TB is crucial for curing patients early in their disease course, thereby limiting community transmission. Rapid commercial tests are now available for TB diagnosis and DST based on the detection of mutations associated with resistance in amplified fragments of TB DNA [5]. Among the rapid tests, Xpert MTB/RIF [6] and MTBDR*plus* [7] have shown sensitivities of 98% for smear-positive and 72% for smear-negative culture positive specimens, with specificities greater than 98% [8]. Both tests are endorsed by the World Health Organization (WHO) for TB diagnosis and the detection of rifampicin (RIF) resistance [9,10] and MTBDR*plus* is also endorsed for the detection of isoniazid (INH) resistance. Culture-based phenotypic tests, which take much longer, are used to confirm the RIF resistance or sensitivity detected by rapid nucleic acid-based tests. Phenotypic DST is also used to detect resistance to drugs that are not included in the available rapid tests. In many settings, however, routine cultures are simply not feasible because of their cost, the absence of BSL3 facilities, and the high work-load and expertise required.

The Xpert MTB/RIF and MTBDR*plus* tests use different technologies – quantitative PCR for Xpert MTB/RIF and line probe assay for MTBDR*plus*. While technological limitations can lead to false results with both tests, the errors are likely to be different for each method. The simultaneous use of both tests can make each test a control for the other, thereby yielding more accurate results than can be obtained when either test is used alone.

We previously showed that the unused remnants of sputa processed for GeneXpert can be tested with MTBDR*plus* to confirm a diagnosis of TB and susceptibility to RIF, and also detect resistance to INH [11]. This prompted us to develop an algorithm employing the Xpert MTB/RIF and MTBDR*plus* tests in the absence of cultures for phenotypic DST. In the present study, however, sputum cultures were routinely made from all sputum specimens, but used only to repeat the MTBDR*plus* test with those samples on which it produced uninterpretable results with the Xpert remnants. The cultures were not used for phenotypic DST.

Our study was conducted at the CCDC of the Nanshan district of Shenzhen. Shenzhen is a rapidly growing city with a large "floating population" that is attracted from all over China for jobs in the many industries in Shenzhen. However, once they are suspected to have developed TB, many patients choose to return to their hometowns for treatment, making follow-up of TB patients difficult [12]. This increases the urgency for the rapid detection of tuberculosis and drug resistance, so that the patients can be started on appropriate therapy promptly to allow them to stay and be treated in Shenzhen or return to their home town after beginning effective treatment. We therefore studied the potential benefit of the simultaneous use of Xpert MTB/RIF and MTBDR*plus* for the rapid diagnosis of TB and detection of drug resistance in all patients suspected of having TB who presented to the TB Centre of the Nanshan CCDC.

## Material and Methods

### Study site and ethics approval

This study was conducted at the laboratory of the Shenzhen Nanshan Center for Chronic Disease Control, Shenzhen, China, and ethics approval was granted by the Ethics Review Committee of the Shenzhen Nanshan Centre for Chronic Disease Control. Signed informed consent was obtained from all participants. The tests employed have been approved by the WHO for the evaluation of TB cases and required no additional patient samples beyond routine sputum specimens. The results were made irreversibly anonymous.

### Specimens

Between April 2018 and March 2019, 711 morning sputum specimens were collected from 711 patients suspected of having TB based on clinical signs and symptoms of the disease. The specimens were collected in the laboratory and then either immediately processed or refrigerated for processing within 24 h. All specimens were prepared and processed according to the international standards recommended by the WHO [13,14].





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The study was carried out in 4 steps. In Step 1, the Xpert MTB/RIF test was performed on sputum samples. In Step 2, the MTBDR*plus* test was performed on the remnants of the Xpert processed sputum samples found to be positive for TB by Xpert. In Step 3 the MTBDR*plus* test was performed on cultures of those sputum samples that gave ambiguous results in Step 2. Finally, in Step 4, the MTBDR*sl* test was performed on cultures considered to be MDR-TB based on the results of Steps 2 and 3.

### Acid-fast bacilli examination

Microscopy examination was performed on all sputa after Ziehl-Neelsen staining [15]. The number of acid-fast bacilli seen on microscopy was classified according to WHO quantification scales. For each glass slide, a total of 300 fields were observed by an experienced technician. Smear acid-fast bacilli (AFB) were graded as – (negative, no AFB/300 fields), scanty (1–8 AFB/300 fields), + (3–9 AFB/100 fields), ++ (1–9 AFB/10 fields), +++ (1–9 AFB/field) and ++++ (≥10 AFB/field) [13,16,17].

### Use of GeneXpert remnants for the GenoType assay

One milliliter (1 mL) of the sputum specimens was mixed with 2 mL of GeneXpert sample reagent. After 15 min at room temperature, 2 mL of the inactivated material was transferred to a cartridge for Xpert MTB/RIF analysis (Version 6.0, Cepheid, USA). For the 200 samples in which TB was detected with the Xpert MTB/RIF test, 1 ml of the remainder of the sputum samples processed for Xpert MTB/RIF was used for the GenoType MTBDR*plus* V2.0 (Hain Lifescience) test, as previously described [11]. The GenoType MTBDR*plus* test and MTBDR*sl* tests (V1.0) were performed according to the manufacturer's instructions. Culture inactivation was done by heating the cultures for 30 min at 95°C.

### MGIT960 culture

All sputum specimens were digested with N-acetyl-L-cysteine and sodium hydroxide (NALC-NaOH) for 15 min. PBS buffer was then added to a total volume of 50 mL and the suspension was centrifuged for 15 min at 3000×g. Following centrifugation, the supernatant was discarded and the sediment was suspended in 1.5 mL PBS buffer. A 7-mL BACTEC MGIT tube was inoculated with 0.5 mL of the suspension and incubated in the MGIT960 system (BD Microbiology Systems, USA). All positive liquid cultures were confirmed by ZN staining and microscopy.

## Results

### Two rapid tests for direct diagnosis on sputa

Over a 12-month period from April 2018 to March 2019, in parallel with the regional TB control program, we obtained 711 fresh sputum samples from patients presenting to the district Shenzhen Nanshan Center for Chronic Disease Control (Nanshan CCDC, Shenzhen, China) with a clinical suspicion of having pulmonary TB. The sputum samples were initially subjected to microscopy for the presence of TB bacilli, and cultures were set up and sent to the central Shenzhen Center for Chronic Disease Control (Shenzhen CCDC, China) where DST was performed using MTBDR*plus*. The sputum samples were also tested in parallel with Xpert MTB/RIF and MTBDR*plus* at the Nanshan District CCDC.

The results of each of the steps are presented in Figure 1, and the microscopy and culture results with the sample characteristics are shown in Table 1. Of the 711 sputum samples, 510 (71.7%) were negative for TB by the Xpert MTB/RIF and the test was considered invalid for 1 sample. The Xpert identified 200 (28.1%) samples as positive for TB. Among these, 186 (93.0%) were found to be sensitive to RIF, 13 (6.5%) resistant to RIF, and 1 (0.5%) had an indeterminate RIF result.

The Xpert MTB/RIF test can only detect RIF resistance. Therefore, in Step 2, for the 200 samples in which TB was detected by Xpert MTB/RIF, the remnants of the sputum processed for Xpert were used with the MTBDR*plus* to confirm the Xpert MTB/RIF results and also to detect INH resistance. MTBDR*plus* performed with the Xpert remnants yielded 131/200 unambiguous results. Ninety-four of these were positive for TB and sensitive to RIF and INH. Eleven of the 13 samples (84.6%) identified as RIF-resistant by Xpert MTB/RIF were confirmed as RIF-resistant by MTBDR*plus*. Seven of these 11 were found to be also INH-resistant and thus MDR-TB, and the other 4 were INH-sensitive and therefore monoresistant to RIF. There were also 14 samples that were monoresistant to INH. Twelve samples positive for TB by Xpert MTB/RIF were negative for TB by MTBDR*plus*, and all 12 exhibited no growth in MGIT cultures.

### Complementary diagnostic with rapid tests on cultures

The sample characteristics are presented in Table 2. MTBDR*plus* tests were performed on cultures from the 69 samples that were positive for TB with the Xpert MTB/RIF, but gave ambiguous results with MTBDR*plus* performed on Xpert remnants (Step 3). This allowed the confirmation of additional Xpert TB-positive cases and antibiotic resistance. Three of the cultures were contaminated and discarded. The remaining 66 cultures gave unambiguous MTBDR*plus* results, including one found to be negative for TB. Of the other 65 cultures, MTBDR*plus* identified 4 samples as monoresistant to INH, 2 that were monoresistant to RIF, and 3 that were MDR. The Xpert had not detected RIF resistance in one of the 4 isolates determined to be mono-RIF-resistant, and one of the 3 isolates determined to be MDR by MTBDR*plus*.





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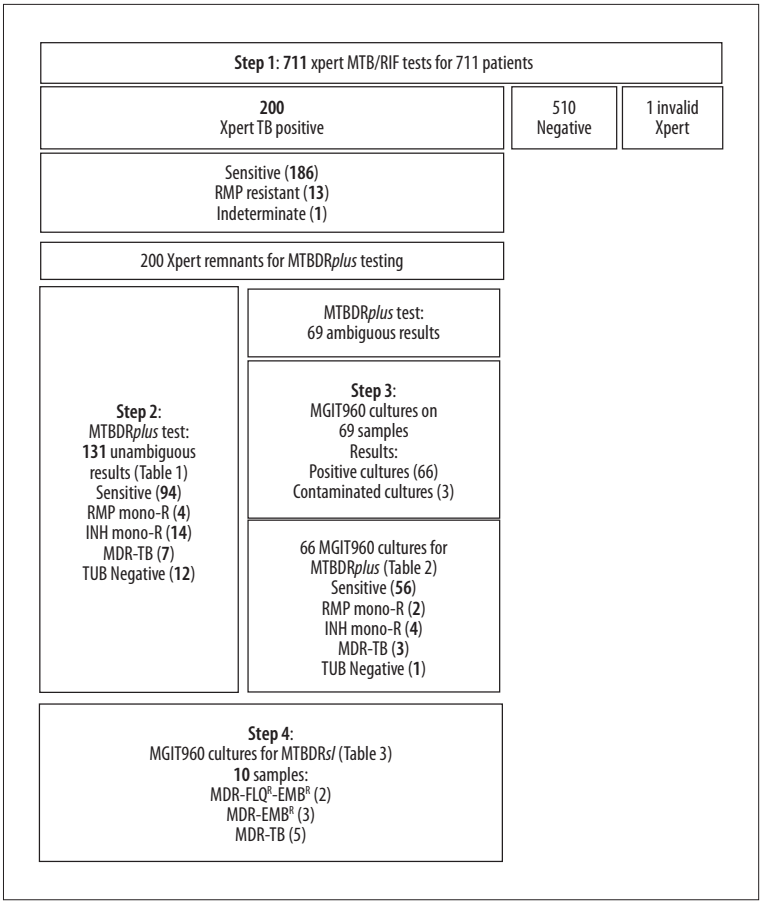


**Figure 1.** Flowchart showing the processing of the 711 sputum samples. RMP mono-R, monoresistant to RIF; INH mono-R, monoresistant to INH; MDR-TB, multidrug-resistant tuberculosis; TUB, Hain MTBDR*plus*/s*l* quality control for *M. tuberculosis* complex; ambiguous result, absence of at least one of the *M. tuberculosis* complex-specific controls (*rpo*B, *kat*G and/or *inh*A locus), making it impossible to evaluate the MTBDR*plus* test; FLQ – fluoroquinolones; EMB – ethambutol; R – resistant.

In Step 4, the MTBDR*sl* test was performed on the cultures from the 10 sputum samples found to be MDR by MTBDR*plus* in Steps 2 and 3–7 detected with the Xpert sputum remnants and 3 detected with cultures. The results are presented in Table 3 with additional characteristics of the MDR genotypes. Two were found to be resistant to the fluoroquinolones and ethambutol and were therefore classified as pre-XDR-TB. Three samples were identified as resistant to ethambutol but sensitive to the other second-line drugs, and in the remaining 5 samples only INH and RIF resistance were detected. With these results, the patients could be started on appropriately adapted drug regimens.

## Discussion

Nucleic acid-based diagnostic tests to detect of TB and determine drug susceptibility are quick and easy, but they are not perfect. To ensure accuracy, they require cultures for confirmation, but this delays appropriate treatment, while patients can continue to transmit the disease. The study described here builds upon previous work (Alame-Emane AK et al. [11]) showing that remnants of sputum processed for Xpert can be used in tests for resistance to additional antibiotics not included in the Xpert/RIF test. The present study assessed the increase in accuracy of a diagnostic algorithm implementing 2 complementary rapid molecular tests performed directly on clinical samples. Sputa were first tested with Xpert, and then the left-over remnants of the sputa processed for GeneXpert were tested with MTBDR*plus* to confirm the Xpert results and also to detect INH resistance, thus diagnosing MDR-TB. Finally, the MTBDR*sl* test was used to detect mutations conferring resistance to fluoroquinolones and the injectable agents, to determine whether any of the MDR cases we found were actually XDR-TB.

Of the 200 samples identified as positive for TB by Xpert, the MTBDR*plus* performed on Xpert remnants gave unambiguous results in 131, and of these, 119 or 63.3% of the total (119/200) were positive for TB, while 12 were TB-negative. MTBDR*plus* on cultures of the specimens that gave ambiguous results with sputum remnants confirmed TB in 94% (65/69), with one negative for TB and 3 contaminated. MTBDR*plus* thus confirmed TB in 98.3% (184/200), and failed to find TB in 13 samples that were TB-positive with Xpert. The Xpert detected RIF resistance in 13 sputa, and all (13/13) were confirmed as RIF-resistant by the MTBDR*plus* test performed on Xpert remnants or cultures. In addition, 2 samples that were RIF-sensitive by Xpert were found to be RIF-R by MTBDR*plus*.





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**Table 1.** Sample characteristics (Xpert MTB/RIF and MTBDR*plus* tests on sputum and Xpert remnants, respectively. *n*=131).

| Number of samples *n* | Microscopy results (AFB smear grading) | Culture results | Xpert MTB/RIF results | | |
|---|---|---|---|---|---|
| | –/scanty/+/++/+++/++++: *n* | Negative/positive | Quantification | Probe Negative | Resistant genotype |
| 94 | –: 6; scanty: 4; +: 18; ++: 21; +++: 22; ++++: 23 | Negative: 6; Positive: 88 | VL/L/M/H | NA | Sensitive |
| 1 | + | Positive | M | NA | Sensitive |
| 2 | ++++/– | Positive | H/VL | Probe D | Resistant |
| 1 | ++ | Positive | M | Probe E | Resistant |
| 6 | +: 1; ++: 1; ++++: 4 | Positive | H/M | NA | Sensitive |
| 1 | + | Positive | L | NA | Sensitive |
| 4 | –: 1; +: 1; ++: 2 | Positive | M/VL/L | NA | Sensitive |
| 1 | ++ | Positive | L | NA | Sensitive |
| 2 | –/+++ | Positive | L/M | NA | Sensitive |
| 4 | ++: 2; ++++: 4 | Positive | H/M | Probe E | Resistant |
| 1 | ++ | Positive | M | Probe D | Resistant |
| 1 | ++ | Positive | L | Probe D | Resistant |
| 1 | – | Positive | L | Probe D | Resistant |
| 12 | –: 9; scanty: 1; +: 2 | Negative: 9; Positive: 3 | VL/L | NA | Sensitive |

| Number of samples *n* | MTBDR*plus* (v2.0) results | | | | |
|---|---|---|---|---|---|
| | TUB probe | *rpo*B | *kat*G | *inh*A | Resistant genotype |
| 94 | Positive | WT | WT | WT | Sensitive |
| 1 | Positive | WT4 and WT5 absent | WT | WT | RMP monoresistance |
| 2 | Positive | H526D | WT | WT | RMP monoresistance |
| 1 | Positive | S531L | WT | WT | RMP monoresistance |
| 6 | Positive | WT | S315T1 | WT | INH monoresistance |
| 1 | Positive | WT | S315T1 | WT1 and WT2 absent | INH monoresistance |
| 4 | Positive | WT | WT absent | WT | INH monoresistance |
| 1 | Positive | WT | WT | WT1 and WT2 absent | INH monoresistance |
| 2 | Positive | WT | WT absent | WT1 and WT2 absent | INH monoresistance |
| 4 | Positive | S531l | S315T1 | WT | MDR |
| 1 | Positive | H526Y | S315T1 | WT | MDR |
| 1 | Positive | WT7 absent | WT | WT1 absent | MDR |
| 1 | Positve | H526Y | WT absent | WT | MDR |
| 12 | Negative | NA | NA | NA | NA |

AFB – acid-fast bacilli; VL – very low; L – low; M – moderate; H – high; NA – not available; WT – wild-type; TUB – Hain MTBDR*plus/sl* quality control for *M. tuberculosis* complex-specific; RMP – rifampicin; INH – isoniazid; MDR – multidrug-resistant.





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**Table 2.** Sample characteristics (Xpert MTB/RIF and MTBDR*plus* tests on cultures. *n*=66).

| Number of samples *n* | Xpert MTB/RIF results | | | MTBDR*plus* (v2.0) results | | | | |
|---|---|---|---|---|---|---|---|---|
| | Quantification | Probe negative | Resistant genotype | TUB probe | *rpo*B | *kat*G | *inh*A | Resistant genotype |
| 55 | VL/L/M | NA | Sensitive | Positive | WT | WT | WT | Sensitive |
| 1 | VL | NA | Indeterminate | Positive | WT | WT | WT | Sensitive |
| 1 | L | Probe E | Resistant | Positive | S531L | WT | WT | RMP monoresistance |
| 1 | L | NA | Sensitive | Positive | WT6 absent | WT | WT | RMP monoresistance |
| 3 | VL | NA | Sensitive | Positive | WT | S315T1 | WT | INH monoresistance |
| 1 | M | NA | Sensitive | Positive | WT | WT | C15T | INH monoresistance |
| 1 | M | Probe B | Resistant | Positive | WT3 and WT4 absent | S315T1 | WT | MDR |
| 1 | VL | NA | Sensitive | Positive | WT3 and WT4 absent | S315T1 | WT | MDR |
| 1 | L | Probe D | Resistant | Positive | H526Y | S315T1 | WT | MDR |
| 1 | L | NA | Sensitive | Negative | NA | NA | NA | NA |

VL – very low; L – low; M – moderate; H – high; NA – not available; WT – wild-type; TUB – Hain MTBDR*plus/sl* quality control for *M. tuberculosis* complex-specific; RMP – rifampicin; INH – isoniazid; MDR – multidrug-resistant.

The 2 tests were thus discordant in a total of 15 samples. There were 13 samples that were TB-positive by Xpert but TB-negative with MTBDR*plus*, and none of these grew in MGIT cultures. These were apparently false positives with the Xpert, and confirming results with MTBDR*plus* could therefore avoid 13 unnecessary TB treatments. False positives with Xpert were recently described in a study performed in Brazil [18] and were attributed to residual TB DNA from TB infection in the absence of active TB disease, and false positives were reported to be more common with the Xpert Ultra cartridges [22].

There were also 2 samples that were RIF-sensitive with the Xpert but RIF-R with MTBDR*plus*, and based on the Xpert results alone, these 2 patients would have been started on ineffective drug regimens. Of the 15 cases found to be RIF-R with MTBDR*plus*, INH resistance was also detected in 10, which were therefore MDR-TB. It is possible, though, that the number of MDR-TB strains was underestimated, because the sensitivity of the MTBDR*plus* for INH is lower than for RIF [6,7].

In collaboration with the regional TB follow-up program, we performed follow-up on all patients diagnosed with TB during the present study. Among the 150 (94+56) patients diagnosed with drug-susceptible TB by both rapid tests, 55 (36.7%) had left Shenzhen (our unpublished epidemiological data). Among the 10 patients diagnosed with MDR-TB by the same tests, 8 (80.0%) had left Shenzhen (our unpublished epidemiological data). Patients who are diagnosed with TB based on clinical symptoms and microscopy are immediately started on therapy unless antibiotic resistance is suspected. When there is suspicion of antibiotic resistance, however, sputum cultures are sent to the central Shenzhen CCDC reference laboratory for molecular DST, and therapy is not initiated until results are available. The time required depends upon the speed of culture growth and the time to obtain the test results, but the minimum is 3 weeks, and the process generally takes longer. Therefore, the time between initial diagnosis and treatment initiation is much longer for MDR-TB patients than for patients with drug-sensitive TB, which might explain why a higher percentage of these had left Shenzhen.

To reduce the prevalence of MDR-TB, these patients must be identified and started on appropriate therapy as quickly as possible to curtail transmission. We believe that the implementation in the district labs of the Xpert and the MTBDR*plus* for all patients presenting with clinical symptoms of TB could reduce the loss of MDR-TB patients, and thus the transmission of MDR-TB. A diagnostic algorithm is presented in Figure 2. Our results suggest that if the rapid tests were performed once directly on sputum specimens, only about one-third of patients would require a culture. Although supplementary tests performed on the cultures at the central reference laboratory will be important





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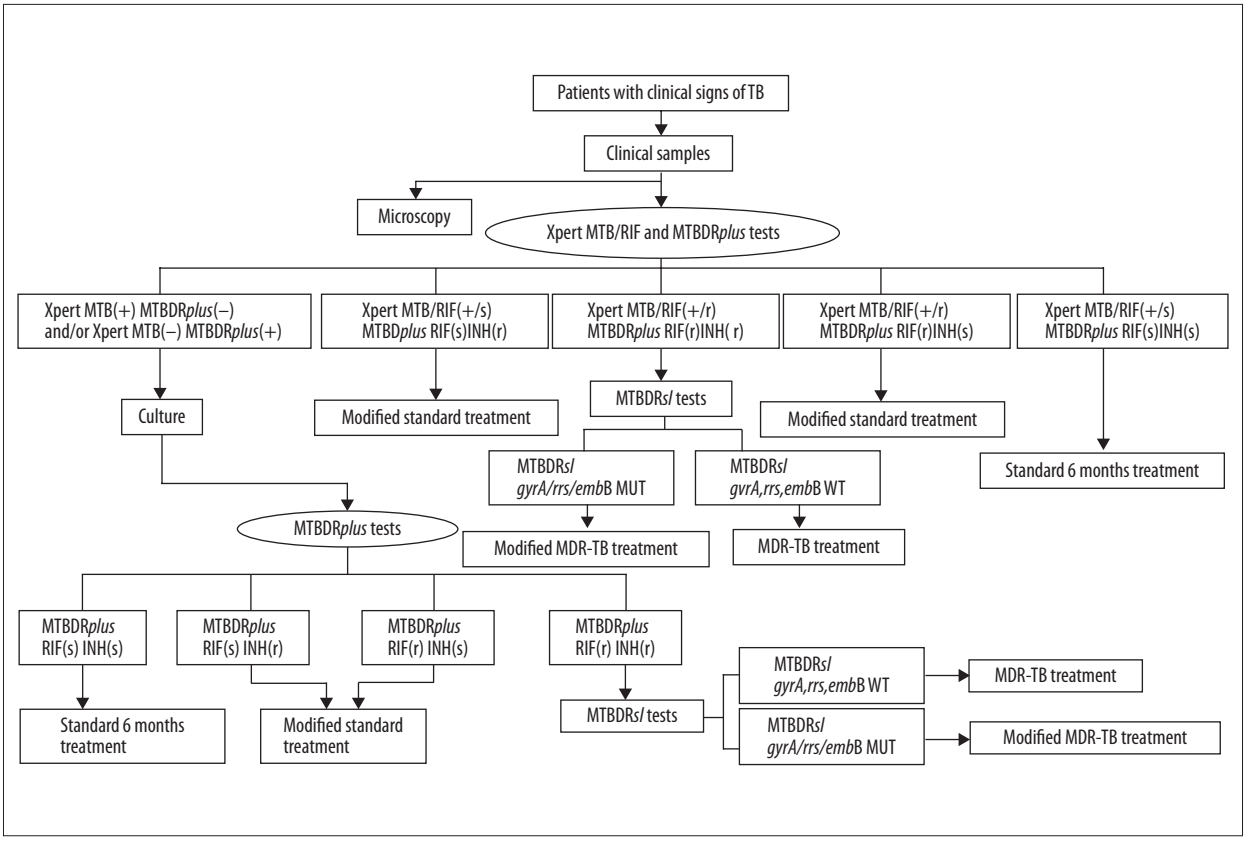


**Figure 2.** Diagnostic algorithm. MDR-TB: multidrug-resistant tuberculosis, –: negative, +: positive, r: resistant, s: sensitive, RIF: rifampicin, INH: isoniazid, *sl*: second-line drug sensitivity testing, *gyr*A/*rrs*/*emb*B MUT: the mutation was detected in at least one of the genes (*gyr*A/*rrs*/*emb*B), *gyr*A,*rrs*,*emb*B WT: all genes (*gyr*A, *rrs*, and *emb*B) were wild-type, *gyr*A: identify the resistance to fluoroquinolones (*e.g.,* ofloxacin or moxifiloxacin), *rrs*: identify the resistance to aminoglycosides (*e.g.* capreomycin or viomycin)/cyclic peptides (*e.g.,* kanamycin or amikacin), *emb*B: identify the resistance to ethambutol.

for cases that are difficult to diagnose and those with more extensive drug resistance, we expect the number of these cases, who may also have delayed initiation of appropriate therapy, will be considerably reduced after implementation of nucleic acid-based diagnosis at the level district. The advent of new Xpert cartridges that can detect resistance to antibiotics other than RIF will provide results that are complementary to those obtained with MTBDR*plus* and MTBDRs*l* [19]. These cartridges could also be used at the district level on samples found to be RIF-R, thus further reducing the need to wait for results to arrive from central laboratories before starting appropriate therapy.

While we used the remnants of sputa processed for Xpert, others studies have extracted the TB DNA from used Xpert MTB/RIF [20] and Xpert Ultra cartridges [21] for accurate second-line genotypic drug susceptibility testing and genotyping, with minimal *rpo*B-amplicon cross-contamination [21]. This approach could likely isolate cleaner DNA than is possible to obtain directly from the inactivated sputum, and thus could improve the sensitivity of subsequent tests and perhaps reduce the number of ambiguous results.

In our study, the accuracy of the tests, especially the Xpert, was lower than results published in other studies [6,7]. Our data represent results observed in a routine TB diagnostic lab not specifically pursuing the optimum performance of these tests, and therefore might be more typical of the accuracy obtained in many peripheral laboratories. Whole-genome sequencing (WGS) has been shown to be very accurate for diagnosis and DST when performed on cultured material (resistance to rifampin was correctly predicted with 97.5% sensitivity and 98.8% specificity [23]), but is less accurate and is cumbersome to perform directly on sputum samples [24,25], and the theoretical minimal time to obtain results with current technology is still 2–3 days. Therefore, the optimal use of WGS on routine clinical material remains uncertain. We believe that our algorithm using 2 test methods can confirm the results obtained by each technique alone and thereby quickly provide very accurate results. This will allow the prompt implementation of appropriate treatment while avoiding treating individuals without confirmed TB.





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**Table 3.** MDR-TB (MTBDR*sl* test on cultures. *n*=10).

| Sample No. | Xpert MTB/RIF results | | | MTBDR*plus* (v2.0) results | | | | MTBDRsl (v1.0) results | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Quantification | Probe negative | Resistant genotype | *rpo*B | *kat*G | *inh*A | Resistant genotype | *gyr*A | *rrs* | *emb*B | Resistant genotype |
| sz181008 | H | Probe E | Resistant | S531L | S315T1 | WT | MDR | D94H | WT | M306V | MDR-FLQ$^R$-EMB$^R$ |
| sz181376 | H | Probe E | Resistant | S531L | S315T1 | WT | MDR | WT | WT | M306I | MDR-EMB$^R$ |
| sz181791 | H | Probe E | Resistant | S531L | S315T1 | WT | MDR | WT | WT | M306V | MDR-EMB$^R$ |
| sz190258 | H | Probe E | Resistant | S531L | S315T1 | WT | MDR | WT | WT | WT | MDR |
| sz180711 | M | Probe D | Resistant | H526Y | S3015T1 | WT | MDR | A90V | WT | M306V | MDR-FLQ$^R$-EMB$^R$ |
| sz181640 | L | Probe D | Resistant | H526Y | WT absent | WT | MDR | WT | WT | WT | MDR |
| sz181039 | L | Probe D | Resistant | WT7 absent | WT | WT absent | MDR | WT | WT | WT | MDR |
| sz180521 | M | Probe B | Resistant | WT3 and WT4 absent | S315T1 | WT | MDR | WT | WT | M306V | MDR-EMB$^R$ |
| sz181674 | VL | WT | Sensitive | WT3 and WT4 absent | S315T1 | WT | MDR | WT | WT | WT | MDR |
| sz190157 | L | Probe D | Resistant | H526Y | S315T1 | WT | MDR | WT | WT | WT | MDR |

MDR – multidrug-resistant; TB – tuberculosis; VL – very low; L – low; M – moderate; H – high; NA – not available; WT – wild-type; FLQ – fluoroquinolones; EMB – ethambutol; R – resistant.

## Conclusions

The use of 2 rapid tests directly performed on sputa for the diagnosis of pulmonary TB quickly provides accurate results and will allow the prompt implementation of appropriate treatment for most patients, while avoiding unnecessary treatment of individuals without confirmed TB.

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Equipment: GeneXpert MTB/RIF (Cepheid, U.S.A.), MGIT 960 (BD Com., U.S.A.), Automated hybridization instrument GT-Blot 48 (bioMérieux, France).

### Conflict of interest

None.

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