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Diagnosis and treatment of TB patients with rifampicin resistance detected using Xpert® MTB/RIF in Zimbabwe

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Setting: In Zimbabwe, there are concerns about the management of tuberculosis (TB) patients with rifampicin (RMP) resistance diagnosed using Xpert® MTB/RIF.

Objective: To assess linkages between diagnosis and treatment for these patients in Harare and Manicaland provinces in 2014.

Design: A retrospective cohort study.

Results: Of 20 329 Xpert assays conducted, 90% were successful, 11% detected *Mycobacterium tuberculosis* and 4.5% showed RMP resistance. Of 77 patients with RMP-resistant TB diagnosed by Xpert, 70% had samples sent to the reference laboratory for culture and drug susceptibility testing (CDST); 53% of the samples arrived. In 21% the samples showed *M. tuberculosis* growth, and in 17% the DST results were recorded, all of which confirmed RMP resistance. Of the 77 patients, 34 (44%) never started treatment for multidrug-resistant (MDR) TB, with documented reasons being death, loss to follow-up and incorrect treatment. Of the 43 patients who started MDR-TB treatment, 12 (71%) in Harare and 17 (65%) in Manicaland started within 2 weeks of diagnosis.

Conclusion: Xpert has been rolled out successfully in two Zimbabwe provinces. However, the process of confirming CDST for Xpert-diagnosed RMP-resistant TB works poorly, and many patients are either delayed or never initiate MDR-TB treatment. These shortfalls must be addressed at the programmatic level.

Zimbabwe is one of the world's 22 high-burden tuberculosis (TB) countries, with an estimated TB incidence of 552 per 100 000 population in 2013.¹ Human immunodeficiency virus (HIV) prevalence is 17%, and 69% of TB patients are co-infected with HIV.^{1,2} For decades, the diagnosis of pulmonary TB has relied on sputum smear microscopy, although the test lacks sensitivity and does not detect drug-resistant TB.^{3,4} The early diagnosis of multidrug-resistant TB (MDR-TB, defined as TB resistant to at least both rifampicin [RMP] and isoniazid [INH]), is essential to institute prompt treatment, reduce mortality and prevent the transmission of infection.⁵ In this light, the Xpert® MTB/RIF assay (Cepheid Inc, Sunnyvale, CA, USA) is revolutionary, requiring minimal laboratory expertise and yielding test results within 2 hours.⁶ Sensitivity and specificity for TB diagnosis is high, and the assay also detects RMP resistance. Studies in several settings have shown the feasibility, accuracy and effectiveness of Xpert,⁷ prompting the World Health Organization (WHO) in 2010 to strongly recommend the wide-

spread use of Xpert, with priority for those with suspected MDR-TB and for patients with TB and HIV coinfection.^{8,9} In 2013, the WHO made a conditional recommendation that Xpert should be the initial diagnostic test for all people requiring investigation for TB.¹⁰

Zimbabwe has been scaling up the implementation of Xpert since 2011. By December 2014, 62 sites in the country were using this technology. All individuals identified with RMP-resistant TB by Xpert should be placed immediately on treatment for MDR-TB, and their specimens should be processed for culture and drug susceptibility testing (CDST), in line with previous WHO recommendations.⁹ There are a number of challenges with implementation, however. First, national data suggest that the performance of CDST after Xpert detection of RMP resistance is poor, although this has not been formally studied. Second, records indicate that not all patients diagnosed with MDR-TB are initiated on treatment. Loss to follow-up between the initial diagnosis of TB and the start of treatment is known as 'initial loss to follow-up' (formerly termed 'initial default'), and is well recognised to occur when sputum smears are used for diagnosis.¹¹⁻¹³ More information is needed about what occurs between the diagnosis of MDR-TB and subsequent treatment, and improving this linkage is a key priority of the WHO End TB control strategy.¹⁴ Third, several sites in Zimbabwe have been repeating Xpert assays on the same patient following an initial RMP-resistant *Mycobacterium tuberculosis* result, which may inadvertently add to the numbers of reported initial losses to follow-up and unnecessarily increase the consumption of expensive Xpert cartridges (approximately US\$10 per cartridge). More information about these challenges will help the National Tuberculosis Programme (NTP) in Zimbabwe, as well as in other countries, to develop better strategic use of Xpert.

The aim of this study was to assess the linkage between diagnostic and treatment services for patients investigated and diagnosed with RMP-resistant TB using Xpert in two provinces in Zimbabwe (Manicaland and Harare City) in 2014. Specific objectives were to determine 1) the Xpert assays performed and the number and proportion showing resistance to RMP (including repeat assays), and 2) the number of patients identified with RMP resistance by Xpert; the number and proportion who had CDST performed along with the results; the number and proportion of patients who never started MDR-TB treatment and the

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reasons why; and, among those who did start treatment, the time taken to initiate MDR-TB treatment.

METHODS

Study design

This was a retrospective cross-sectional study of Xpert and a cohort study using routinely collected data to follow patients through the process of CDST and MDR-TB treatment.

General setting and study sites

Country and provinces

Zimbabwe is a landlocked country in southern Africa with an estimated population of 15 million and a gross domestic product of US\$830 per capita in 2013.¹⁵ The study was conducted in two provinces, Harare City and Manicaland, which have populations of approximately 2 million and 1.8 million, respectively.¹⁶ Public health services in the two provinces are discharged through the City Health Department and the Provincial Health Directorate. Xpert instruments were made available in the provinces in 2012 and 2013, and by December 2014, nine Xpert instruments were available in each of the two provinces.

The National Tuberculosis Programme and management of presumed MDR-TB

The management of MDR-TB in Zimbabwe is coordinated through a designated national MDR-TB focal person, and there is a committee in each province and district to oversee the clinical and programmatic management of MDR-TB. The committees have the mandate of initiating patients on MDR-TB treatment as soon as possible.

Patients are deemed to have suspected MDR-TB if they are symptomatic and 1) have failed to sputum smear convert at 2 months during first-line anti-tuberculosis treatment, 2) have a history of previous anti-tuberculosis treatment, 3) are contacts of a known index patient with MDR-TB, 4) have travelled from a high MDR-TB burden country, or 5) have come from high-risk congregate settings such as prisons. It is recommended that these patients and those with HIV-associated presumptive TB have Xpert performed on one sputum specimen.

The Xpert assay results are recorded in the registers of the nine laboratories in Harare City and the nine laboratories throughout the province of Manicaland. If the Xpert assay shows *M. tuberculosis* and RMP resistance, further sputum specimens should be submitted for CDST at the Harare-based National Microbiology Reference Laboratory (NMRL). Once diagnosed with RMP-resistant TB by Xpert, all patients should start MDR-TB treatment immediately using standardised recommended regimens.¹⁷ These regimens consist of five drugs (kanamycin [KM], levofloxacin [LVX], cycloserine [CS], ethionamide [ETH] and pyrazinamide [PZA]) for the initial phase of 6–8 months, followed by four drugs (LVX, CS, ETH and PZA) for the continuation phase of 14 months. The initial phase is administered either in hospital or at home and is directly observed, while the continuation phase is administered

from home. Prior to treatment, the district MDR-TB committee discusses the model of care to be used in the management of the patient, whether as an out-patient or an in-patient for the initial phase. The latter model is only used for very ill patients or when infection control is not achievable at home. Baseline biochemical tests are then conducted before treatment is initiated.

Study population

All patients who were tested using Xpert and registered in the laboratory registers in the Harare City and Manicaland provinces between January and December 2014 were included in the study.

Data variables, sources of data, data collection tools and data validation

Data variables were collected from the Xpert laboratory registers and archive files, the CDST register in the Harare NMRL and the MDR-TB treatment registers. To follow the process of CDST, the names of those found to have *M. tuberculosis* or RMP resistance detected in the Xpert registers were searched for in the NMRL register in Harare for up to 6 months after the last patient was registered in the Xpert laboratory registers.

For data validation, Xpert results in the laboratory registers were cross-checked with data extracted from the Xpert machines, and data in the treatment registers were cross-checked with facility-based patient medical files. Study data were collected into paper-based questionnaires between March and November 2015.

Analysis and statistics

Data from the paper-based questionnaires were double entered and analysed using EpiData software (version 3.1 for entry and version 2.2.2.182 for analysis, EpiData Association, Odense, Denmark). Data were analysed by frequencies and percentages, with comparisons between the two provinces and between patient categories assessed using the χ^2 test, risk ratios and 95% confidence intervals (CI). Levels of significance were set at 5%.

Ethics

Permission for the study was obtained from the NTP and the Medical Research Council, Harare, Zimbabwe. The study met the Médecins Sans Frontières (MSF) Ethics Review Board (Geneva, Switzerland) approved criteria for studies of routinely collected data and was approved by the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease, Paris, France. As this was a record review study with anonymised data, informed patient consent was not required.

RESULTS

Xpert assays

The number of Xpert assays performed and their results in both Harare and Manicaland provinces in 2014 are shown in Figure 1. Of 20 329 assays performed in both provinces, 90% were successful, and of these, 11% detected *M. tuberculosis*. There were 97

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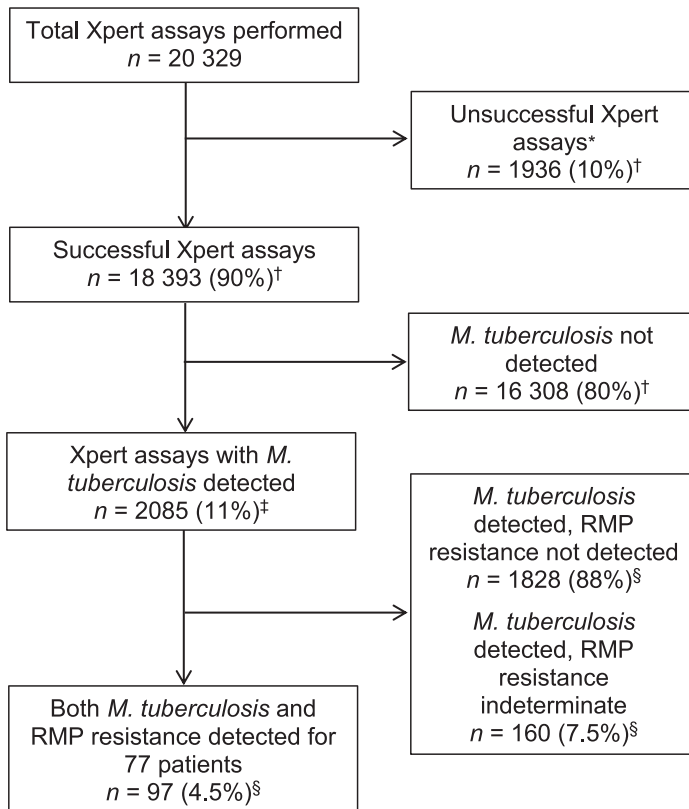


FIGURE 1 Xpert® MTB/RIF assays performed and results in both Harare and Manicaland provinces, Zimbabwe, 2014. *Unsuccessful test = error result, invalid or no result. †Denominator = total Xpert assays performed. ‡Denominator = successful Xpert assays. §Denominator = Xpert assays with *M. tuberculosis* detected. RMP = rifampicin.

assays (4.5% of those detecting *M. tuberculosis*) that showed RMP resistance. A comparison between Harare and Manicaland of the number of assays performed and their results is shown in Table 1. There were some programmatic differences between the

two sites: the proportion of assays detecting *M. tuberculosis* was higher in Harare, but the proportion of *M. tuberculosis* assays that showed RMP resistance was higher in Manicaland. Altogether, of 77 patients who had RMP resistance on Xpert, 60 had one Xpert assay, 14 had two assays and 3 had three assays. Thus, 17 (22%) patients with RMP resistance had two or more assays done.

Patients with rifampicin resistance on Xpert and CDST results

Of the 77 patients who were RMP-resistant on Xpert, the outcomes of sending samples to the NMRL for CDST for both provinces combined are shown in Figure 2. There were losses at almost all stages. Of the 77 patients, 70% had samples sent to the reference laboratory for CDST; 53% of the samples arrived and were registered at the reference laboratory; 21% of these showed growth of *M. tuberculosis*; and 17% ($n = 13$) had a DST result recorded. All 13 patients were RMP-resistant, and 11 were also INH-resistant. The outcomes of sending samples for CDST in Harare compared with Manicaland are shown in Table 2. There were no significant differences at any stage between the two provinces.

MDR-TB treatment initiation in rifampicin-resistant patients on Xpert

Of the 77 patients detected with RMP-resistant *M. tuberculosis*, 34 (44%) were never initiated on MDR-TB treatment. Reasons for never starting MDR-TB treatment are shown in Table 3. In two thirds of the patients there was no documented reason. Starting a first-line anti-tuberculosis treatment regimen, loss to follow-up and death were the three documented reasons for not starting appropriate treatment. Sex, HIV status, category of TB and the province where the diagnosis was made were not associated with never starting MDR-TB treatment (see Table 4).

For the 43 patients who initiated MDR-TB treatment, the time from diagnosis to treatment initiation in both provinces is shown in Table 5. Most patients (71% in Harare and 65% in Manicaland) were initiated on treatment within 2 weeks of diagnosis. There were no significant differences in the time from diagnosis to treatment initiation in the provinces.

TABLE 1 Number of Xpert® MTB/RIF assays performed and the results in Harare and Manicaland provinces, Zimbabwe, 2014

Xpert assays and results	Harare n (%)	Manicaland n (%)	P value
Xpert assays performed	13 384	6 945	
Successful Xpert assays	12 149 (91)	6 244 (90)	0.02
Xpert assays with <i>M. tuberculosis</i> detected	1 129 (9)	956 (15)	<0.001
Xpert assays with <i>M. tuberculosis</i> detected that showed:			
RMP-susceptible bacilli	1 012 (90)	816 (85)	<0.001
RMP-resistant bacilli	36 (3)	61 (6)	0.001
RMP-indeterminate bacilli	81 (7)	79 (8)	0.41
Unsuccessful Xpert assays	1 235 (9)	701 (10)	0.02
Error results*	857 (69)	423 (60)	<0.001
No results†	276 (22)	195 (28)	0.003
Invalid results‡	101 (8)	84 (12)	0.004

* Error results: probe check control failed and the assay was aborted due to the following: 1) the reaction tube being filled improperly; 2) a reagent probe integrity problem detected; 3) the maximum pressure limits were exceeded; 4) an Xpert module failure.

† No results: insufficient data were collected due to 1) power failure; 2) test stopped by the operator.

‡ Invalid results: presence or absence of *M. tuberculosis* could not be determined due to the following: 1) sample processing control did not meet acceptance criteria; 2) sample was not properly processed; 3) PCR was inhibited.

RMP = rifampicin; PCR = polymerase chain reaction.

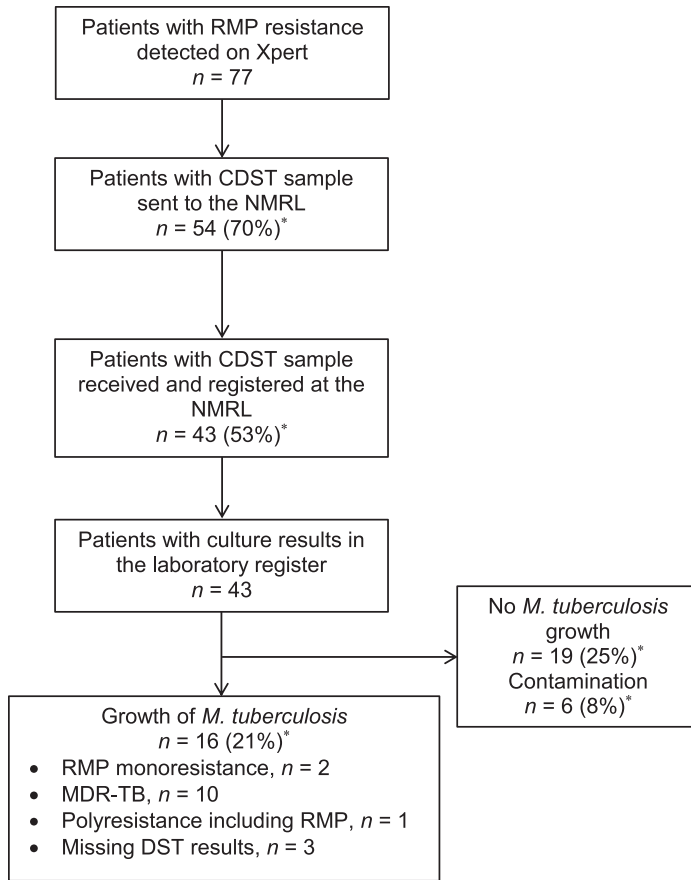


FIGURE 2 Patients with RMP resistance on Xpert® MTB/RIF and process and performance of CDST in both Harare and Manicaland provinces, Zimbabwe, 2014. *Denominator = patients diagnosed RMP-resistant on Xpert. RMP = rifampicin; CDST = culture and drug susceptibility testing; NMRL = National Microbiology Reference Laboratory; MDR-TB = multidrug-resistant tuberculosis; DST = drug susceptibility testing.

DISCUSSION

This is the first study in Zimbabwe to assess linkages between diagnosis and treatment for patients detected with RMP-resistant TB using Xpert. There were some important findings. First, large numbers of Xpert assays were successfully performed in the two

TABLE 3 Reasons for never starting MDR-TB treatment in patients with RMP resistance on Xpert® MTB/RIF in both Harare and Manicaland provinces, Zimbabwe, 2014

Reason for never starting MDR-TB treatment	n (%)
Started treatment with first line anti-tuberculosis drugs	5 (15)
Lost to follow-up	3 (9)
Death	4 (12)
Not documented	22 (64)
Total	34

MDR-TB = multidrug-resistant tuberculosis; RMP = rifampicin; TB = tuberculosis.

provinces in the 12-month period studied. Nearly 5% of *M. tuberculosis* strains showed resistance to RMP, and repeat tests were performed in about one fifth of these patients, although we have no information about why the tests were repeated.

Second, the process of sending specimens and obtaining CDST results was poor, with only one fifth of the patients detected with RMP-resistant strains on Xpert being confirmed by CDST. On a positive note, when CDST was performed successfully, all those with RMP resistance on Xpert were also confirmed as having RMP resistance in the reference laboratory.

Third, almost half of the patients detected with RMP resistance on Xpert never started MDR-TB treatment, and the reasons were often not documented. Finally, about one third of those who did begin MDR-TB treatment had a treatment delay of >2 weeks from the date of diagnosis.

The strengths of this study were that it included all Xpert assays performed in the two provinces during a 12-month period, and included all patients detected with RMP-resistant TB. There was therefore no need for any sampling framework. The study was conducted under routine programmatic conditions, and adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for conducting and reporting on observational studies.¹⁸ Limitations included the retrospective nature of the study using already collected secondary data in registers and archived Xpert files, where some data are missing and some may be inaccurately recorded.

There are some important lessons to be learnt. The high success rate of the Xpert assays in our programmatic setting study compares favourably with recent results reported from a national programme study in nearby Swaziland, although the proportion

TABLE 2 Patients resistant to RMP on Xpert® MTB/RIF and the process and performance of CDST at the Harare-based NMRL, Harare and Manicaland provinces, Zimbabwe, 2014

Characteristics	Harare n (%)	Manicaland n (%)	P value
Patients with RMP-resistant TB strains	35	42	
Patients with CDST sample sent to the NMRL	22 (63)	32 (76)	0.20
Patients with CDST sample received and registered at the NMRL	19 (54)	22 (52)	0.86
Patients with CDST results in the NMRL register	19 (54)	22 (52)	0.86
Culture results			
No growth	10 (29)	9 (21)	0.47
<i>M. tuberculosis</i> growth*	5 (14)	11 (26)	0.20
Contamination	4 (11)	2 (5)	0.51
CDST results received by the referring facility	16 (46)	17 (40)	0.64

*DST showed: RMP mono-resistance (n = 2); MDR (n = 10); polydrug resistance, including RMP (n = 1); missing DST results (n = 3).

RMP = rifampicin; CDST = culture and drug susceptibility testing; NMRL = National Microbiology Reference Laboratory; TB = tuberculosis; MDR = multidrug resistance; DST = drug susceptibility testing.

TABLE 4 Factors associated with never starting MDR-TB treatment in patients with RMP resistance on Xpert® MTB/RIF in both Harare and Manicaland, Zimbabwe, 2014

Characteristics	Patients with RMP resistance on Xpert <i>n</i>	Patients who never started MDR-TB treatment <i>n</i> (%)	RR (95%CI)	<i>P</i> value
Total	77	34 (44)		
Sex				
Female	31	6 (19)	1	
Male	27	9 (33)	1.7 (0.7–4.2)	0.22
Missing data	19	19 (100)	–	
HIV status				
Negative	15	3 (20)	1	
Positive	35	7 (20)	1.0 (0.3–3.4)	0.04
Unknown	27	24 (89)	–	
Category of TB				
Retreatment	23	2 (9)	1	
New	27	6 (22)	2.6 (0.6–11.5)	0.26
Missing data	26	27 (92)	–	
Province				
Manicaland	42	16 (38)	1	
Harare	35	18 (51)	1.4 (0.8–2.2)	0.24

MDR-TB = multidrug-resistant tuberculosis; RMP = rifampicin; RR = risk ratio; CI = confidence interval; HIV = human immunodeficiency virus; TB = tuberculosis.

of unsuccessful assays in Zimbabwe was higher than in Swaziland.¹⁹

The system of sending sputum specimens and receiving the results back between the peripheral health facilities and the central reference laboratory in Harare did not work. At each stage there were losses, and when the specimens finally did arrive at the laboratory, over half failed to successfully grow *M. tuberculosis*. This problem of sending samples to a central reference laboratory is not unique to Zimbabwe; similar challenges are encountered in many other countries.^{20–24} Trying to fix these challenges is also not easy, as described in a case study from Malawi.²⁰ As several studies, including our own, have highlighted the high sensitivity and specificity of Xpert compared with phenotypic CDST under routine programme settings,^{7,9,25} we question the need for CDST to confirm RMP-resistant TB. CDST might be better used 1) to diagnose resistance to second-line anti-tuberculosis results and thus help to diagnose extensively drug resistant (XDR) TB (MDR-TB that is also resistant to both any fluoroquinolone and one of the injectable second-line drugs) or pre-XDR-TB (MDR-TB resistant to either any fluoroquinolone or one of the injectable second-line drugs); and 2) to follow up patients who are failing MDR-TB treatment.

It is unacceptable for any patient diagnosed with MDR-TB never to start treatment or to start treatment after several weeks of delay. Again, this problem is not unique to Zimbabwe. Of the 300 000 notified TB patients estimated to have MDR-TB globally in 2014, only 110 000 (37%) started MDR-TB treatment, and of these, only 50% successfully completed treatment.²⁶ Possible reasons for delays in starting treatment in Zimbabwe might be the time taken in conducting the baseline biochemistry tests on liver and renal function and the decision to start MDR-TB treatment, which is made by the clinical management team. Previous studies

TABLE 5 Time from diagnosis to MDR-TB treatment among patients with RMP resistance detected using Xpert® MTB/RIF in both Harare and Manicaland provinces, Zimbabwe, 2014

Time from diagnosis to treatment initiation, days	Harare <i>n</i> (%)	Manicaland <i>n</i> (%)	<i>P</i> value
0–14	12 (71)	17 (65)	0.72
15–28	2 (12)	4 (15)	0.91
>28	1 (6)	2 (8)	0.70
Unknown	2 (12)	3 (12)	0.64
Total	17	26	

MDR-TB = multidrug-resistant tuberculosis; RMP = rifampicin.

conducted elsewhere have shown that delayed treatment is due to a combination of patient and health system factors,^{27–29} and these need to be addressed.

This study has several implications for the NTP. First, Xpert instruments need to be functional at all times, with unsuccessful tests reduced to a minimum. This means attention by the NTP to maintenance, calibration, uninterrupted power supplies and consistent external back-up of data. Second, we suggest that the current recommendations of using CDST for confirming Xpert RMP resistance be revised. Third, all patients who are diagnosed with MDR-TB must start MDR-TB treatment. The process of initiating a patient on MDR-TB treatment after diagnosis is quite complicated in Zimbabwe, requiring biochemical tests that may not always be available at the clinical level and a decision by a specific committee; all of these steps may delay the start of treatment. This process needs to be reviewed to see whether it can be simplified. Also, instead of evaluating treatment outcomes on those registered for treatment, it would be better and more honest, as suggested previously,^{12,13} to evaluate outcomes in those diagnosed with MDR-TB and recording as a treatment outcome 'initial loss to follow-up'. Finally, we need qualitative research to better understand why some patients do not start MDR-TB treatment.

In conclusion, although the roll-out of Xpert technology in two provinces in Zimbabwe has been successful, there were shortcomings with respect to the central reference laboratory confirmation of RMP-resistant TB diagnosis and the timely linkage of patients to MDR-TB treatment. These shortcomings must be addressed. With the international community signed up to end the TB epidemic by 2030,³⁰ attention to these programme issues will be essential if this goal is to be realised.

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Contexte : Au Zimbabwe, la prise en charge des patients tuberculeux ayant une résistance à la rifampicine (RMP) diagnostiqués par Xpert® MTB/RIF est préoccupante.

Objectif : Evaluer les liens entre le diagnostic et le traitement de ces patients dans les provinces de Harare et de Manicaland en 2014.

Schéma : Etude rétrospective de cohorte.

Résultats : Sur 20 329 tests Xpert, 90% ont été réussis, 11% ont détecté *Mycobacterium tuberculosis* et 4,5% ont mis en évidence une résistance à la RMP. Il y a eu 77 patients atteints d'une tuberculose (TB) résistante à la RMP diagnostiqués par Xpert. Parmi eux, 70% ont bénéficié d'un envoi d'échantillon au laboratoire de référence pour une culture et un test de pharmacosensibilité (CDST) ; pour 53% d'entre eux, les échantillons sont arrivés à bon port ; pour 21%, les échantillons ont mis en évidence une

croissance de *M. tuberculosis* ; et chez 17%, les résultats du CDST ont été enregistrés et tous ont confirmé la résistance à la RMP. Sur 77 patients, 34 (44%) n'ont jamais mis en route un traitement pour le TB multirésistant (TB-MDR) ; les motifs documentés étaient le décès, la perte de vue ou un traitement incorrect. Des 43 patients qui ont débuté le traitement de TB-MDR, 12 (71%) à Harare et 17 (65%) au Manicaland ont commencé dans les 2 semaines suivant le diagnostic.

Conclusion : L'Xpert a été lancé avec succès dans deux provinces du Zimbabwe. Cependant, le processus de confirmation du CDST pour une TB résistante à la RMP diagnostiquée par Xpert ne fonctionne pas bien, et de nombreux patients sont soit traités avec retard, soit ne démarrent jamais le traitement de TB-MDR. Ces problèmes doivent être examinés par le programme.

Marco de referencia: En Zimbabwe, el tratamiento de los pacientes cuyo diagnóstico de tuberculosis (TB) resistente a la rifampicina (RMP) se determina mediante la prueba Xpert® MTB/RIF es fuente de inquietud.

Objetivo: Evaluar los nexos entre el diagnóstico y el tratamiento de los pacientes diagnosticados mediante la prueba Xpert en las provincias de Harare y Manicaland en el 2014.

Método: Fue este un estudio retrospectivo de cohortes.

Resultados: Se obtuvieron resultados satisfactorios en el 90% de las 20 329 pruebas Xpert realizadas; se detectó *Mycobacterium tuberculosis* en el 11% y el 4,5% reveló resistencia a RMP. Con la prueba Xpert se diagnosticaron 77 casos de TB resistente a RMP y se enviaron muestras del 70% de estos casos al laboratorio de referencia, con el fin de practicar el cultivo y las pruebas de sensibilidad (CDST) a los medicamentos antituberculosos. El 53% de estas muestras llegaron al laboratorio, en un 21% se obtuvo crecimiento de *M.*

tuberculosis y en el 17% de los casos existía un registro de los resultados de la CDST; todos los resultados confirmaron la resistencia a RMP. De los 77 pacientes, 34 nunca comenzaron el tratamiento contra la TB multidrogoresistente (TB-MDR) (44%); las causas documentadas fueron el fallecimiento, la pérdida durante el seguimiento y un tratamiento inadecuado. De los 43 pacientes que iniciaron el tratamiento por TB-MDR, 12 casos en Harare (71%) y 17 casos en Manicaland (65%) lo comenzaron en las 2 primeras semanas después del diagnóstico.

Conclusión: El despliegue de la prueba Xpert en dos provincias de Zimbabwe fue satisfactorio. Sin embargo, el mecanismo de confirmación de la resistencia a RMP mediante el CDST en los casos diagnosticados por la prueba Xpert fue deficiente y en muchos pacientes se retrasó el tratamiento de la TB-MDR o nunca se comenzó. Es preciso abordar estas deficiencias en el marco programático.