INT J TUBERC LUNG DIS 19(9):1078–1083

http://dx.doi.org/10.5588/ijtld.14.0951
E-published ahead of print 30 June 2015

Routine use of Xpert® MTB/RIF in areas with different prevalences of HIV and drug-resistant tuberculosis

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SUMMARY

SETTING: Despite the widespread introduction of Xpert® MTB/RIF in developing countries, reports of its use and value in routine conditions remain limited.

OBJECTIVE: To describe Xpert results in relation to microscopy, treatment initiation, cost and workload under routine conditions at four sites in Cambodia, Georgia, Kenya and Swaziland.

DESIGN: Laboratory and clinical information on presumed TB patients were obtained from routine registers over a period of at least 6 months between March and November 2012.

RESULTS: Among the 6086 presumed TB patients included in the analysis, Xpert testing increased the number of biologically confirmed cases by 15% to 67% compared to microscopy. Up to 12% of the initial Xpert results were inconclusive. Between 56% and 83% of patients were started on treatment based on microscopy and/or Xpert results, with median delays of 1–16 days. Rifampicin resistance was detected in 3–19% of Xpert-positive patients.

CONCLUSION: Despite the additional numbers of cases detected by Xpert compared to microscopy, large proportions of patients are still started on treatment empirically in routine practice. Patient and specimen flow should be optimised to reduce delays in treatment initiation. Simple, non-sputum-based point-of-care tests with high sensitivity are needed to improve TB diagnosis and management.

KEY WORDS: diagnostic test; cost; tuberculosis; routine conditions

TUBERCULOSIS (TB) REMAINS the second most common cause of death due to an infectious agent worldwide, and approximately one third of all TB cases are believed to go undetected due to the poor sensitivity of current diagnostic techniques.[1] The recent introduction of an integrated molecular assay for the diagnosis of TB and detection of rifampicin (RMP) resistance has opened new perspectives. This test, the Xpert® MTB/RIF assay (Cepheid, Sunnyvale, CA, USA), shows a sensitivity of respectively 86% and 79% compared to culture in human immunodeficiency virus (HIV) negative and -positive patients, and a specificity of 98%, according to a meta-analysis of published studies.[2] It is easy to use and provides results in <2 h, thus facilitating decentralised and same-day testing.[3]

The World Health Organization (WHO) recommends using Xpert as the initial diagnostic test instead of microscopy in adults presumed to have HIV-associated or multidrug-resistant TB (MDR-TB).[4,5] In other patients, the current policy recommends using Xpert either as the initial diagnostic test or as an add-on test following a negative microscopy result, where resources are available. In practice, many facilities use Xpert as an add-on test.[6]

Recent studies on how the introduction of Xpert impacts patient outcomes have shown increases in same-day diagnosis, but limited or no benefit in terms of proportions of patients on treatment, morbidity or mortality.[7–10] This apparent lack of impact may reflect the high proportion of patients started on treatment empirically, without laboratory confirmation, and/or difficulties in defining and adopting diagnostic and treatment algorithms.[11] The impact might be even lower in routine conditions, where there are other additional challenges, such as lack of national guidance on testing algorithms, high rates of failed tests and delays in testing, that prevent same-day diagnosis; however, routine data remain scarce.[6]

Here, we present data on the use of Xpert under routine conditions in four TB programmes in different settings as regards HIV prevalence and MDR-TB risk. We report on per-patient analysis of Xpert results when compared to microscopy, treat-

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Article submitted 15 December 2014. Final version accepted 10 April 2015.

ment initiation and delay, as well as cost and workload issues.

STUDY POPULATION AND METHODS

Sites and population

The analysis was conducted on routine data collected from four TB programmes supported by Médecins Sans Frontières (MSF) in Kampong Cham, Cambodia, Sukhumi, Georgia, Mathare, Kenya, and Nhlangano, Swaziland. These sites were non-randomly selected to illustrate settings with different human immunodeficiency virus (HIV) prevalence and multidrug-resistant TB (MDR-TB) risks (Appendix Table A.1).* All sites had been using the Xpert assay for at least 6 months prior to the start of data collection to ensure that data reflected established routine use.

The laboratory received specimens from the health structure where it was located, as well as from peripheral health centres or clinics (Appendix Table A.1). The population consisted of all patients presumed to have TB for whom at least one diagnostic specimen was sent to the laboratory. Patients started on treatment without providing a diagnostic specimen were also included based on data collected in the clinical register. There was no minimal sample size for this descriptive study.

In high HIV prevalence settings (Mathare and Nhlangano), the recommended definition of a presumed TB patient was cough for >2 weeks; or any cough with at least one of the following signs: weight loss, night sweat, fever; or suspicion based on clinical judgment. The diagnostic algorithm included Xpert testing for all presumptive TB patients and repeated testing for patients with presumed TB who are initially negative and not recovering on broad-spectrum antibiotics.

In low HIV prevalence settings (Kampong Cham and Sukhumi), the recommended definition of a presumed TB patient was cough for >2 weeks. The diagnostic algorithm was smear microscopy as first-line test and Xpert testing for patients at high risk of MDR-TB or smear-negative suspects not recovering on broad-spectrum antibiotics. In addition, in high MDR-TB settings (Sukhumi), all smear-positive patients were tested with Xpert to assess RMP resistance.

When anti-tuberculosis treatment is initiated on clinical grounds, the MSF guidelines do not recommend stopping treatment if subsequent laboratory test results are negative.

Microscopy and culture

Smear microscopy was performed by experienced technicians at all sites. Auramine fluorescence microscopy using light-emitting diode-based microscopes on two sputum samples were used at all sites except for Sukhumi, where three sputum samples were submitted for Ziehl-Neelsen staining. Positive slides were read and graded according to WHO guidelines.[12]

In Kampong Cham, Löwenstein-Jensen and MGIT™ (Mycobacteria Growth Indicator Tube, BD, Sparks, MD, USA) cultures were performed systematically, each on one specimen submitted for microscopy. In Nhlangano, thin-layer agar (TLA) culture was started during the monitoring period on a limited number of specimens.

Cost estimation

Test costs were estimated based on the current cost of Xpert cartridges by MSF-Logistique (excluding shipment costs), plus additional costs of materials as needed, as reported by the field sites. Staff cost was calculated by multiplying the time spent on each test (estimated at approximately 15 min) by hourly wages. The cost per test was multiplied by the average number of tests per patient to obtain a testing cost/patient. Microscopy costs were not reported here, but a generic cost of €2.7/patient was considered based on published data from an MSF-supported site.[13]

Data collection and analysis

Data collected from the laboratory and clinical registers were entered into an Excel file (MicroSoft, Redmond, WA, USA) designed for routine monitoring. Data were analysed using Stata® 12.1 (StataCorp, College Station, TX, USA). Patients were identified by a unique identification number.

The relative gain of Xpert was defined as the ratio between the number of smear-negative patients detected using Xpert and the number of smear-positive patients.

Ethics

The protocol was submitted to the MSF ethical review board (Geneva, Switzerland), which waived the need for ethics approval, as this was a quality assurance study that used routine anonymised data for analysis.

RESULTS

Description of the study population

Data collected from 1 March 2012 in Nhlangano and Sukhumi, 1 May 2012 in Kampong Cham and 15 May 2012 in Mathare until 31 November 2012, are presented here. During this period, a total of 6086 TB suspects provided specimens at the four sites, and 1124 were started on treatment (Appendix Table A.2).

* The appendix is available in the online version of this article, at http://www.ingentaconnect.com/content/iuatld/ijtld/2015/00000019/00000008/art00016

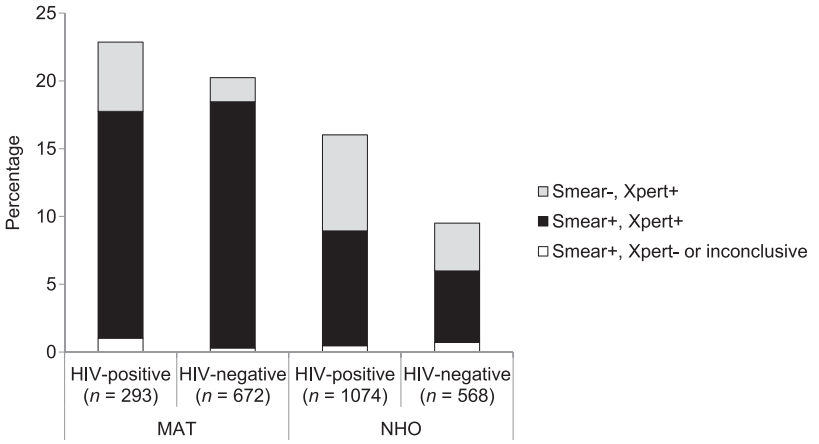

Figure 1 Proportion of presumed tuberculosis patients detected by microscopy only, Xpert and microscopy, and Xpert only among HIV-positive and HIV-negative patients in high HIV prevalence settings. HIV = human immunodeficiency virus; MAT = Mathare; NHO = Nhlangano.

There were differences in the population characteristics among sites, with a higher proportion of males in Sukhumi, younger age in Mathare and Nhlangano, and a higher proportion of presumptive extra-pulmonary cases in Kampong Cham (Appendix Table A.2). Among patients started on treatment, retreatment cases represented more than one in five patients in Mathare and Sukhumi (Appendix Table A.2).

Xpert results and relative gain over microscopy in high HIV prevalence settings

In Mathare and Nhlangano, almost all patients underwent at least one Xpert test; the proportion of those with two or three Xpert tests varied from 2.9% in Nhlangano to 13.5% in Mathare (Appendix Table A.2). At both sites, the main reason for repeating the Xpert test was that the initial test was inconclusive (error, invalid, no result: 123/145, 84.8%, in Mathare and 62/76, 81.6%, in Nhlangano), followed by repeated testing for presumed TB patients not recovering on broad spectrum antibiotics ($n = 17$, 11.7% in Mathare; $n = 6$, 7.9% in Nhlangano).

The proportion of inconclusive initial results was 12.2% in Mathare and 7.0% in Nhlangano; this decreased to respectively 4.3% and 4.2% after repeated testing. The proportion of Xpert-positive, smear-negative patients was higher among HIV-positive than among HIV-negative patients at the two sites, and higher in Nhlangano than in Mathare (Figure 1), with relative gains over microscopy of respectively 28.8%, 9.7% and 15.5% in HIV-positive, HIV-negative patients and overall in Mathare, and 79.2%, 58.8% and 66.7% in Nhlangano.

Reasons for performing Xpert and additional yield in low HIV prevalence settings

In the low HIV prevalence settings, the proportion of patients tested with Xpert was 39.5% in Sukhumi and 54.6% in Kampong Cham (Appendix Table A.2). The main reasons for requesting Xpert are presented in Table 1. The proportions of Xpert-positive patients among those tested was respectively 30.3% (88/290)

Table 1 Reasons for requesting Xpert in low HIV prevalence settings

	Kampong Cham ($n = 1016$) *n* (%)	Sukhumi ($n = 235$) *n* (%)
Included in the algorithm	617 (60.7)	123 (52.3)
Presumed pulmonary TB after antibiotic treatment	297 (29.2)	47 (20.0)
Presumed drug resistance*	317 (31.2)	17 (7.2)
DST in smear-positive patients	0	59 (25.1)
Presumed TB in HIV patient	3 (0.3)	0
Not included in the algorithm	358 (35.2)	112 (47.7)
Presumed pulmonary TB patient†	208 (20.5)	112 (47.7)
Extra-pulmonary	144 (14.2)	0
Presumed TB in children	2 (0.2)	0
Presumed non-tuberculous mycobacteria	4 (0.4)	0
Unknown	41 (4.0)	0

* Including drug-resistant contacts, failure and relapse.
† Before broad spectrum antibiotics or unspecified.
HIV = human immunodeficiency virus; TB = tuberculosis; DST = drug susceptibility testing.

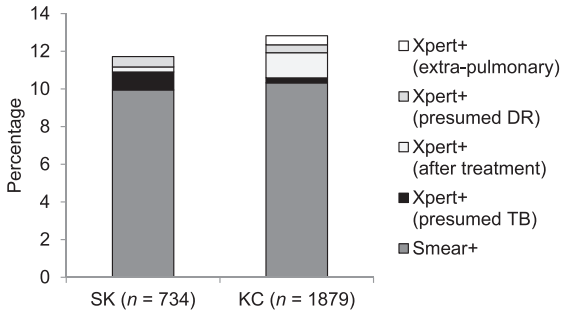

Figure 2 Proportion of patients detected by microscopy or by Xpert only, stratified by reason for requesting Xpert. SK = Sukhumi; KC = Kampong Cham; DR = drug resistance; TB = tuberculosis.

and 14.0% (144/1025) overall, and 8.2% (18/219) and 5.7% (52/912) among presumptive smear-negative TB patients in Sukhumi and Kampong Cham. The proportion of additional cases detected using Xpert compared to microscopy by setting and type of request is presented in Figure 2. The relative gain was 17.8% in Sukhumi and 24.2% in Kampong Cham.

Patients on treatment

The proportion of patients confirmed by microscopy, Xpert or both varied between 56% and 83% among adult pulmonary TB patients started on treatment and from 6% to 26% among adult extra-pulmonary TB patients (Table 2). The time between the collection of the first specimen and treatment start varied substantially across sites and type of biological confirmation (Table 2).

Rifampicin resistance

The proportion of RMP resistance detected among Xpert-positive patients was 3.3% 5/152) in Kampong Cham, 19.1% (17/89) in Sukhumi, 4.9% (10/203) in Mathare and 11.4% (31/271) in Nhlangano. The proportion of indeterminate RMP resistance results varied between 0% in Sukhumi and 4.4% (12/271) in Nhlangano.

Among patients from sites with clinical information available, the majority of the patients with RMP resistance detected were started on MDR-TB treatment (7/10 in Mathare, 25/30 in Nhlangano, 12/15 in Sukhumi and 3/3 in Kampong Cham), with median delays of 10 days in Nhlangano, 12.5 days in Sukhumi and 17 days in Kampong Cham and Mathare. The median time to obtaining culture drug susceptibility testing (DST) results among those for whom this test was performed was 13 days in Nhlangano ($n = 89$, using the TLA method onsite), 23 days in Mathare ($n = 10$), 52 days in Kampong Cham ($n = 25$) and 77 days in Sukhumi ($n = 54$).

Laboratory workload and turnaround time

The median number of Xpert tests performed per day was 9 (interquartile range [IQR] 7–12) in Mathare, 13.5 (IQR 8–18.5) in Nhlangano, 3 (IQR 2–4) in Sukhumi and 8 (IQR 5–13) in Kampong Cham. The median time between receipt of a specimen in the

Table 2 Type of laboratory confirmation and time between collection of first specimen and treatment initiation among patients started on treatment

	Kampong Cham		Sukhumi		Mathare		Nhlangano	
	n (%)	Delay, days median [IQR]	*n* (%)	Delay, days median [IQR]	*n* (%)	Delay, days median [IQR]	*n* (%)	Delay, days median [IQR]
Adult pulmonary TB patients	257		115		179		278	
Xpert+, smear−	15 (5.8)	16 [6–33]	14 (12.2)	6 [4–9]	17 (9.5)	4 [2–7]	63 (22.7)	6.5 [3–10]
Xpert+, smear+	54 (21.0)	5 [2–9]	64 (55.7)	3 [2–6]	128 (71.5)	1 [1–3]	97 (34.9)	6 [1–8]
Smear+*	77 (30.0)	4 [2–6]	0 (0)	NA	3 (1.7)	1 [1–35]	7 (2.5)	8 [1–11]
Culture+†	39 (15.2)	25 [9–61]	NA		NA		NA	
No laboratory confirmation	46 (17.9)	12 [2–18]	22 (19.1)	7 [4–14]	22 (12.3)	7 [1–22]	81 (29.1)	0 [0–5]
No specimen	26 (10.1)	1 [1–10]	15 (13.0)	7.5 [1–18]	9 (5)	0 [0–0.5]	30 (10.8)	1 [0–2]
Adult extra-pulmonary TB patients	69		18		35		36	
Xpert+, smear−	6 (8.7)	12.5 [5–13]	0 (0)	NA	2 (5.7)	1 [0–2]	2 (5.6)	4.5 [3–6]
Xpert+, smear+	7 (10.1)	3 [3–4]	1 (5.6)	55.0	3 (8.6)	3 [3–5]	2 (5.6)	5.5 [4–7]
Smear+*	0 (0)	NA	0 (0)	NA	0 (0)	NA	2 (5.6)	7.5 [0–15]
Culture+†	9 (13.0)	14 [10–15]	NA		NA		NA	
No laboratory confirmation	28 (40.6)	6 [2–11]	11 (61.1)	4.5 [1–7]	18 (51.4)	6 [4–11]	21 (58.3)	1 [0–6]
No specimen	19 (27.5)	5 [1–13]	6 (33.3)	3 [3–6]	12 (34.3)	4 [0–6]	9 (25.0)	8 [1–8]
Children	62		3		29		39	
Xpert+, smear−	0	NA	0	NA	0	NA	2 (5.1)	0;2
Xpert+, smear+	1 (1.6)	1.0	0	NA	0	NA	2 (5.1)	1;12
Smear+*	0	NA	0	NA	0	NA	1 (2.6)	13.0
Culture+†	3 (4.8)	3 [0–25]	NA		NA		NA	
No laboratory confirmation	15 (24.2)	8 [7–18]	1 (33.3)	11	6 (20.7)	2.5 [0–6]	13 (33.3)	0 [0–1]
No specimen	43 (69.4)	4 [1–10]	2 (66.7)	1;10	23 (79.3)	1 [1–4]	21 (53.9)	0 [0–1]

* Smear-positive and Xpert not performed, negative or inconclusive.
† Culture-positive, smear-negative, and Xpert not performed, negative or inconclusive.
IQR = interquartile range; TB = tuberculosis; + = positive; − = negative; NA = not available.

laboratory and availability of a result was 6 h (IQR 4–26) in Mathare, 26 h (IQR 21–51) in Nhlangano, 28 h (IQR 27–75) in Sukhumi and 45 h (IQR 24–95) in Kampong Cham, resulting in same-day testing for most specimens only in Mathare (Appendix Figure A).

Cost

At a cost of €9.19 per cartridge, we estimated that the cost/patient detected varied between €32.8 and €91.4 across sites (Appendix Table A.3). Around 80% and 92% of the total costs were for testing smear-negative patients in Mathare and Nhlangano, respectively. If we assume a cost of €2.7/patient for microscopy, the total cost/patient detected would have been respectively €51.3 and €96.3 had Xpert been used as an add-on test to microscopy in Mathare and Nhlangano.

DISCUSSION

The results of Xpert use in these four programmes illustrate the variety of use and added value of Xpert compared to traditional methods depending on the context and the algorithm used. As expected, given its widely demonstrated greater sensitivity,[2,3] Xpert detected more TB cases than microscopy overall. In high HIV prevalence settings, the relative gain of Xpert compared to microscopy in initial patient screening varied greatly between Mathare and Nhlangano, but was within the wide range of relative gains reported by MSF or calculated in a multicentric implementation study by other authors (7% to 150%).[14] The reasons for such variations are unclear, but could include several factors such as differences in populations attending the clinics in terms of HIV prevalence and health care use, which could also explain the difference in the proportions of smear-positive patients between the two sites. Differences in microscopy sensitivity could also be a reason.

Despite the additional number of cases detected by Xpert, a large proportion of patients were started on treatment empirically at all sites. In Nhlangano, most of these patients were started on the day of first specimen collection, suggesting that the clinicians did not wait for the biological results. This might be partly due to the suboptimal turnaround times to obtain results, which also delayed treatment start for laboratory-confirmed patients. Several reasons could have contributed to these laboratory delays, including high workload, preparation of specimens for culture at sites performing both methods in parallel, as well as the complexity of the diagnostic algorithm at sites that did not perform Xpert systematically. Same-day testing in the laboratory should be ensured to reduce delays in treatment initiation and loss to follow-up.[15]

Adherence to the recommended use of Xpert was low in both high and low HIV prevalence settings. In high prevalence settings, only a few patients underwent a repeat Xpert after broad-spectrum antibiotic treatment, probably due to the complexity of following the algorithm in the absence of well-kept clinical files for presumptive TB patients, as reported informally by clinicians on site. In low HIV prevalence settings, many smear-negative patients were tested prior to broad-spectrum antibiotic treatment, against recommendations. It is difficult to restrain clinicians from using an efficient tool where available. As a consequence, the added value of these strategies could not be evaluated, and the global added value of the diagnostic algorithm using Xpert might have been underestimated.

Although it was not possible to evaluate the impact of introducing Xpert on treatment initiation or outcomes due to the lack of comparative data in our settings, the large proportion of patients started on empirical treatment might have undermined this effect, as reported elsewhere.[11] However, considering the imperfect sensitivity of Xpert, we believe that empirical treatment is still justified in certain cases, and that this does not undermine the added value of Xpert in increasing biological confirmation of TB diagnosis. In addition, the median delay of 10–17 days in initiating MDR-TB treatment among RMP-resistant TB patients probably represents a real improvement over the pre-Xpert era, as suggested by the long delays in obtaining conventional DST results at some sites.

Modelled costs of using Xpert as a replacement or add-on test after microscopy were very similar in Mathare and Nhlangano, arguing in favour of the simpler and less time-consuming use of Xpert only as initial test whenever possible. However, considering the high rate of inconclusive results reported here and elsewhere,[6] some smear-positive cases might be missed by this strategy and a system should be in place to ensure second specimen collection to repeat Xpert and reduce the number of inconclusive results.

Routine data collection represents the main strength of this study, providing valuable data to document the use of Xpert in a real-life situation, but also its main weakness. Some data on screening and clinical information were missing or lacking in precision. In particular, the identification of patients providing several specimens for diagnosis was difficult, and reasons for requesting Xpert in low HIV prevalence settings were sometimes imprecise. In addition, our data did not include the date the results were made available to clinicians, probably leading to an underestimation of the proportion of patients started on treatment without laboratory confirmation.

In conclusion, these data confirm the added value of Xpert compared to microscopy for the biological confirmation of TB and detection of RMP resistance, although with considerable variations across different sites. However, the proportion of patients put on empirical treatment remained high, and most extra-

pulmonary cases were still not confirmed. The organisation of patient, specimen and result flow should be optimised to ensure same-day testing in the laboratory and reduce the time to treatment initiation. Diagnostic and clinical algorithms should be as simple as possible, and training should focus on both clinicians and laboratory staff to ensure optimal adherence. Where budget allows, Xpert should be considered as the initial test and not as an add-on test to microscopy, as the latter strategy is not cost-effective. Finally, non-sputum-based point-of-care diagnostic tests are still needed for rapid diagnosis of TB, particularly in extra-pulmonary patients and children.

Acknowledgements

The authors would like to thank all the persons who participated in supervising or collecting data for the study, in particular R Kaitano and T Zanamwe in Swaziland, L Nyangau Obonyo, G Mumbua Kyalo and N Odhoch Odidi in Kenya, B Poepping and J-P Dousset in Cambodia, and H Pangtey in Georgia. We would also like to thank C Lauro for her help in data collection and extraction in Cambodia; and M Zedevic and P Kahn for editorial input.

This work was supported by the Paris and Geneva Operational Centers of Médecins Sans Frontières.

Conflicts of interest: none declared.

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Appendix Table A.1 Description of the monitoring sites

Site, country	Type of setting	Laboratory	Sites sending specimens	Number of Xpert machines and installation date	Recommended Xpert testing algorithm
Kampong Cham, Cambodia	Low HIV, low MDR-TB prevalence	Provincial reference laboratory, Kampong Cham Provincial Hospital	District hospital + 1 health centre	1 four-module (2011)	Smear-negative patients after broad-spectrum antibiotic treatment Patients at high risk of MDR-TB
Sukhumi, Georgia	Low HIV, high MDR-TB prevalence*	TB laboratory, Gulripch TB Hospital, Abkhazia	Hospital + 7 peripheral health centres	1 four-module (May 2011)	All smear-positive patients Smear-negative patients after broad-spectrum antibiotic treatment
Mathare, Kenya	High HIV,† low MDR-TB prevalence	TB laboratory, TB-HIV clinic, Mathare	TB-HIV clinic	1 four-module (May 2011)	All presumed TB patients in parallel with smear microscopy Repeat Xpert in smear-negative patients after broad-spectrum antibiotic treatment
Nhlangano, Swaziland	High HIV,† high MDR-TB prevalence*	TB laboratory, Nhlangano Health Centre	Health centre + 13 rural clinics	2 four-module (August 2011 and May 2012)	All presumed TB patients in parallel with smear microscopy Repeat Xpert in smear-negative patients after broad-spectrum antibiotic treatment

* Defined as >5% prevalence in new TB cases. MDR-TB prevalence obtained from WHO TB country profiles (www.who.int/tb/country/data/profiles/en).
† Defined as >5% prevalence among adults aged 15–49 years. HIV prevalence obtained from AIDSinfo country fact sheets (www.unaids.org/en/dataanalysis/datatools/aidsinfo).
HIV = human immunodeficiency virus; MDR-TB = multidrug-resistant tuberculosis.

Appendix Table A.2 Characteristics of patients providing specimens and patients started on treatment per site

	Kampong Cham *n* (%)	Sukhumi *n* (%)	Mathare *n* (%)	Nhlangano *n* (%)
Patients providing a specimen	1879	734	1047	2426
Males	970 (51.8)	524 (71.4)	610 (58.3)	1069 (44.2)
Age, years, median [IQR]	52 [35–65]	47 [32–61]	32 [25–42]	36 [27–52]
Children (<15 years)	121 (6.5)	4 (0.6)	67 (6.4)	198 (8.5)
Known HIV result	286 (15.2)	59 (8.0)	965 (92.2)	1642 (67.9)
HIV-positive	10 (3.5)	8 (13.6)	293 (30.4)	1074 (65.4)
Presumed extra-pulmonary TB	182 (9.7)	0	6 (0.6)	70 (2.9)
Smear-positive TB	194 (10.3)	73 (13.4)	181 (17.3)	178 (7.4)
Underwent Xpert testing	1025 (54.6)	290 (39.5)	1028 (98.2)	2407 (99.2)
Xpert repeated	106 (10.3)	14 (4.8)	139 (13.5)	71 (2.9)
Patients started on treatment	388	136	243	357
Males	215 (55.4)	95 (69.9	147 (60.5)	179 (50.1)
Age, years, median [IQR]	45 [25–61]	43 [33–52]	30 [22–39]	33 [26–45]
Children (<15 years)	62 (16.0)	3 (2.2)	29 (11.9)	39 (10.9)
Known HIV result	360 (92.8)	51 (37.2)	235 (96.7)	331 (92.7)
HIV-positive	26 (7.2)	5 (9.8)	90 (38.3)	247 (74.6)
Retreatment cases	51 (13.6)	36 (26.3)	55 (22.7)	34 (9.5)
Extra-pulmonary TB	69 (17.8)	18 (13.2)	36 (14.8)	35 (9.8)
Treatment category				
Category 1	323 (87.1)	94 (69.1)	188 (77.4)	298 (83.5)
Category 2	42 (11.3)	29 (21.3)	48 (19.7)	21 (5.9)
Category 3	0	0	0	13 (3.6)
MDR-TB	6 (1.6)	13 (9.5)	7 (2.9)	25 (7.0)
No specimen provided	88 (22.7)	12 (8.8)	44 (18.1)	60 (17.8)

IQR = interquartile range; HIV = human immunodeficiency virus; MDR-TB = multidrug-resistant tuberculosis.

Appendix Table A.3 Cost estimates based on a cartridge cost of €9.19

	Kampong Cham	Sukhumi	Mathare	Nhlangano
Monthly salary	500	160	660	400
Salary/test*	0.89	0.29	1.18	0.71
Additional material	0.07	0.2	0.00	0.07
Cost/test	10.15	9.68	10.37	9.97
Number of Xpert tests performed during period	1 115	302	1 226	2 483
Number of Xpert tests in smear-negative patients	986	229	989	2 288
Number of patients tested	1 032	290	1 087	2 407
Average number of tests/patient	1.08	1.04	1.13	1.03
Number of patients detected by Xpert	152	89	238	271
Number of smear-negative patients detected by Xpert	55	18	31	110
Total cost	11 320.44	2 922.07	12 711.87	24 766.15
Cost/patient	10.97	10.08	11.69	10.29
Cost/patient detected	74.48	32.83	53.41	91.39
Total cost in smear-negative patients	10 010.72	2 215.74	10 254.52	22 821.17
Cost/smear-negative patient detected	182.01	123.10	330.79	207.47

* Estimated based on 140 h/month and 15 min per test.

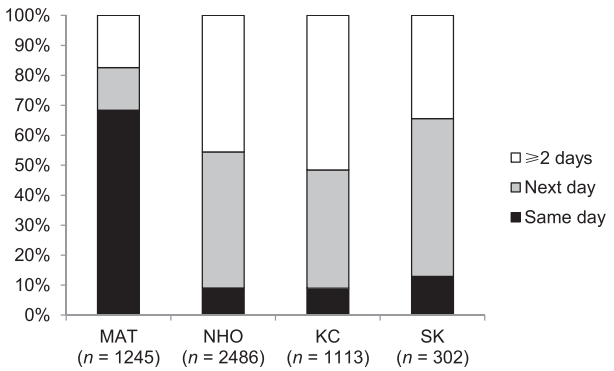

Figure A Proportion of Xpert tests performed on same day, next day or ⩾2 days after receipt of specimen in the laboratory. MAT = Mathare; NHO = Nhlangano; KC = Kampong Cham; SK = Sukhumi.

RESUME

CONTEXTE : Malgré l'introduction du test Xpert® MTB/RIF dans de nombreux pays en voie de développement, il y a encore peu de données sur son utilisation et sa valeur ajoutée en conditions de routine.
OBJECTIF : Décrire les résultats du test Xpert par rapport à la microscopie, l'initiation du traitement, le coût et la charge de travail en conditions de routine dans quatre sites au Cambodge, en Géorgie, au Kenya et au Swaziland.
MÉTHODE : Les données cliniques et de laboratoire de patients avec présomption de tuberculose (TB) consultant aux sites d'étude entre mars et novembre 2012 ont été obtenues grâce aux registres de routine.
RÉSULTATS : Parmi les 6086 cas présumés de TB inclus dans l'analyse, le test Xpert a augmenté le nombre de cas biologiquement confirmés de 15% à 67% par rapport à la microscopie. Jusqu'à 12% des échantillons n'ont pas donné de résultats concluants. Entre 56% et 83% des patients ont été mis sous traitement sur la base de la microscopie et/ou du test Xpert avec des délais médians de 1 à 16 jours. La résistance à la rifampicine a été détectée dans 3% à 19% des patients positifs par Xpert.
CONCLUSIONS : Malgré le nombre supplémentaire de cas détectés par Xpert par rapport à la microscopie, de nombreux patients sont encore mis sous traitement de façon empirique en routine. Les circuits de patients et d'échantillons devraient être optimisés afin d'améliorer le délai à l'initiation du traitement. Des tests simples et rapides à partir d'échantillons autres que le crachat et avec une haute sensibilité sont encore nécessaires pour améliorer le diagnostic et la prise en charge de la TB.

RESUMEN

MARCO DE REFERENCIA: Pese a la introducción generalizada de la prueba Xpert® MTB/RIF en los países en desarrollo, existen aún pocos datos fidedignos sobre su uso y sus ventajas en las condiciones de la práctica corriente.
OBJETIVO: Describir los resultados obtenidos con la prueba Xpert, en comparación con el examen microscópico, la iniciación del tratamiento, los costos y la carga de trabajo en las condiciones de la práctica ordinaria en cuatro centros en Camboya, Georgia, Kenya y Swazilandia.
MÉTODO: Se obtuvo información de laboratorio y datos clínicos de los pacientes con presunción diagnóstica de tuberculosis (TB) a partir de los registros sistemáticos durante un período mínimo de 6 meses de marzo a noviembre del 2012.
RESULTADOS: En los 6086 pacientes con presunción clínica de TB que se incluyeron en el análisis, la prueba Xpert aumentó de 15% a 67% la proporción de casos confirmados bacteriológicamente en comparación con el examen microscópico. Hasta un 12% de los resultados iniciales de la prueba fueron no concluyentes. Del 56% al 83% de los pacientes que recibían tratamiento lo habían iniciado con base en la baciloscopia, la prueba Xpert o ambas, con una mediana del retraso de 1 a 16 días. Se detectó resistencia a rifampicina en 3% a 19% de los pacientes con resultado positivo a la prueba Xpert.
CONCLUSIÓN: Si bien la prueba Xpert aumentó el número de casos detectados en comparación con la baciloscopia, en la práctica corriente una gran proporción de pacientes comienza aun el tratamiento con bases empíricas. Es preciso optimizar el flujo de los pacientes y las muestras, con el propósito de disminuir el retraso en el comienzo del tratamiento. Se necesitan pruebas diagnósticas inmediatas en el punto de atención y que sean sencillas y muy sensibles a fin de mejorar el diagnóstico y el tratamiento de la TB.