

Using the Xpert MTB/RIF assay
to detect pulmonary
and extrapulmonary tuberculosis
and rifampicin resistance
in adults and children

NEW DIAGNOSTIC TESTS
TB
PULMONARY TB
RIFAMPICIN
DIAGNOSIS
RESISTANCE
EXPERT GROUP MEETING REPORT
DRUG-RESISTANCE
TUBERCULOSIS
TB/HIV
RAPID TB TEST
PERFORMANCE
ACCURACY
RECOMMENDATIONS
MYCOBACTERIUM
MOLECULAR DIAGNOSTICS



World Health
Organization

Using the Xpert MTB/RIF
assay to detect pulmonary
and extrapulmonary tuberculosis
and rifampicin resistance
in adults and children

Expert Group Meeting Report

2013



This report contains the collective views of an international group of experts, and does not necessarily represent the decisions or the stated policy of the World Health Organization. Mention of a technology in the report does not imply endorsement of any specific commercial product.



**World Health
Organization**

© World Health Organization 2013

All rights reserved. Publications of the World Health Organization are available on the WHO web site (www.who.int) or can be purchased from WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel.: +41 22 791 3264; fax: +41 22 791 4857; e-mail: bookorders@who.int).

Requests for permission to reproduce or translate WHO publications – whether for sale or for noncommercial distribution – should be addressed to WHO Press through the WHO web site (http://www.who.int/about/licensing/copyright_form/en/index.html).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area, or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.

Designed by GPS Publishing

WHO/HTM/TB/2013.14

Contents

1. EXECUTIVE SUMMARY	X
2. BACKGROUND	1
3. EVIDENCE BASE	2
3.1. EVIDENCE SYNTHESIS	2
3.2. MEETING OBJECTIVES	2
3.3. GRADE EVALUATION	3
3.3.1. PICO QUESTIONS FOR EACH REVIEW	4
3.3.2. DETERMINING THE RELATIVE IMPORTANCE OF PATIENTS' OUTCOMES	6
3.3.3. ASSESSMENT OF STUDY QUALITY	6
3.4. PROCEDURAL ISSUES	6
4. RESULTS	7
4.1. USING XPERT MTB/RIF TO DIAGNOSE PULMONARY TB	7
4.1.1. CHARACTERISTICS OF THE STUDIES	7
4.1.2. QUALITY OF THE STUDIES	8
4.1.3. USING XPERT MTB/RIF AS AN INITIAL TEST TO REPLACE SMEAR MICROSCOPY	9
4.1.4. INVESTIGATIONS OF HETEROGENEITY: TB DETECTION IN SMEAR-POSITIVE AND SMEAR-NEGATIVE INDIVIDUALS SUSPECTED OF HAVING TB	11
4.1.5. DETECTING TB IN HIV-NEGATIVE AND HIV-POSITIVE INDIVIDUALS SUSPECTED OF HAVING PULMONARY TB	13
4.1.6. DETECTING TB AMONG HIV-POSITIVE INDIVIDUALS BY SMEAR STATUS	13
4.1.7. EFFECT OF THE CONDITION OF THE SPECIMEN	14
4.1.8. EFFECT OF SPECIMEN PREPARATION	14
4.1.9. EFFECT OF THE PROPORTION OF CULTURE-CONFIRMED CASES OF TB ON A STUDY	15
4.1.10. EFFECT OF A COUNTRY'S INCOME STATUS	15
4.1.11. DETECTING RIFAMPICIN RESISTANCE	15
4.1.12. INVESTIGATIONS OF HETEROGENEITY: DETECTING RIFAMPICIN RESISTANCE	16
4.1.13. SUMMARY OF FINDINGS AND GRADE EVIDENCE PROFILES	19
4.1.14. STRENGTHS AND LIMITATIONS OF THE EVIDENCE BASE	19
4.1.15. GRADE EVALUATION AND RECOMMENDATIONS	20
4.2. USING XPERT MTB/RIF TO DIAGNOSE EXTRAPULMONARY TB AND RIFAMPICIN RESISTANCE IN ADULTS AND CHILDREN	30
4.2.1. CHARACTERISTICS OF THE STUDIES	30
4.2.2. QUALITY OF THE STUDIES	36

4.2.3.	USING XPERT MTB/RIF TO DETECT EXTRAPULMONARY TB	37
4.2.4.	DETECTING RIFAMPICIN RESISTANCE	44
4.2.5.	SUMMARY OF FINDINGS AND GRADE EVIDENCE PROFILES	44
4.2.6.	STRENGTHS AND LIMITATIONS OF THE EVIDENCE BASE	46
4.2.7.	GRADE EVALUATIONS AND RECOMMENDATIONS	46
4.2.8.	FURTHER RESEARCH NEEDS	56
4.3.	USING XPERT MTB/RIF TO DIAGNOSE PULMONARY TB, PERIPHERAL LYMPH NODE TB, TB MENINGITIS AND RIFAMPICIN RESISTANCE IN CHILDREN	56
4.3.1.	CHARACTERISTICS OF THE STUDIES	56
4.3.2.	QUALITY OF THE STUDIES	57
4.3.3.	USING XPERT MTB/RIF AS THE INITIAL TEST TO DETECT PULMONARY TB	58
4.3.4.	XPERT MTB/RIF COMPARED WITH SMEAR MICROSCOPY	60
4.3.5.	INVESTIGATIONS OF HETEROGENEITY	62
4.3.6.	USING XPERT MTB/RIF TO DETECT PERIPHERAL LYMPH NODE TB IN CHILDREN	66
4.3.7.	USING XPERT MTB/RIF TO DETECT TB MENINGITIS IN CHILDREN	67
4.3.8.	USING XPERT MTB/RIF TO DETECT RIFAMPICIN RESISTANCE IN CHILDREN	67
4.3.9.	SUMMARY OF FINDINGS AND GRADE EVIDENCE PROFILES	68
4.3.10.	STRENGTHS AND LIMITATIONS OF THE EVIDENCE BASE	68
4.3.11.	GRADE EVALUATIONS AND RECOMMENDATIONS	69
4.4.	AFFORDABILITY AND COST EFFECTIVENESS OF USING XPERT MTB/RIF TO DIAGNOSE TB	82
4.4.1.	SUMMARY OF COST ANALYSES	82
4.4.2.	SUMMARY OF COST-EFFECTIVENESS ANALYSES	82
4.4.3.	SUMMARY OF FINDINGS	83
4.4.4.	RECOMMENDATIONS	83
ANNEX 1.	MEETING PARTICIPANTS	84
ANNEX 2.	MEETING AGENDA	86
ANNEX 3.	DECLARATIONS OF INTERESTS	91
ANNEX 4.	SELECTION OF STUDIES EVALUATING THE ACCURACY OF XPERT MTB/RIF IN DIAGNOSING PULMONARY TB AND RIFAMPICIN RESISTANCE IN ADULTS	92
ANNEX 5.	SELECTION OF STUDIES EVALUATING THE ACCURACY OF XPERT MTB/RIF IN DIAGNOSING EXTRAPULMONARY TB AND RIFAMPICIN RESISTANCE IN ADULTS AND CHILDREN	102
ANNEX 6.	SELECTION OF STUDIES EVALUATING THE ACCURACY OF XPERT MTB/RIF IN DIAGNOSING PULMONARY AND EXTRAPULMONARY TB, AND RIFAMPICIN RESISTANCE IN CHILDREN	108
ANNEX 7.	LITERATURE REVIEW OF AFFORDABILITY AND COST EFFECTIVENESS OF XPERT MTB/RIF FOR THE DIAGNOSIS OF TB	112

Tables

TABLE 1.	POOLED SENSITIVITY AND SPECIFICITY OF THE XPERT MTB/RIF ASSAY FOR DETECTING PULMONARY TB AND RIFAMPICIN RESISTANCE	10
TABLE 2.	IMPACT OF COVARIATES ON THE HETEROGENEITY OF THE SENSITIVITY AND SPECIFICITY OF XPERT MTB/RIF IN DETECTING PULMONARY TB IN 24 STUDIES (33 STUDY CENTRES)	12
TABLE 3.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DIAGNOSING PULMONARY TB IN ADULTS	21
TABLE 4.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DIAGNOSING PULMONARY TB IN SPUTUM SMEAR-POSITIVE ADULTS	22
TABLE 5.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DIAGNOSING PULMONARY TB IN SPUTUM SMEAR-NEGATIVE ADULTS	23
TABLE 6.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DIAGNOSING PULMONARY TB IN ADULTS LIVING WITH HIV	24
TABLE 7.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DIAGNOSING PULMONARY TB IN ADULTS WITHOUT HIV INFECTION	25
TABLE 8.	GRADE EVIDENCE PROFILE: THE INCREMENTAL YIELD OF XPERT MTB/RIF COMPARED WITH MICROSCOPY IN PATIENTS WITH CULTURE-CONFIRMED TB	26
TABLE 9.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DIAGNOSING PULMONARY TB IN ADULTS AS AN ADD-ON TEST FOLLOWING NEGATIVE SPUTUM-SMEAR MICROSCOPY	27
TABLE 10.	SENSITIVITY OF XPERT MTB/RIF IN SMEAR-NEGATIVE CULTURE-CONFIRMED PULMONARY TB IN INDIVIDUALS, BY HIV STATUS	28
TABLE 11.	GRADE EVIDENCE PROFILE: ADDITIONAL YIELD OF XPERT MTB/RIF OVER MICROSCOPY IN SMEAR-NEGATIVE TB	28
TABLE 12.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DETECTING RIFAMPICIN RESISTANCE, WHERE XPERT MTB/RIF REPLACES PHENOTYPIC CULTURE-BASED DRUG-SUSCEPTIBILITY TESTING AS THE INITIAL TEST	29
TABLE 13.	SAMPLE TYPES AND PROCESSING METHODS USED IN THE 22 STUDIES INCLUDED IN THE REVIEW OF THE ACCURACY OF XPERT MTB/RIF IN DIAGNOSING EXTRAPULMONARY TB AND RIFAMPICIN RESISTANCE IN ADULTS AND CHILDRENA	31
TABLE 14.	SENSITIVITY AND SPECIFICITY OF XPERT MTB/RIF IN DETECTING EXTRAPULMONARY TB, BY SAMPLE TYPE	39
TABLE 15.	ACCURACY OF XPERT MTB/RIF IN DETECTING TB IN LYMPH NODE FLUID AND TISSUE (A. EVIDENCE PROFILE, B. SUMMARY OF FINDINGS)	47
TABLE 16.	ACCURACY OF XPERT MTB/RIF IN DETECTING TB IN PLEURAL FLUID (A. EVIDENCE PROFILE, B. SUMMARY OF FINDINGS)	49
TABLE 17.	ACCURACY OF XPERT MTB/RIF IN DETECTING TB IN CEREBROSPINAL FLUID (A. EVIDENCE PROFILE, B. SUMMARY OF FINDINGS)	51

TABLE 18.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DETECTING TB IN GASTRIC FLUID	53
TABLE 19.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DETECTING TB IN TISSUE SAMPLES	54
TABLE 20.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DETECTING RIFAMPICIN RESISTANCE IN NONRESPIRATORY SPECIMENS	55
TABLE 21.	META-ANALYSIS OF THE ESTIMATED SENSITIVITY AND SPECIFICITY OF XPERT MTB/RIF IN DIAGNOSING PULMONARY TB, PERIPHERAL LYMPH NODE TB AND TB MENINGITIS IN CHILDREN COMPARED AGAINST CULTURE AS A REFERENCE STANDARD (IN PUBLISHED AND UNPUBLISHED STUDIES) AS WELL AS AGAINST THE CLINICAL TB REFERENCE STANDARD	60
TABLE 22.	META-ANALYSIS OF THE ESTIMATED SENSITIVITY AND SPECIFICITY OF SMEAR MICROSCOPY IN DIAGNOSING PULMONARY TB, PERIPHERAL LYMPH NODE TB AND TB MENINGITIS IN CHILDREN COMPARED AGAINST CULTURE AS A REFERENCE STANDARD IN PUBLISHED AND UNPUBLISHED STUDIES	61
TABLE 23.	META-ANALYSIS OF THE SENSITIVITY AND SPECIFICITY OF XPERT MTB/RIF IN DIAGNOSING PULMONARY TB, PERIPHERAL LYMPH NODE TB AND TB MENINGITIS COMPARED AGAINST CULTURE AS A REFERENCE STANDARD IN SMEAR-NEGATIVE AND SMEAR-POSITIVE CHILDREN IN PUBLISHED AND UNPUBLISHED STUDIES	63
TABLE 24.	META-ANALYSIS COMPARING XPERT MTB/RIF FOR DIAGNOSING PULMONARY TB, PERIPHERAL LYMPH NODE TB AND TB MENINGITIS USING CULTURE AS A REFERENCE STANDARD IN HIV-POSITIVE AND HIV-NEGATIVE CHILDREN, STRATIFIED BY SMEAR STATUS	64
TABLE 25.	METAREGRESSION MODEL FOR XPERT MTB/RIF USING SAMPLES OF EXPECTORATED OR INDUCED SPUTUM FROM CHILDREN, CONTROLLING FOR SMEAR STATUS AND HIV STATUS	64
TABLE 26.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DETECTING TB IN CHILDREN COMPARED WITH CULTURE AS A REFERENCE STANDARD (A. EXPECTORATED SPUTUM AND INDUCED SPUTUM, B. GASTRIC LAVAGE OR ASPIRATE, C. SUMMARY OF FINDINGS)	70
TABLE 27.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DETECTING TB IN CHILDREN COMPARED WITH A CLINICAL REFERENCE STANDARD (A. EXPECTORATED SPUTUM AND INDUCED SPUTUM, AND GASTRIC LAVAGE AND ASPIRATE, B. SUMMARY OF FINDINGS)	73
TABLE 28.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DETECTING TB IN CHILDREN FOLLOWING NEGATIVE SMEAR MICROSCOPY (A. EVIDENCE PROFILE, B. SUMMARY OF FINDINGS, C. ADDITIONAL YIELD OF XPERT MTB/RIF OVER MICROSCOPY)	75
TABLE 29.	INCREMENTAL YIELD OF XPERT MTB/RIF COMPARED WITH SMEAR MICROSCOPY IN CHILDREN WITH CULTURE-CONFIRMED TB (A. EXPECTORATED SPUTUM AND INDUCED SPUTUM, B. GASTRIC LAVAGE OR ASPIRATE)	78
TABLE 30.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DETECTING RIFAMPICIN RESISTANCE IN RESPIRATORY SPECIMENS FROM CHILDREN	79
TABLE 31.	GRADE EVIDENCE PROFILE: ACCURACY OF XPERT MTB/RIF IN DETECTING PERIPHERAL LYMPH NODE TB IN CHILDREN	80
TABLE 32.	GRADE EVIDENCE PROFILE AND SUMMARY OF FINDINGS: ACCURACY OF XPERT MTB/RIF IN DETECTING TB MENINGITIS IN CHILDREN	81

Figures

FIGURE 1.	RISKS OF BIAS (%) AND JUDGEMENTS ABOUT APPLICABILITY (%) FOR EACH DOMAIN OF THE QUADAS-2 TOOL IN STUDIES ASSESSING THE USE OF XPERT MTB/RIF TO DIAGNOSE PULMONARY TB FOR 36 STUDY CENTRES INCLUDED IN 27 STUDIES	9
FIGURE 2.	FOREST PLOT OF THE SENSITIVITY AND SPECIFICITY OF XPERT MTB/RIF FOR DETECTING PULMONARY TB IN 27 STUDIES (36 STUDY CENTRES)	11
FIGURE 3.	FOREST PLOT OF THE SENSITIVITY AND SPECIFICITY OF XPERT MTB/RIF FOR DETECTING PULMONARY TB IN SMEAR-NEGATIVE INDIVIDUALS SUSPECTED OF HAVING TB IN 24 STUDIES (33 STUDY CENTRES)	11
FIGURE 4.	FOREST PLOTS OF THE SENSITIVITY AND SPECIFICITY OF XPERT MTB/RIF FOR DETECTING PULMONARY TB IN HIV-NEGATIVE INDIVIDUALS SUSPECTED OF HAVING TB (9 STUDIES, 18 STUDY CENTRES) AND HIV-POSITIVE INDIVIDUALS SUSPECTED OF HAVING TB (10 STUDIES, 16 CENTRES)	14
FIGURE 5.	FOREST PLOTS OF THE SENSITIVITY AND SPECIFICITY OF XPERT MTB/RIF FOR DETECTING RIFAMPICIN RESISTANCE WHEN XPERT MTB/RIF WAS USED AS AN INITIAL TEST REPLACING PHENOTYPIC CULTURE-BASED DRUG-SUSCEPTIBILITY TESTING IN 24 STUDIES (33 STUDY CENTRES) (STUDIES ARE PRESENTED IN ORDER OF DECREASING SENSITIVITY AND DECREASING NUMBER OF TRUE-POSITIVE RESULTS)	16
FIGURE 6.	RISKS OF BIAS (%) AND JUDGEMENTS ABOUT APPLICABILITY (%) FOR EACH DOMAIN OF THE QUADAS-2 TOOL IN STUDIES USING CULTURE AS THE REFERENCE STANDARD FOR TB DETECTION AND USING XPERT MTB/RIF TO DIAGNOSE EXTRAPULMONARY TB AND RIFAMPICIN RESISTANCE IN ADULTS AND CHILDREN	36
FIGURE 7.	RISKS OF BIAS (%) AND JUDGEMENTS ABOUT APPLICABILITY (%) FOR EACH DOMAIN OF THE QUADAS-2 TOOL IN STUDIES USING AN AUTHOR-DEFINED COMPOSITE REFERENCE STANDARD FOR TB DETECTION AND XPERT MTB/RIF TO DIAGNOSE EXTRAPULMONARY TB AND RIFAMPICIN RESISTANCE IN ADULTS AND CHILDREN	36

预览已结束，完整报告链接和

<https://www.yunbaogao.cn/report/index/report>