OBJN
Online Brazilian Journal of Nursing
ISSN: 1676 - 4285 | www.objnursing.uff.br

**Submission:** 05-Aug-2024
**Approved:** 02-May-2025

# RAPID MOLECULAR TEST IN THE DIAGNOSIS OF EXTRAPULMONARY TUBERCULOSIS: PROTOCOL FOR A SYSTEMATIC REVIEW OF DIAGNOSTIC TEST ACCURACY

## TESTE RÁPIDO MOLECULAR NO DIAGNÓSTICO DA TUBERCULOSE EXTRAPULMONAR: PROTOCOLO DE REVISÃO SISTEMÁTICA DE ACURÁCIA DIAGNÓSTICA

**Rafaele Oliveira Bonfim**[1] ORCID: 0000-0001-8157-2323
**Mariana Gaspar Botelho Funari de Faria**[1] ORCID: 0000-0002-5544-910X
**Felipe Mendes Delpino**[2] ORCID: 0000-0002-3562-3246
**Pedro Augusto Bossonario**[3] ORCID: 0000-0001-6287-174X
**Quezia Rosa Ferreira**[1] ORCID: 0000-0001-5796-4546
**Rubia Laine de Paula Andrade**[1] ORCID: 0000-0001-5843-1733
**Juan Ramon Lacalle Remigio**[4] ORCID: 0000-0002-2648-0191
**Aline Aparecida Monroe**[1] ORCID: 0000-0003-4073-2735

[1] Universidade de São Paulo, Escola de Enfermagem de Ribeirão Preto, SP, Brazil
[2] Universidade Federal de Pelotas, RS, Brazil
[3] Universidade Estadual de Maringá, PR, Brazil
[4] Universidade de Sevilha, Andalucia, Spain

**How to cite:** Bonfim RO, Faria MGBF, Delpino FM, Bossonario PA, Ferreira QR, Andrade RLP, et al. Rapid molecular test in the diagnosis of extrapulmonary tuberculosis: protocol for a systematic review of diagnostic test accuracy. Online Braz J Nurs. 2025;24(Suppl 1):e20256826. https://doi.org/10.17665/1676-4285.20256826

## RESUMO

**Objetivo:** Sintetizar o conhecimento científico produzido sobre a acurácia do teste rápido molecular no diagnóstico da tuberculose extrapulmonar. **Método:** Trata-se de um protocolo de revisão sistemática, cuja questão da pesquisa foi elaborada a partir da estratégia PIRD (na qual População (P) corresponde às pessoas de qualquer idade; Teste Índice (I), ao teste rápido molecular (Gene Xpert MTB/RIF e/ou Gene Xpert Ultra); Teste de Referência (R), à cultura; por fim, Diagnóstico (D), à tuberculose extrapulmonar). As buscas na literatura foram realizadas com a utilização dos vocabulários controlados e livres em cinco bases de dados da literatura científica e dois sites de literatura cinzenta. Ademais, os resultados encontrados foram exportados para o software Rayyan da Qatar Computing Research Institute (QCRI) (literatura científica) e arquivos do Word (literatura cinzenta), por meio dos quais serão possíveis a exclusão de materiais duplicados e a seleção das publicações por três revisores. Além disso, a extração dos dados das publicações selecionadas será realizada a partir de uma planilha elaborada com base em recomendações da Joanna Briggs Institute (JBI), a qual também apresenta um instrumento de avaliação da qualidade metodológica de estudos de acurácia de testes diagnósticos e que será utilizado nesta revisão. Por fim, os resultados dos estudos serão sintetizados narrativamente e por meio de metanálise.

**Descritores:** Tuberculose Extrapulmonar; Diagnóstico; Técnicas de Diagnóstico Molecular; Testes de Diagnóstico Rápido.

## ABSTRACT

**Objective:** to synthesize the scientific knowledge produced on the accuracy of the rapid molecular test in the diagnosis of extrapulmonary tuberculosis. **Method:** This is a systematic review protocol, whose research question was drawn up using the PIRD strategy (where Population (P) corresponds to people of any age; Index Test (I), to the molecular rapid test (Gene Xpert MTB/RIF and/or Gene Xpert Ultra); Reference Test (R), to culture; Diagnosis (D), to extrapulmonary tuberculosis). Literature searches were carried out using controlled and free vocabularies in five scientific literature databases and two gray literature sites. The results found were exported to the Qatar Computing Research Institute's (QCRI) Rayyan software (scientific literature) and word files (grey literature), through which it will be possible to exclude duplicate material and the selection of publications by three reviewers. The data from the selected publications will be extracted using a spreadsheet based on the recommendations of the Joanna Briggs Institute (JBI), which also has an instrument for assessing the methodological quality of studies on the accuracy of diagnostic tests, which will be used in this review. The results of the studies will be synthesized narratively and by means of meta-analysis.

**Descriptors:** Extrapulmonary tuberculosis; Diagnosis; Molecular Diagnostic Techniques; Rapid Diagnostic Tests.



**Publisher:**
Escola de Enfermagem Aurora de Afonso Costa – UFF
Rua Dr. Celestino, 74 – Centro, CEP: 24020-091 – Niterói, RJ, Brazil
Journal email: objn.cme@id.uff.br

**Corresponding author:**
Rubia Laine de Paula Andrade
Email: rubia@eerp.usp.br

## INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis, and was the leading cause of death by a single agent in the world until the start of the COVID-19 pandemic. It is estimated that in 2022, 10.6 million people fell ill with TB, a higher estimate than in 2021 (10.3 million) and 2020 (10 million)[1].

Extrapulmonary tuberculosis (ETB) refers to the occurrence of TB in the human body outside the lungs, such as the meninges, lymph nodes, pleura, genitourinary tract, skin, joints and bones, among others[2-3]. TB accounts for around 16% of TB cases worldwide[4], and this percentage can vary according to certain risk factors, such as age, gender, HIV infection or other comorbidities. It should also be noted that TB mainly affects children and people living with HIV[3-4].

The diagnosis of TBE has some challenges, such as its paucibacillary nature and the difficulty in obtaining material samples[5]. Thus, failure to diagnose and delay in starting treatment negatively affects patients, leading to increased morbidity and mortality, as well as the development of drug resistance[6-8].

Microscopy is generally negative in extrapulmonary samples and does not differentiate between resistant strains and non-tuberculous mycobacteria. Although culture is considered the reference test for diagnosis in extrapulmonary samples, its results are not rapid, which delays patient care and compromises treatment outcomes[9]. Rapid and timely diagnosis is essential for achieving favorable outcomes, given that TB is a curable disease[7]. Thus, the World Health Organization (WHO) endorses the use of the Rapid Molecular Test for TB (RMT-TB), which amplifies nucleic acid for the diagnosis of TB and rifampicin resistance in two hours. The RMT-TB indicated by the WHO corresponds to the GeneXpert system, which requires minimal biosafety facilities and training and is not prone to cross-contamination, characteristics that make it a potential alternative for detecting TB in extrapulmonary samples and for reducing the time between diagnosis and treatment[7,10-11].

The RMT-TB was initially recommended by regulatory agencies only for the diagnosis of pulmonary TB with sputum samples. A preliminary search of databases identified a systematic review and meta-analysis that evaluated the accuracy of the test in 2014 for extrapulmonary samples[12]. As a result, the use of the test to detect TBE, which had been off-label until 2014[10,13], is now recommended by the WHO[14]. Bearing in mind that the review on the subject was carried out 11 years ago with the first version of the test (Xpert MTB/RIF), as well as the change with the new Ultra version in 2019, this study aims to identify the scientific knowledge produced on the accuracy of RMT-TB in the diagnosis of TBE.

## METHOD

This is a systematic review protocol of diagnostic test accuracy registered with PROSPERO (CRD42023470149) and prepared in accordance with the recommendations of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P)[15], JBI Reviewer's Manual for Diagnostic Test Accuracy Systematic Reviews[16]. We chose to carry out a Systematic Review, since it allows us to gather and synthesize the scientific knowledge produced on a given subject, evaluate the data obtained individually and publish the evidence found on the accuracy of a diagnostic test, in order to contribute to decision-making and the gathering of information in the face of an elaborate question[17].

The systematic review of accuracy compares a diagnostic test of interest (I) to an existing diagnostic test (R), which is known to be a standard and available test to accurately identify the presence or absence of the condition of interest. In this way, the results of the two tests, I and R, are compared with each other to assess the accuracy of I[16].

This protocol specifies, in detail, the steps that will be carried out throughout the study: elaboration of the research question; definition of the inclusion and exclusion criteria for the selection of primary studies; selection of the databases to be used; search for studies that meet the established criteria; screening of the articles found by reading the titles and abstracts; complete reading of the studies filtered in the previous step; assessment of the eligibility of the selected studies; extraction of the necessary information; analysis of the risk of bias of the included studies; synthesis of the results obtained and assessment of the strength of the evidence[16].

### Research question

The research question was developed using the acronym PIRD, whose structure was constructed as follows: Population (P) corresponds to people of any age; Index Test (I), to MDR-TB (Gene Xpert MTB/RIF and/or Gene Xpert Ultra); Reference Test (R), to culture; Reference Diagnosis (D), to extrapulmonary tuberculosis, as described by the JBI[16].

Thus, the following guiding question was developed: "What is the accuracy of the rapid molecular test for the diagnosis of extrapulmonary TB in people of any age compared to culture?"

### Eligibility criteria

In order to select the studies, the following inclusion criteria were established: studies dealing with the accuracy of the RMT-TB in samples of extrapulmonary material and comparing it with reference tests (culture); studies whose study population included children and/or adults. Exclusion criteria: studies not presented in full, review studies and studies involving animal experimentation.

### Information sources and research strategy

The search for studies was carried out in October 2023 in the following databases: Excerpta Medica DataBASE (Embase); MEDLINE (accessed via the PubMed platform); Scopus, an Elsevier domain (SciVerse Scopus), Latin American and Caribbean Health Sciences Literature (LILACS) and Web of Science.

The gray literature was surveyed by searching Google Scholar and the Brazilian Digital Library of Theses and Dissertations (BDTD). The keywords and descriptors used for the research were checked in the Health Sciences Descriptor (DeCS), Medical Subject Headings (MeSH) and Emtree, as well as preliminary searches in data repositories. The search strategies were adjusted according to each database, using the Boolean operators OR and AND[17], as shown in Figure 1. The search did not apply language restrictions; however, the studies were selected based on the publication period from 2010 to 2023, considering that 2010 was the year in which the WHO recommended RMT-TB[10].

| Database | Search strategy |
|---|---|
| Embase, MEDLINE, Scopus and *Web of Science* | "Extrapulmonary Tuberculosis" OR "Tuberculous Peritonitis" OR "Peritoneal Tuberculosis" OR "Cardiovascular Tuberculosis" OR "Tuberculous Pericarditis" OR "Central nervous System Tuberculosis" OR "Intracranial Tuberculoma" OR "Meningeal Tuberculosis" OR "Cutaneous Tuberculosis" OR tuberculide OR escrofuloderma OR "Endocrine Tuberculosis" OR "Gastrointestinal Tuberculosis" OR "Hepatic Tuberculosis" OR "Laryngeal Tuberculosis" OR "Lymph Node Tuberculosis" OR "Kings Evil" OR "Tuberculous Lymphadenitis" OR "Lymphatic Nodes Tuberculosis" OR "Cervical Tuberculous Lymphadenitis" OR "Mycobacterial Cervical Lymphadenitis" OR scrofula OR "Oral Tuberculosis" OR "Osteoarticular Tuberculosis" OR "Bone Tuberculosis" OR "Articular Tuberculosis" OR "Spinal Tuberculosis" OR "Potts Disease" "Tuberculosis Pleural" OR "Tuberculous Pleurisy" OR "Splenic Tuberculosis" OR "Tuberculosis Urogenital" OR "Female Genital Tuberculosis" OR "Male Genital Tuberculosis" OR "Renal Tuberculosis" OR "Miliary Tuberculosis" OR "Abdominal tuberculosis" OR "Pancreatic tuberculosis" OR "Cardiac tuberculosis" OR "Tuberculous encephalitis" OR "Tuberculous meningitis" OR "Adrenal tuberculosis" OR "Thyroid tuberculosis" OR "Ocular tuberculosis" OR "Tuberculous arthritis" OR "Tuberculous sacroiliitis" OR "Tuberculous osteomyelitis" OR "Tuberculous spondylitis" OR "Potts paraplegia" OR "Skin tuberculosis" OR "Lichen scrofulosorum" OR "Lupus vulgaris" OR scrofuloderma OR tuberculid OR "Erythema induratum" OR "Papulonecrotic tuberculid" OR "Dry pleurisy" OR "Tuberculous empyema" OR "Urinary tuberculosis"<br><br>AND<br><br>"Molecular diagnostic techniques" OR "Molecular Diagnostic Technique" OR "Molecular Diagnostic Techniques" OR "Molecular Diagnostic Technics" OR "Molecular Diagnostic Technic" OR "Molecular Testing" OR "Molecular Diagnostic Testing" OR "Xpert" OR genexpert OR diagnostic OR "Molecular diagnostic" OR "Molecular diagnostics" OR "Molecular diagnosis" OR "Molecular biology methods" OR "Molecular Biology Techniques" OR "Molecular probe techniques" OR "Genetic techniques" |
| LILACS and *Biblioteca Digital Brasileira de Teses e Dissertações* | "Tuberculose Extrapulmonar" OR "Tuberculoses Extrapulmonares" OR "Peritonite Tuberculosa" OR "Tuberculose Peritoneal" OR "Tuberculose Cardiovascular" OR "Pericardite Tuberculosa" OR "Tuberculose do Sistema Nervoso Central" OR "Tuberculoma Intracraniano" OR "Tuberculose Meníngea" OR "Tuberculose Cutânea" OR "Tuberculose Endócrina" OR "Tuberculose Gastrointestinal" OR "Tuberculose Gastrintestinal" OR "Tuberculose Hepática" OR "Tuberculose Laríngea" OR "Tuberculose dos Linfonodos" OR "Linfadenite Tuberculosa" OR "Tuberculose dos Gânglios Linfáticos" OR "Linfadenite Tuberculosa Cervical" OR "Tuberculose Bucal" OR "Tuberculose Osteoarticular" OR "Tuberculose Óssea" OR "Tuberculose Articular" OR "Tuberculose da Coluna Vertebral" OR "Tuberculose Pleural" OR "Pleurisia Tuberculosa" OR "Tuberculose Esplênica" OR "Tuberculose Urogenital" OR "Tuberculose dos Genitais Femininos" OR "Tuberculose dos Genitais Masculinos" OR "Tuberculose Renal" OR "Tuberculose Miliar" OR "Extrapulmonary Tuberculosis" OR "Tuberculous Peritonitis" OR "Peritoneal Tuberculosis" OR "Cardiovascular Tuberculosis" OR "Tuberculous Pericarditis" OR "Central nervous System Tuberculosis" OR "Intracranial Tuberculoma" OR "Meningeal Tuberculosis" OR "Cutaneous Tuberculosis" OR tuberculide OR escrofuloderma OR "Endocrine Tuberculosis" OR "Gastrointestinal Tuberculosis" OR "Hepatic Tuberculosis" OR "Laryngeal Tuberculosis" OR "Lymph Node Tuberculosis" OR "Kings Evil" OR "Tuberculous Lymphadenitis" OR "Lymphatic Nodes Tuberculosis" OR "Cervical Tuberculous Lymphadenitis" OR "Mycobacterial Cervical Lymphadenitis" OR scrofula OR "Oral Tuberculosis" OR "Osteoarticular Tuberculosis" OR "Bone Tuberculosis" OR "Articular Tuberculosis" OR "Spinal Tuberculosis" OR "Potts Disease" "Tuberculosis Pleural" OR "Tuberculous Pleurisy" OR "Splenic Tuberculosis" OR "Tuberculosis Urogenital" OR "Female Genital Tuberculosis" OR "Male Genital Tuberculosis" OR "Renal Tuberculosis" OR "Miliary Tuberculosis" OR "Abdominal tuberculosis" OR "Pancreatic tuberculosis" OR "Cardiac tuberculosis" OR "Tuberculous encephalitis" OR "Tuberculous meningitis" OR "Adrenal tuberculosis" OR "Thyroid tuberculosis" OR "Ocular tuberculosis" OR "Tuberculous arthritis" OR "Tuberculous sacroiliitis" OR "Tuberculous osteomyelitis" OR "Tuberculous spondylitis" OR "Potts paraplegia" OR "Skin tuberculosis" OR "Lichen scrofulosorum" OR "Lupus vulgaris" OR scrofuloderma OR tuberculid OR "Erythema induratum" OR "Papulonecrotic tuberculid" OR "Dry pleurisy" OR "Tuberculous empyema" OR "Urinary tuberculosis" OR "Tuberculosis Extrapulmonar" OR "Peritonitis Tuberculosa" OR "Peritonitis Tuberculosa" OR "Tuberculosis Cardiovascular" OR "Pericarditis Tuberculosa" OR "Tuberculosis del Sistema Nervioso Central" OR "Tuberculoma Intracraneal" OR "Tuberculosis Meníngea" OR "Tuberculosis Cutánea" OR "Tuberculosis Endocrina" OR "Tuberculosis Gastrointestinal" OR "Tuberculosis Hepática" OR "Tuberculosis Laríngea" OR "Tuberculosis de los Ganglios Linfáticos" OR "Lifadenitis Tuberculosa" OR "Tuberculosis de los ganglios linfáticos" OR "Linfadenitis Tuberculosa Cervical" OR "Linfadenitis Cervical Micobacteriana" OR "Tuberculosis Bucal" OR "Tuberculosis Osteoarticular" OR "Tuberculose Ósea" OR "Tuberculosis Articular" OR "Tuberculosis Espinal" OR "Tuberculosis Pleural" OR "Pleurisía Tuberculosa" OR "Tuberculosis Esplénica" OR "Tuberculosis Urogenital" OR "Tuberculosis de los Genitales Femeninos" OR "Tuberculosis de los Genitales Masculinos" OR "Tuberculosis Renal" OR "Tuberculosis Miliar"<br><br>AND<br><br>"Técnicas de Diagnóstico Molecular" OR "Teste molecular" OR "Teste diagnóstico molecular" OR "Diagnóstico molecular" OR "Teste de diagnóstico molecular" OR diagnóstico OR "Molecular diagnostic techniques" OR "Molecular Diagnostic Technique" OR "Molecular Diagnostic Techniques" OR "Molecular Diagnostic Technics" OR "Molecular Diagnostic Technic" OR "Molecular Testing" OR "Molecular Diagnostic Testing" OR "Xpert" OR genexpert OR diagnostic OR "Molecular diagnostic" OR "Molecular diagnostics" OR "Molecular diagnosis" OR "Molecular biology methods" OR "Molecular Biology Techniques" OR "Molecular probe techniques" OR "Genetic techniques" OR "Técnicas de diagnóstico molecular" OR "Prueba molecular" OR "Prueba de diagnóstico molecular" OR "Diagnostico molecular" |
| *Google Scholar* | Xpert “tuberculose extrapulmonar”<br>Xpert “extrapulmonary tuberculosis”<br>Xpert “tuberculosis extrapulmonar” |

**Figure 1 -** Strategies used to search for studies for the systematic review on the accuracy of the rapid molecular test for the diagnosis of extrapulmonary tuberculosis. Ribeirão Preto, SP, Brazil, 2023

### Selection of studies

The studies found in the scientific literature databases were exported to the Rayyan QCRI application[18], which will allow the exclusion of duplicate publications and subsequent screening of the publications by reading the titles and abstracts by two autonomous evaluators. If there is disagreement between the reviewers about the inclusion of a study, a third reviewer will be called in to resolve the issue. Finally, to validate the decision to include or exclude the articles, all the materials considered relevant will be examined in full. The studies found on Google Scholar and BDTD were copied and pasted into a word file for subsequent manual selection of studies. This selection will also be carried out by two independent reviewers and by a third reviewer in the event of divergences in the selection.

A flowchart will be drawn up to present the search process for the materials found and included in this review study, as recommended by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 Statement (PRISMA)[19].

### Data extraction and synthesis

For data extraction, a standardized form was drawn up in Microsoft Excel and will be filled in by a reviewer, who will then check it with another reviewer. The data extraction form was designed based on the items suggested by the JBI for extracting data from systematic reviews of the accuracy of diagnostic tests[16]: authors, year of publication, study site, journal, study objective, sample size, disease site, clinical specimen, I (GeneXpert MTB/RIF or GeneXpert Ultra), R (culture), test accuracy in terms of sensitivity, specificity, positive and negative predictive value, positive and negative likelihood ratio, as well as the accuracy of other tests.

The articles included in the review will undergo a narrative synthesis and a quantitative synthesis (meta-analysis). To carry out the meta-analysis, the following information will also be extracted: true positive (VP), true negative (VN), false positive (FP) and false negative (FN).

### Risk of bias assessment

The methodological quality of the articles selected for the review will be analyzed using the tools suggested by the JBI for evaluating the accuracy of diagnostic tests[14], thus making it possible to verify the conformity between the items used in the studies and those provided by the evaluation instruments. No study will be excluded on the basis of its methodological limitations.

### Certainty of evidence

At the end of all the stages, the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system will be used to grade the quality of the evidence.

## CONFLICT OF INTERESTS

The authors have declared that there is no conflict of interests.

## FUNDING

This work was carried out with the support of the Coordination for the Improvement of Higher Education Personnel - Brazil (CAPES) - Funding Code 001, the São Paulo State Research Foundation (FAPESP) - 2022/00025-2 and the National Council for Scientific and Technological Development (CNPq) - Research productivity grant - process 317170/2021-0.

## REFERENCES

1. World Health Organization. Global tuberculosis report 2023 [Internet]. Geneva: WHO; 2023 [cited 31 Jan 2024]. Available from: https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023
2. Yu Y, Xiang Y, Liu H, Yang S, Li M, Liu B, et al., Analysis of epidemiological characteristics of extrapulmonary tuberculosis from South-Central China. Front Public Health. 2024;12:1405358. https://doi.org/10.3389/fpubh.2024.1405358
3. Seo YS, Kang JM, Kim DS, Ahn JG. Xpert MTB/RIF assay for diagnosis of extrapulmonary tuberculosis in children: a systematic review and meta-analysis. BMC Infect Dis. 2020;20(1):14. https://doi.org/10.1186/s12879-019-4745-1
4. World Health Organization. Global tuberculosis report 2020 [Internet]. Geneva: WHO; 2020 [cited 31 Jan 2024]. Available from: https://www.who.int/publications/i/item/9789240013131
5. Gopalaswamy R, Dusthackeer VNA, Kannayan S, Subbian S. Extrapulmonary tuberculosis—an update on the diagnosis, treatment and drug resistance. J Respir. 2021; 1(2):141-164. https://doi.org/10.3390/jor1020015
6. Berra TZ, Bruce ATI, Alves YM, Ramos ACV, Giacomet CL, Arcêncio RA. Impact of the GeneXpert® MTB/RIF rapid molecular test on tuberculosis detection: temporal trends and vulnerable territories. Rev Lat Am Enfermagem. 2021;29:e3441. https://doi.org/10.1590/1518.8345.4412.3441
7. Santos APFB, Feliciano CS, Bollela VR. Papel do teste Xpert MTB/RIF Ultra® no diagnóstico de tuberculose extrapulmonar em um hospital terciário de São Paulo. Braz J Infect Dis. 2023;27(1):102812. https://doi.org/10.1016/j.bjid.2023.103645
8. Silva DR, Rabahi MF, Sant'Anna CC, Silva-Junior JLR, Capone D, Bombarda S, et al. Consenso sobre o diagnóstico da tuberculose da Sociedade Brasileira de Pneumologia e Tisiologia. J Bras Pneumol. 2021;47(2):e20210054. https://doi.org/10.36416/1806-3756/e20210054
9. Dong B, He Z, Li Y, Xu X, Wang C and Zeng J (2022) Improved Conventional and New Approaches in the Diagnosis of Tuberculosis. Front Microbiol.

2022;13:924410. https://doi.org/10.3389/fmicb.2022.924410

10. World Health Organization. WHO consolidated guidelines on tuberculosis. Module 3: diagnosis – rapid diagnostics for tuberculosis detection, third edition [Internet]. Geneva: WHO; 2024 [cited 21 Feb 2025]. Available from: https://www.who.int/publications/i/item/9789241501545
11. World Health Organization. Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF system [Internet]. Geneva: WHO; 2011 [cited 13 Mar 2024]. Available from: https://www.who.int/publications/i/item/9789241501545
12. Denkinger CM, Schumacher SG, Boehme CC, Dendukuri N, Pai M, Steingart KR. Xpert MTB/RIF essay for the diagnosis of extrapulmonary tuberculosis: a systematic review and meta-analysis. Eur Respir J. 2014;44:435-466. https://doi.org/10.1183/09031936.00007814
13. Mokaddas E, Ahmad S, Eldeen H. Performance comparison of GeneXpert MTB/RIF and Probetec Et Tests for rapid molecular diagnosis of extrapulmonary tuberculosis in a low TB/MDR-TB incidence country. Med Princ Pract. 2021;30(3):277-284. https://doi.org/10.1159/000515254
14. World Health Organization. Standard Operating Procedure (SOP): specimen processing of CSF, lymph nodes and other tissues for Xpert MTB/RIF [Internet]. Geneva: WHO; 2014 [cited 28 Apr 2024]. Available from: https://tbcindia.mohfw.gov.in/wp-content/uploads/2023/05/190623097905-Annexure-05-GeneXpert_SOP_Xpert_processing_EPTB_specimens_.pdf
15. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1. https://doi.org/10.1186/2046-4053-4-1
16. Campbell JM, Klugar M, Ding S, Carmody DP, Hakonsen SJ, Jadotte YT, et al. Chapter 9: diagnostic test accuracy systematic reviews. In: Aromataris E, Munn Z, editors. JBI Manual for Evidence Synthesis. Adelaide: JBI, 2020. https://doi.org/10.46658/JBIMES-20-10
17. Khan KS, Zamora J. Systematic Reviews to support Evidence-Based Medicine: how to appraise conduct and publish reviews. London: CRC Press, 2022.
18. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan - a web and mobile app for systematic reviews. Syst Rev. 2016;5:210. https://doi.org/10.1186/s13643-016-0384-4
19. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:71. https://doi.org/10.1136/bmj.n71
20. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011;155(8):529-536. https://doi.org/10.7326/0003-4819-155-8-201110180-00009

**AUTHORSHIP CONTRIBUTIONS**

Project design: Bonfim RO, Andrade RLP, Remigio JRL, Monroe AA.
Data collection: Faria MGBF, Delpino FM, Bossonario PA, Ferreira QR.
Data analysis and interpretation: Faria MGBF, Delpino FM, Bossonario PA, Ferreira QR.
Writing and/or critical review of the intellectual content: Bonfim RO, Faria MGBF, Delpino FM, Bossonario PA, Ferreira QR, Andrade RLP, Remigio JRL, Monroe AA.
Final approval of the version to be published: Bonfim RO, Faria MGBF, Delpino FM, Bossonario PA, Ferreira QR, Andrade RLP, Remigio JRL, Monroe AA.
Responsibility for the text in ensuring the accuracy and completeness of any part of the paper: Bonfim RO, Faria MGBF, Delpino FM, Bossonario PA, Ferreira QR, Andrade RLP, Remigio JRL, Monroe AA.