INPLASY PROTOCOL

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None declared.

Exploring the eligibility of all reported lipoarabinomannan-testing assays in different clinical situations: A systematic review and meta-analysis of 97 articles

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Review question / Objective: **This work summarized all reported LAM-testing assays, collected all data about the diagnostic capacity of these assays, scientifically pooled data and compared the performance of these different assays in the same situations. This work aimed to identify the application scopes of all reported LAM-testing assays and then offer guidance for clinicians to make correct medical decision in different clinical situations.**
Information sources: **A search in 3 databases (PubMed, Embase, and Web of Science) with a series of subject headings [(tuberculosis OR TB) AND (lipoarabinomannan OR LAM)] up to August 23, 2020 was conducted. Bibliographies of relevant researches and a forward search were also manually assessed. Language restriction was set at English.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 August 2021 and was last updated on 06 August 2021 (registration number INPLASY202180020).

INTRODUCTION

Review question / Objective: **This work summarized all reported LAM-testing assays, collected all data about the diagnostic capacity of these assays, scientifically pooled data and compared the performance of these different assays in the same situations. This work aimed to identify the application scopes of all reported LAM-testing assays and then offer guidance for clinicians to make correct**

medical decision in different clinical situations.

Condition being studied: Tuberculosis (TB) is a major infectious disease and also, the ninth leading cause of death worldwide. The key to reducing TB burden is early diagnosis. However, current diagnostic methods do not meet clinical needs. As a new TB diagnostic biomarker, lipoarabinomannan (LAM) has been paid much attention by many scholars. Various teams and companies have developed a number of tests for LAM. These various detection methods also pose a serious problem for clinicians that how to select proper LAM-testing methods in different, complex and varied clinical situations. Some studies reported the performance of different LAM-testing assays. However, the studied cohort was usually specific population with similar characteristics and the studied LAM-testing assay was also specific one. Different study designs bring the great variation of reported diagnostic performance that further adds to clinician confusion. How to give medical orders to select appropriate LAM-testing assay according to different sample types offered by TB patients? How to choose LAM-testing assay to improve detection rate when TB patients have different ages, TB subtypes, CD4 counts or HIV status? These questions that clinicians have always been most concerned about still remain unanswered. Therefore, we summarized all reported LAM-testing assays, collected all data about the diagnostic capacity of these assays, scientifically pooled data and compared the performance of these different assays in the same situations.

METHODS

Search strategy: Two independent authors conducted a search in 3 databases (PubMed, Embase, and Web of Science) with a series of subject headings [(tuberculosis OR TB) AND (lipoarabinomannan OR LAM)] up to August 23, 2020. Bibliographies of relevant researches and a forward search were also manually assessed. Language restriction was set at English.

Participant or population: Suspected tuberculosis participants.

Intervention: Using LAM-testing assays to detect participant samples.

Comparator: Using reference standard to detect participant samples.

Study designs to be included: Cohort studies, cross-sectional studies or randomized controlled trials.

Eligibility criteria: (I) study design was cohort studies, cross-sectional studies, or randomized controlled trials; (II) the focus of study was to investigate the diagnostic performance of LAM-testing assays for TB patients; (III) reference standard was etiological diagnosis (culture, Xpert, etc.) or clinical comprehensive diagnosis; (IV) details of study design (patient characteristics, the types of LAM-testing assay, etc.) and accurate data about diagnostic performance were provided. Otherwise, studies would be discarded.

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Main outcome(s): This meta is an diagnostic meta. All participants should receive both LAM-testing and diagnostic reference detection (culture, Xpert, etc.). True positive, false positive, true negative and false negative of each included study are calculated by comparing with the result of reference detection. Then, a bivariate mixed model was used to pool sensitivity and specificity. Collectively, pooled sensitivity, specificity and area under curve of each LAM-testing assay are main outcomes.

Additional outcome(s): Chi-square and inconsistency square will be calculated to assess the heterogeneity among studies.

Diagnostic odds ratio will be also computed to evaluate the performance of each assay.

Quality assessment / Risk of bias analysis: Each included article needs to undergo the evaluation of risk of bias according to Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2). Four parts (patient selection, index test, reference standard, and study flow and timing) were taken into this assessment. According to information extracted from text, each included article would be rated as high, unclear, or low risk in each term of QUADAS-2. This evaluation was carried out by 2 independent authors and any divergence was resolved by discussion.

Strategy of data synthesis: Considering the potential influence of threshold effect, a bivariate mixed model was applied to yield pooled sensitivity, specificity, diagnostic odds ratio, and area under the curve (AUC), each with a 95% confidence interval (CI). Forest plot was generated to visualize pooled sensitivity and specificity, while the hierarchical summary receiver operating characteristic (sROC) curve was plotted to show the performance of LAM-testing assays. All analyses were realized by Review Manager Version 5.3 and STATA Version 15.

Subgroup analysis: All cases also would be divided into different subgroups based on their characteristics, and meta-regression analysis was applied to explore the performance of each LAM-testing assay in subgroups to explore their optimal application scopes. The following factors will be taken into consideration: age, sex, ethnicity, TB subtypes, HIV status, smear status and sample types.

Sensitivity analysis: Trough removing low-quality trials, a sensitivity analysis was carried out to examine the robustness of results by removing low-quality trials.

Country(ies) involved: China.

Keywords: tuberculosis, diagnosis, lipoarabinomannan, application scope.

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