# INPLASY PROTOCOL

To cite: Zhu et al. Diagnostic Value of Combination of Biomarkers for Malignant Pleural Mesothelioma: Systematic Review and Meta-Analysis. Inplasy protocol 2022100043. doi: 10.37766/inplasy2022.10.0043

Received: 12 October 2022

Published: 12 October 2022

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Support: CY2020-MS09.

Review Stage at time of this submission: Data analysis.

Conflicts of interest: None declared.

# Diagnostic Value of Combination of Biomarkers for Malignant Pleural Mesothelioma: Systematic Review and Meta-Analysis

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**Review question / Objective:** Tumor biomarkers have become increasingly attractive due to their non-invasive properties and relatively inexpensive nature for early diagnosis of Malignant pleural mesothelioma (MPM) .Many scholars have published studies on DNA and protein as biomarkers for early diagnosis of MPM, which might be a new breakthrough. A new meta-analysis is necessary to compare the accuracy of combination of three kinds of DNA and three kinds of proteins.

Condition being studied: XAs the previous studies have a certain controversy about DNA as a biomarker of MPM, we conducted a systematic search using EMBASE, PubMed and Cochrane Library to identify relevant studies from the inception to October 2021. we used QUADAS-2 for Quality Assessment to Diagnostic Accuracy Studies to evaluate the quality of eligible studies. We used Stata 15.0 and Review Manager 5.4 software to perform the meta-analysis to compare the accuracy of combination of three kinds of DNA and three kinds of proteins.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 October 2022 and was last updated on 12 October 2022 (registration number INPLASY2022100043).

## INTRODUCTION

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#### **METHODS**

Participant or population: Patients diagnosed with MPM by histopathological examination.

**Intervention:** Patient with distant metastasis of MPM.

**Comparator:** The accuracy of combination of three kinds of DNA and three kinds of proteins.

Study designs to be included: (a)Study type: We prospectively or retrospectively assessed the diagnostic accuracy of MPM antibody markers. (b) Participants: patients diagnosed with MPM by histopathological examination, excluding patients with distant metastasis of MPM. (c) Reference standard: pleural biopsy tissue obtained by surgery for histopathological diagnosis. (d) Results: area under the curve (AUC), sensitivity (SEN), specificity (SPE), diagnostic odds ratio (DOR).

Eligibility criteria: (a)Study type: We prospectively or retrospectively assessed the diagnostic accuracy of MPM antibody markers. (b) Participants: included patients diagnosed with MPM by histopathological examination, excluding patients with distant metastasis of MPM. (c) Reference standard: pleural biopsy tissue obtained by surgery for histopathological diagnosis. (d) Results: area under the curve (AUC), sensitivity (SEN), specificity (SPE), diagnostic odds ratio (DOR), positive likelihood ratio (PLR), negative likelihood ratio (NLR). Information sources: https:// www.cochranelibrary.com/, https:// www.ncbi.nlm.nih.gov/, https:// www.embase.com/landing?status=grey

Main outcome(s): We assessed 15 studies to compare the diagnostic accuracy of the combination of three kinds of DNA and three kinds of proteins. We concluded that the combination of MTAP + Fibulin-3 might be more appropriate for early diagnosis of MEM. However, due to the limitations of the included samples, the conclusions may require further studies.

Quality assessment / Risk of bias analysis: Quality was assessed using the revised Diagnostic Accuracy Research Quality Assessment Tool (QUADAS-2). Deek's funnel plot was conducted to detect publication bias where there were more than 10 studies available for an index test.

Strategy of data synthesis: We utilized Stata 15.0 and Review Manager 5.4 statistical software programs to test the heterogeneity of the research and perform meta-analysis. We obtained a 2×2 contingency table by extracting the sensitivity and specificity data of each study. The SEN, SPE, PLR, NLR and DOR of the study were calculated, and the SROC curve is generated.

Subgroup analysis: Clinical information included tumor stage, histologic subtype (epithelioid, sarcomatous, biphasic), age, and gender.

Sensitivity analysis: Sensitivity analysis was performed to compare the accuracy of the different combinations of DNA and proteins.

Language restriction: English.

Country(ies) involved: China.

**Keywords: MPM; diagnostic; combination of biomarkers; meta-analysis; prognosis; bioinformatics analysis** 

### Contributions of each author:

Author 1 - Mucheng Zhu - The author provided concept, design, and manuscript preparation.

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Author 2 - Zhenhua Lu - The author developed the search strategies, conducted literature and study selection. Email: luzhh20@lzu.edu.cn

Author 3 - Hao Guo - The author contributed to the development of selection criteria and the risk of bias assessment strategy. The author contributed to the development of bioinformatics analysis.

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