

# INPLASY PROTOCOL

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**Support:** None.

**Review Stage at time of this submission:** Formal screening of search results against eligibility criteria.

**Conflicts of interest:**  
None declared.

## The diagnostic value of miR-221/222 in glioma : a systematic review and meta-analysis

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**Review question / Objective:** Based on the biological characteristics of miRNA, many researchers at home and abroad have published studies on the diagnostic role of miR-221 and miR-222 in human glioma in recent years. This aroused our interest in exploring the effectiveness of miR-221/222 as a biomarker. A single study may not be enough to draw comprehensive and reliable conclusions. Therefore, we performed a comprehensive meta-analysis of these published studies to evaluate the diagnostic value of miR-221 and miR-222 in glioma.

**Condition being studied:** Previous studies have shown that miR221/222 is highly expressed in a variety of cancer types and may serve as a biomarker for tumor diagnosis and prognosis. Mir221/222 is present not only in tissues, but also in a wide variety of extracellular fluids, including cerebrospinal fluid (CSF), serum, plasma, saliva, and gastrointestinal fluids. Although many studies have proposed the diagnostic value of MIR221/222 in glioma, the results have been inconclusive. The primary purpose of this study was to examine the diagnostic accuracy of miR221/222 in the detection of glioma to determine whether miR221/222 should be considered for screening of patients with suspected glioma.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 March 2021 and was last updated on 19 March 2021 (registration number INPLASY202130064).

### INTRODUCTION

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published studies on the diagnostic role of miR-221 and miR-222 in human glioma in recent years. This aroused our interest in exploring the effectiveness of miR-221/222 as a biomarker. A single study may not be

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## METHODS

**Participant or population:** Patients with glioma including World Health Organization (WHO) grade I to IV providing blood (serum or plasma), tissue, and CSF samples.

**Intervention:** Diagnostic performance of miR221/222 in tumor tissues or circulation (serum, plasma and cerebrospinal fluid, etc.) for gliomas.

**Comparator:** The gold reference standard (histopathological examinations).

**Study designs to be included:** The following exclusion criteria were established :(1) study targets were patients with pathologically diagnosed glioma;(2) The expression of miR-221 or miR-222 in tumor tissues or circulation (serum, plasma and cerebrospinal fluid, etc.) was detected;(3) The diagnostic accuracy of miR-221 or miR-222 expression in glioma was evaluated. In addition, the exclusion criteria were as follows:(1) duplicated.

**Eligibility criteria:** (1) study targets were patients with pathologically diagnosed glioma;(2) The expression of miR-221 or miR-222 in tumor tissues or circulation (serum, plasma and cerebrospinal fluid, etc.) was detected;(3) The diagnostic accuracy of miR-221 or miR-222 expression in glioma was evaluated.

**Information sources:** We searched PubMed, Embase and Web of Science from inception to March 2021 by using medical subject headings (MeSH), Emtree, and text word with no language limitations.

**Main outcome(s):** All outcomes are dichotomous variables, including true positive (TP), false positive (FP), true negative (TN), and false negative (FN). The summary sensitivity, specificity and receiver operating characteristic (SROC) curves will be generated to test diagnostic accuracy.

**Data management:** The extracted data include the following information: (1) Study characteristics: the name of the first author, year of publication and country;(2) Subject characteristics: miRNA type, tumor grade, sample type;(3) Relevant data required for Meta analysis: for diagnostic Meta analysis, sensitivity (SEN), specificity (SPE), AUC (area under ROC curve), and 2x2 data tables including false negative (FN), true negative (TN), true positive (TP) and false positive (FP) were extracted.

**Quality assessment / Risk of bias analysis:** The quality was assessed according to the criteria of Quality-Assessment for Diagnostic Accuracy Studies 2 (QUADAS-2). The guidelines include the following 4 categories (including 7 items) : patient selection (2 items), indicator testing (2 items), reference criteria (2 items), and process and timing (1 item) to determine the suitability and risk of deviation of diagnostic studies.

**Strategy of data synthesis:** MetaDisc software was used for diagnostic meta-analysis. Cochran's-Q and I<sup>2</sup> statistical indices were used to assess inter-study

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heterogeneity. We used a bivariate mixed effects regression model to pooled the diagnostic indicators. Receiver operating curve (ROC) and Spearman correlation coefficient were used to evaluate the threshold effect between diagnostic studies.

**Subgroup analysis:** Subgroup analysis was used to explain the sources of heterogeneity. Subgroup analysis of samples from circulation (serum, plasma, and cerebrospinal fluid) can also assess whether miR-221 and miR-222 can be used for the noninvasive diagnosis of glioma.

**Sensitivity analysis:** This meta-analysis was a diagnostic analysis with few references included, and sensitivity analysis was not planned.

**Language:** English.

**Country(ies) involved:** China.

**Keywords:** glioma , miR-221 , miR-222.

**Contributions of each author:**

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Author 2 - Yuhua Hu.

Author 3 - Haihua Zhan.

Author 4 - Yawei He.