

# INPLASY PROTOCOL

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**Conflicts of interest:**  
None declared.

## Gut microbiome-based machine learning for diagnostic prediction of liver fibrosis and cirrhosis: a systematic review and meta-analysis

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**Review question / Objective:** The invasive liver biopsy is the gold standard for the diagnosis of liver cirrhosis. Other non-invasive diagnostic approaches, have been used as alternatives to liver biopsy, however, these methods cannot identify the pathological grade of the lesion. Recently, studies have shown that gut microbiome-based machine learning can be used as a non-invasive diagnostic approach for liver cirrhosis or fibrosis, while it lacks evidence-based support. Therefore, we performed this systematic review and meta-analysis to evaluate its predictive diagnostic value in liver cirrhosis or fibrosis.

**Condition being studied:** Liver fibrosis and cirrhosis. Liver fibrosis refers to excessive deposition of liver fibrous tissue caused by various pathogenic factors, such as hepatitis virus, alcohol, and drug-induced chemical injury. Continuous progression of liver fibrosis can lead to liver cirrhosis.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 May 2022 and was last updated on 23 May 2022 (registration number INPLASY202250133).

### INTRODUCTION

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however, these methods cannot identify the pathological grade of the lesion. Recently, studies have shown that gut microbiome-based machine learning can be used as a non-invasive diagnostic approach for liver cirrhosis or fibrosis, while it lacks evidence-based support. Therefore, we

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## METHODS

**Participant or population:** Cohort studies that reported gut microbiome-based machine learning for liver fibrosis or cirrhosis were included. There were no restrictions on gender, age, and regions of participants.

**Intervention:** None.

**Comparator:** None.

**Study designs to be included:** Cohort study and control trial.

**Eligibility criteria:** (1) Cohort studies that reported gut microbiome-based machine learning for liver fibrosis or cirrhosis were included. There were no restrictions on gender, age, and regions of participants. (2) Predictive outcomes included at least one of the following indicators: receiver operating characteristic curve (ROC), sensitivity, specificity, TP, and TN, in which TP and TN could be calculated indirectly.

**Information sources:** PubMed, Embase, Cochrane Library, and Web of Science were searched, from inception to April 29th, 2022, for studies that applied gut microbiome metagenomic sequencing modeling technology for diagnostic prediction of liver cirrhosis or fibrosis.

**Main outcome(s):** Liver fibrosis (LF) is the excessive deposition of liver fibrous tissue due to various pathogenic factors, and persistent liver fibrosis can lead to liver cirrhosis (LC). Early liver fibrosis is reversible, but progression to liver cirrhosis

is irreversible and has a poor prognosis. Therefore, the early diagnosis of liver fibrosis is critical. In recent years, the Gut Microbiome (GM) has been introduced into the liver fibrosis or cirrhosis's diagnosis, to enable accurate, non-invasive detective diagnosis. With the help of meta-analysis, this research evaluated the diagnostic efficacy, generalization, and practicability of the machine learning approach (established based on the gut microbiome) to predict liver cirrhosis or liver fibrosis.

### Quality assessment / Risk of bias analysis:

Two authors separately implemented the quality assessment scale of the included 18 articles via employing the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool, which contains four domains: patient selection, index test, reference standard, and flow and timing. And every domain can be rated as a high (red), unclear (yellow), or low (green) risk bias. Similarly, applicability concerns in the first three domains were also evaluated through high, unclear, or low risk bias ratings.

**Strategy of data synthesis:** The "Midas" command of Stata 15.0 (StataCorp LLC, College Station, TX) was used to fit the bivariate mixed-effects model to evaluate the sensitivity (SEN), specificity (SEP), positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR). Point-estimates with 95% confidence intervals (95% CIs) were calculated. The summary receiver operating characteristic curves (SROC) were plotted, and area under curve (AUC) with 95%CI was calculated. Deek's funnel plot was employed to determine publication bias, and Q statistic and I<sup>2</sup> statistic were used for heterogeneity test. I<sup>2</sup>>50% indicated significant heterogeneity. A p value less than 0.05 was considered to be statistically significant.

**Subgroup analysis:** We did a subgroup analysis based on fibrosis and cirrhosis.

**Sensitivity analysis:** None.

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**Country(ies) involved:** School of Basic Medicine, Shaanxi University of Chinese Medicine, Shaanxi Province, China. Xianyang, Shaanxi.

**Keywords:** Gut microbiome; Machine learning; Liver cirrhosis/fibrosis; Prediction/ diagnosis; Meta-analysis.

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