# INPLASY PROTOCOL

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Review question / Objective: Periprosthetic joint infection (PJI) is a severe complication after total joint arthroplasty (TJA), representing the leading cause of revision TJA. The diagnosis and treatment of PJI remain difficult for surgeons, especially for cases caused by low-virulence bacteria, which produce biofilms. In recent years, a large number of diagnostic markers have been used in the diagnosis of PJI. Neutrophil gelatinase-associated lipocalin(NGAL) is a secreted protein first found in neutrophils and is a member of the lipocalin family. Several studies have confirmed that NGAL performs extremely well in the diagnosis of PJI, with a high sensitivity and specificity. The diagnostic value of NGAL for PJI varies from study to study, and to our knowledge, there is no systematic evaluation addressing the diagnostic value of NGAL in PJI. The aim of this study is to develop a metaanalysis of seven studies to systematically evaluated the diagnostic value of NGAL in PJI.

**Condition being studied:** Periprosthetic joint infection(PJI) is a catastrophic complication after total joint arthroplasty. As the treatment of different PJI stage is different, it is extremely important to accurately diagnose PJI timely. Nowdays, accurate diagnosis of PJI was still a challenge for surgeon. A number of biomarkers for PJI are finding on the road.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 December 2022 and was last updated on 23 December 2022 (registration number INPLASY2022120098).

## **INTRODUCTION**

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TJA. The diagnosis and treatment of PJI remain difficult for surgeons, especially for cases caused by low-virulence bacteria, which produce biofilms. In recent years, a large number of diagnostic markers have

been used in the diagnosis of PJI. Neutrophil gelatinase-associated lipocalin(NGAL) is a secreted protein first found in neutrophils and is a member of the lipocalin family. Several studies have confirmed that NGAL performs extremely well in the diagnosis of PJI, with a high sensitivity and specificity. The diagnostic value of NGAL for PJI varies from study to study, and to our knowledge, there is no systematic evaluation addressing the diagnostic value of NGAL in PJI. The aim of this study is to develop a meta-analysis of seven studies to systematically evaluated the diagnostic value of NGAL in PJI.

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#### **METHODS**

Search strategy: (((Prosthesis-Related Infections[MeSH]) OR ((((((((Prosthesis Related Infections[Title/Abstract]) OR (Prosthesis Related Infection[Title/ Abstract])) OR (Infection, Prosthesis Related[Title/Abstract])) OR (Related Infection, Prosthesis[Title/Abstract])) OR (Related Infections, Prosthesis[Title/ Abstract])) OR (Prosthesis-Related Infection[Title/Abstract])) OR (Infections, Prosthesis-Related[Title/Abstract])) OR (periprosthetic joint infection[Title/ Abstract])) OR (prosthetic infection[Title/ Abstract])) OR (peri-prosthetic joint infection[Title/Abstract])) OR (periprosthetic infection[Title/Abstract])) OR (prosthetic joint infection[Title/ Abstract]))) AND (("Lipocalin-2"[Mesh]) OR ((((((((neutrophil gelatinase-associated lipocalin[Title/Abstract]) OR (neutrophil gelatinase associated lipocalin[Title/ Abstract])) OR (NGAL protein[Title/ Abstract])) OR (LCN2[Title/Abstract])) OR (NGAL[Title/Abstract])) OR (oncogene 24p3 protein[Title/Abstract])) OR (siderocalin protein[Title/Abstract])) OR (lipocalin-2 protein[Title/Abstract])) OR (lipocalin 2 protein[Title/Abstract])) OR (acute-phase proteins [Title/Abstract])) OR (acute-phase proteins[Title/Abstract])) OR (protooncogene proteins[Title/Abstract]))) AND (sensitiv\*[Title/Abstract] OR sensitivity and specificity[MeSH] OR (predictive[Title/ Abstract] AND value\*[Title/Abstract]) OR predictive value of tests[MeSH] OR accuracy\*[Title/Abstract]).

Participant or population: Periprosthetic joint infection.

Intervention: Neutrophil gelatinaseassociated lipocalin(NGAL).

**Comparator:** Aseptic arthroplasty revision surgery.

Study designs to be included: Cohort study.

Eligibility criteria: The inclusion criteria included: (1) assessing the diagnostic value of NGAL in PJI; (2) owning sufficient data to establish a 2×2 contingency table. The exclusion criteria included: (1) systematic evaluation; (2) animal studies; (3) case reports; (4) expert reviews; (5) insufficient data to construct a 2×2 contingency table; (6) duplicate studies. Two researchers conducted literature searching and reading independently, with a third researcher making decisions when conflicts were encountered.

**Information sources:** Cochrane Library, Scopus, OVID, PubMed, Web of Science, and Embase.

Main outcome(s): Pooled sensitivity, specificity, positive likelihood ratio(PLR), negative likelihood ratio(NLR), diagnostic score, and diagnostic odds ratio(DOR).

Additional outcome(s): The summarized receiver operating characteristic curve(SROC) and calculated the area under the SROC curve(AUSROC).

Data management: NoteExpress.

Quality assessment / Risk of bias analysis: QUADAS-2.

Strategy of data synthesis: In the presence of heterogeneity, random effects were chosen to combine the data; in the absence of heterogeneity, fixed effects were chosen to combine the data.

Subgroup analysis: Subgroup studies based on country, sample size, and diagnostic criteria.

Sensitivity analysis: If the combined results of the remaining studies are not significantly different from those without the deletion of any one of them, it means that the sensitivity analysis is passed.

**Country(ies) involved:** China (Yulin No.2 Hospital).

Keywords: periprosthetic joint infection, diagnosis, NGAL.

#### Contributions of each author:

Author 1 - Huhu WANG conceived the idea, designed the study and wrote framework and manuscript of the paper.

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Author 5 - Ting FU planned the project, wrote the main manuscript text and critically revised the paper. Email: 327180723@gg.com