

INPLASY PROTOCOL

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**Review Stage at time of this
submission:** The review has
not yet started.

Conflicts of interest:
None declared.

Clinical efficacy and safety of the combination of mesenchymal stem cells and scaffolds in the treatment of knee osteoarthritis: A systematic review and meta-analysis of randomized controlled trials

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Feng, H⁸.

Review question / Objective: The aim of this review is to evaluate clinical efficacy and safety of the combination of mesenchymal stem cells and scaffolds in the treatment of knee osteoarthritis.

Condition being studied: Knee osteoarthritis (KOA) is already one of the considerable causes of physical disability Worldwide with no known cure for KOA so far. Due to the enormous osteogenic potential and immunomodulatory biological properties of MSCs, numerous researchers have evaluated the use of MSCs for cartilage repair in knee osteoarthritis. However, the low survival rate of cells during transplantation and injection, and the most suitable stem cell type and dose are controversial, resulting in limited improvement in knee function and cartilage repair. To battle this limitation, bioactive scaffold materials as an adjunct to mesenchymal stem cells for the treatment of knee osteoarthritis are growing in interest.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 July 2021 and was last updated on 08 July 2021 (registration number INPLASY202170021).

INTRODUCTION

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METHODS

Participant or population: Patients with knee osteoarthritis.

Intervention: The combination of mesenchymal stem cells and scaffolds injection is the main intervention.

Comparator: In different studies, the control group included only scaffolds treatment, only mesenchymal stem cells, other current treatment methods or no treatment.

Study designs to be included: Randomized controlled trials (RCTs) will be included.

Eligibility criteria: Participant or population: Patients with knee osteoarthritis. Intervention: The combination of mesenchymal stem cells and scaffolds injection is the main intervention. Comparator: In different studies, the control group included only scaffolds treatment, only mesenchymal stem cells, other current treatment methods or no treatment. Outcomes: Mean changes in The visual analog scale (VAS). Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). The Knee Injury and Osteoarthritis Outcome Score (KOOS). Study designs to be included: Randomized controlled trials (RCTs) will be included.

Information sources: Cochrane Library; MEDLINE; Embase; PubMed; OpenGrey; Scopus; Web of Science; CNKI; VIP; WanFang; CBM. No language restrictions. No date restrictions.

Main outcome(s): Mean changes in The visual analog scale (VAS). Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). The Knee Injury and Osteoarthritis Outcome Score (KOOS).

Additional outcome(s): Lequesne algofunctional indices (Lequesne). Lysholm knee scale (Lysholm).

Quality assessment / Risk of bias analysis: Two independent reviewers (J.C. and Q.Z.) will screen through each article and assess for risk of bias using SYRCLE's Risk of Bias tool, which assesses for selection bias, performance bias, detection bias and attrition bias. Both reviewers will attempt to agree on the study risk of bias. If no agreement can be reached, a third reviewer (A.L.) will be consulted.

Strategy of data synthesis: Statistical analysis will be conducted using RevMan 5.4 software. For continuous data, will be used mean difference (MD) as the effect indicator with 95% confidence interval, and dichotomous data will be calculated as risk ratio (RR) or odds ratio (OR) as the effect index with 95% confidence interval. If the studies with no statistical homogeneity, the fixed-effect model can be used for analysis; if the studies with significant statistical heterogeneity, random effects model analysis will be used.

Subgroup analysis: The overall analysis will combine the data from the use of all bioactive scaffolds and compared with cell-only controls or scaffolds-only controls. Data will be further analyzed by subgroup analysis based on two major criteria: type of scaffold, type of stem cell, animal model and time interval from injury to treatment. Therefore, a separate subgroup meta regression will be performed for these criteria.

Sensitivity analysis: Sources of heterogeneity will be explored by sensitivity analysis via systematic removal of individual trials for each outcome measure.

Language: No language limitation.

Country(ies) involved: China.

Keywords: Mesenchymal Stem Cells; Stem Cell Transplantation; Tissue scaffolds; Knee osteoarthritis.

Contributions of each author:

Author 1 - Jixin Chen designed the review and drafted the manuscript.

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