

Intra-articular Bone Marrow and Adipose-Derived Mesenchymal Stem Cells in Primary Knee Osteoarthritis: A Systematic Review of Clinical Outcomes in Randomized Controlled Trials

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Objective

- Knee osteoarthritis (OA) is the most prevalent joint disease in the world, and a significant cause of chronic pain and disability.
- Mesenchymal Stem Cells (MSCs) have emerged as possible disease-modifying treatments.
- This review investigates the efficacy of intra-articular injections of bone marrow-derived mesenchymal stem cells (BM-MSCs) and adipose tissue-derived mesenchymal stem cells (AT-MSCs) in treating knee OA compared to other established non-surgical interventions as measured by validated pain and function outcome scores.

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Design

- Systematic review of three databases was performed using the search terms:
 - ((bone marrow aspirate) OR (bone marrow concentrate) OR (bone marrow stem cells)) AND ((knee OA) OR (knee osteoarthritis)) AND (randomized controlled trial),
 - ((adipose tissue stem cells) OR (microfragmented adipose tissue) OR (stromal vascular fraction) OR (adipose stem cells)) AND ((knee OA) or (knee osteoarthritis)) AND (randomized controlled trial).
- Inclusion criteria:**
 - RCTs reporting clinical results following the intra-articular injection of either BM-MSC or AT-MSC in human knees with OA.
- Risk of bias was assessed using the Cochrane Collaboration's risk of bias tool.
- Data was extracted for patient demographics, study and treatment protocols, clinical outcomes, and adverse events.
- Clinical outcomes were further recorded as significance from baseline in experimental treatment group, and significance of experimental treatment group compared to control group.

RESULTS

- 13 studies were included.
- All studies employed a clinical outcome questionnaire (WOMAC, KOOS, IKDC, etc.)
- All studies reported pain outcomes by VAS or a pain questionnaire.
- Controls included:
 - Exercise
 - Platelet rich plasma (PRP)
 - Corticosteroid (CSI)
 - Hyaluronic acid (HA)
 - Placebo.
- All studies reported a **significant improvement** in clinical outcome questionnaire score and pain scores.
- Compared to control groups, eight had significant improvement in primary outcome measures, three were not significant, and two did not evaluate statistically against their controls.
- Pain outcomes compared to control, five had statistical improvement, four were not significant, and four were not statistically analyzed against a control.

- MSC groups outperformed exercise in two of two studies,
- CSI in one of one study,
- HA in three of three studies.
- There were mixed results compared to placebo in five studies,
- No significance compared to PRP in one of one study.

CONCLUSIONS

- This systematic review demonstrates a benefit of intraarticular injections of bone marrow and adipose tissue-derived MSCs over other non-surgical interventions
- MSC treated groups had significant improvement compared to controls in seven of the ten studies that compared treatment groups a control in at least one of their outcome measures.
- MSC treatment seems favorable compared to exercise and conservative treatment options such as CSI or HA.
- However in these limited studies it is equivocal to placebo and PRP.

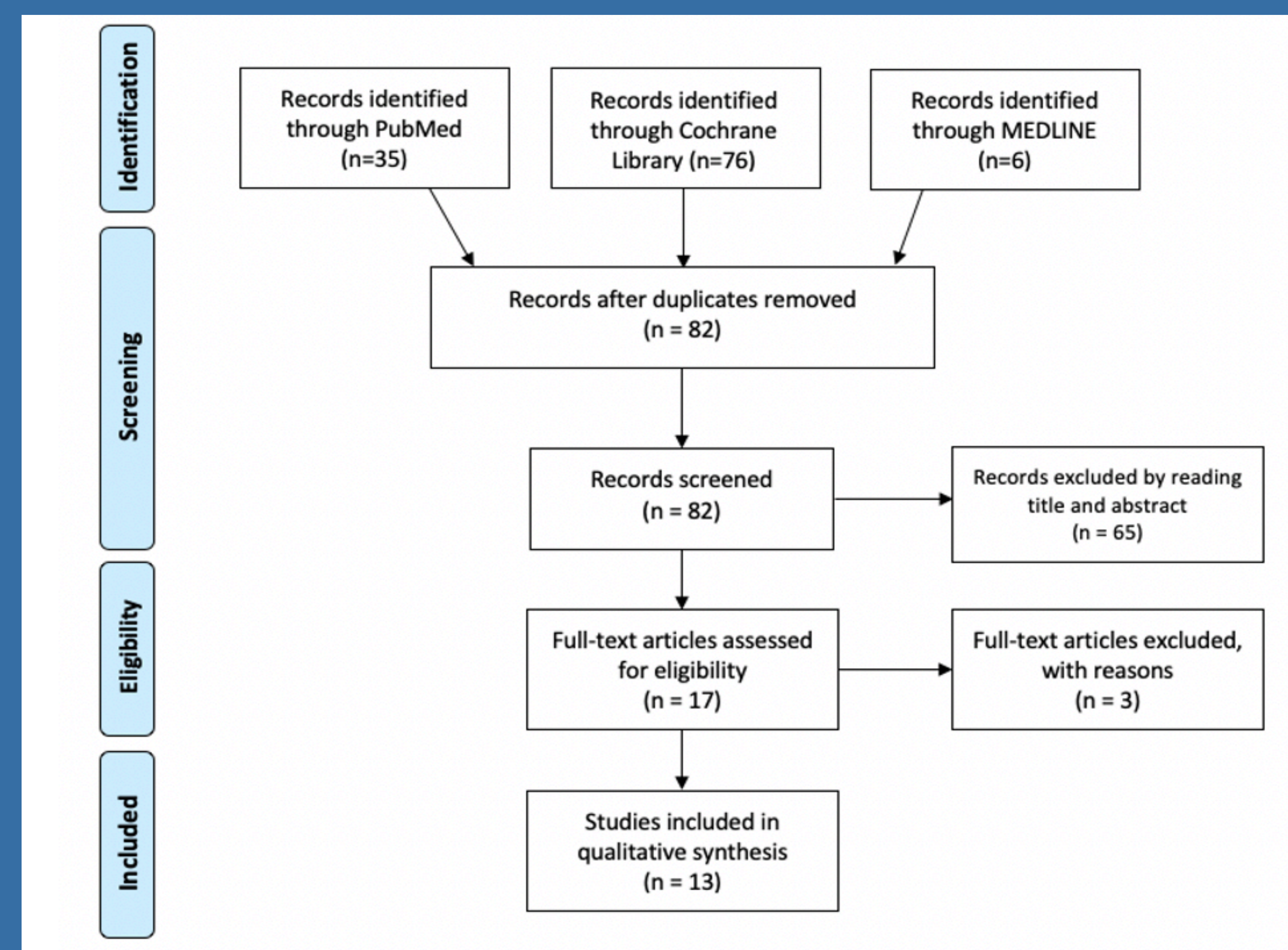


Figure 1. Prisma Flowchart of included studies

Variable	Results	Reference No.
Placebo/Normal Saline	Equivocal	[23, 25, 17, 18, 22, 25]
Exercise/Conservative	Favorable	[16, 24]
CSI	Favorable	[19]
HA	Favorable	[26, 14, 20, 21]
PRP	Equivocal	[15]

Table 1. Suggestion of BM-MSC and AT-MSC versus other non-surgical interventions based on summation of number of studies with significant improvement in outcomes compared to control. “Favorable” is defined as more total studies of that variable control with significant improvement compared to control than non-significant; “equivocal” is defined as total studies with mixed results, or non-significant outcomes between MSC and control groups.